ព្រះរាជាណាចក្រកម្ពុជា

ជាតិ សាសនា ព្រះមហាក្សត្រ

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិក

CLINICAL PRACTICE GUIDELINES

ផ្នែក

FOR

វេជ្ជសាស្ត្រកុមារ

PEDIATRICS

ភាគ ១

ឆ្នាំ ២០២៥

Kingdom of Cambodia

Nation Religion King

CLINICAL PRACTICE GUIDELINES

FOR

PEDIATRICS

Part 1

Department of Health Services

December 2025

Ministry of Health

CLINICAL PRACTICEGUIDELINES FOR

PEDIATRICS

Part

1

December 2025

ព្រះរាជាណាចក្រកម្ពុជា
ជាតិ សាសនា ព្រះមហាក្សត្រ

ក្រសួងសុខាតិបាល
លេខ ០៣៤៨ សហប/អ.ស.ស.ប្រ.ក

ប្រកាស
ស្តីពី
ការជាក់ឱ្យអនុវត្តមគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិក ផ្នែកវេជ្ជសាស្ត្រកុមារ

រដ្ឋមន្ត្រីក្រសួងសុខាតិបាល

- បានឃើញរដ្ឋធម្មនុញ្ញនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០៨២៣/១៩៨១ ចុះថ្ងៃទី២២ ខែសីហា ឆ្នាំ២០២៣ ស្តីពីការតែងតាំងរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០២២៤/២០៥ ចុះថ្ងៃទី២១ ខែកុម្ភៈ ឆ្នាំ២០២៤ ស្តីពីការបំពេញបន្ថែមសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/០៩២៤/១១៦៩ ចុះថ្ងៃទី២០ ខែកញ្ញា ឆ្នាំ២០២៤ ស្តីពីការកែសម្រួល និងតែងតាំងសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រឹត្យលេខ នស/រកត/១១២៤/១៤៧៧ ចុះថ្ងៃទី២០ ខែវិច្ឆិកា ឆ្នាំ២០២៤ ស្តីពីការកែសម្រួល និងតែងតាំងសមាសភាពរាជរដ្ឋាភិបាលនៃព្រះរាជាណាចក្រកម្ពុជា
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/០៦១៨/០១២ ចុះថ្ងៃទី២៨ ខែមិថុនា ឆ្នាំ២០១៨ ដែលប្រកាសឱ្យប្រើច្បាប់ ស្តីពីការរៀបចំ និងការប្រព្រឹត្តទៅនៃគណៈរដ្ឋមន្ត្រី
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/០១៩៦/០៦ ចុះថ្ងៃទី២៤ ខែមករា ឆ្នាំ១៩៩៦ ដែលប្រកាសឱ្យប្រើច្បាប់ស្តីពីការបង្កើតក្រសួងសុខាភិបាល
- បានឃើញព្រះរាជក្រមលេខ នស/រកម/១១១៦/០១៤ ចុះថ្ងៃទី១៦ ខែវិច្ឆិកា ឆ្នាំ២០១៦ ដែលប្រកាសឱ្យប្រើច្បាប់ ស្តីពីការគ្រប់គ្រងអ្នកប្រកបវិជ្ជាជីវៈសុខាភិបាល
- បានឃើញអនុក្រឹត្យលេខ២៣៩ អនក្រ.បក ចុះថ្ងៃទី០៣ ខែធ្នូ ឆ្នាំ២០២៥ ស្តីពីការរៀបចំ និងការប្រព្រឹត្តទៅរបស់ក្រសួងសុខាភិបាល
- យោងតាមការចាំបាច់របស់ក្រសួងសុខាភិបាល

អាសយដ្ឋាន៖ ដីឡូតិ៍លេខ៨០ វិថីសម្តេច ប៉ែន នុត (២៨៩) សង្កាត់បឹងកក់ទី២ ខណ្ឌទួលគោក រាជធានីភ្នំពេញ
ទូរស័ព្ទ៖(+៨៥៥) ២៣ ៨៨៥ ៩៧០ អ៊ីមែល៖ info@moh.gov.kh
គេហទំព័រ៖ www.moh.gov.kh តេឡេក្រាម៖ t.me/MOHCambodia

សម្រេច

ប្រការ១.-

ត្រូវបានដាក់ឱ្យអនុវត្តមគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិក ផ្នែកវេជ្ជសាស្ត្រកុមារ (Clinical Practice Guidelines For Pediatrics) ដែលជាឧបសម្ព័ន្ធនៃប្រកាសនេះ។

ប្រការ២.-

ប្រកាសនេះមានវិសាលភាពអនុវត្តចំពោះគ្រប់មូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជនក្នុងព្រះរាជាណាចក្រកម្ពុជា។

ប្រការ៣.-

បទប្បញ្ញត្តិទាំងឡាយណាដែលផ្ទុយនឹងប្រកាសនេះ ត្រូវទុកជានិរាករណ៍។

ប្រការ៤.-

អគ្គលេខាធិការ អគ្គនាយកបច្ចេកទេសសុខាភិបាល អគ្គាធិការក្រសួងសុខាភិបាល គ្រប់ប្រធានអង្គភាពក្រោមឱវាទក្រសួងសុខាភិបាល ទាំងមូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជន ត្រូវទទួលបន្ទុកអនុវត្តតាមប្រកាសនេះឱ្យមានប្រសិទ្ធភាព ចាប់ពីថ្ងៃចុះហត្ថលេខាតទៅ។

ថ្ងៃ ៣ ៨ ១២ កើត ខែ បុស្ស ឆ្នាំម្សាញ់ សប្តស័ក ព.ស.២៥៦៩
ធ្វើនៅរាជធានីភ្នំពេញ ថ្ងៃទី ៣១ ខែ ម៉ឺ ឆ្នាំ២០២៥

រដ្ឋមន្ត្រីក្រសួងសុខាភិបាល

សាស្ត្រាចារ្យ **ឈាង ប៉ា**

កន្លែងទទួលៈ
- ទីស្តីការគណៈរដ្ឋមន្ត្រី
- ក្រសួងសេដ្ឋកិច្ចនិងហិរញ្ញវត្ថុ
- ខុទ្ទកាល័យឯកឧត្តមសាស្ត្រាចារ្យរដ្ឋមន្ត្រីក្រសួងសុខាភិបាល
- ដូចប្រការ៤
- រាជកិច្ច
- ឯកសារ កាលប្បវត្តិ

អារម្ភកថា

ក្រោមកិច្ចដឹកនាំរបស់រាជរដ្ឋាភិបាលនីតិកាលទី៧ នៃរដ្ឋសភា នៃ **ព្រះរាជាណាចក្រកម្ពុជា** ក្រសួងសុខាភិបាល យកចិត្តទុកដាក់ខ្ពស់ដល់សុខភាព និងសុខុមាលភាពប្រជាជនគ្រប់រូប និងប្តេជ្ញាចិត្តយ៉ាងមុឺងម៉ាត់លើកកម្ពស់ការផ្តល់សេវាសុខាភិបាលប្រកបដោយ គុណភាព សុវត្ថិភាព និងសមធម៌ ដោយផ្តោតលើអ្នកជំងឺ ជូនដល់ប្រជាជនកម្ពុជាគ្រប់រូប ស្របតាម ផែនការយុទ្ធសាស្ត្រសុខាភិបាល ២០២៥-២០៣៤ ក៏ដូចជា ផែនទីបង្ហាញផ្លូវឆ្ពោះទៅការគ្របដណ្តប់សុខភាពជាសកលនៅកម្ពុជា ឆ្នាំ ២០២៤-២០៣៥ របស់រាជរដ្ឋាភិបាល។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកផ្នែកវេជ្ជសាស្ត្រកុមារនេះជាមគ្គុទ្ទេសក៍ណែនាំថ្នាក់ជាតិពាក់ព័ន្ធនឹង ពិធីសារនៃការគ្រប់គ្រងបញ្ហាសុខភាពពាក់ព័ន្ធផ្នែកវេជ្ជសាស្ត្រកុមារជាអាទិភាពនៅកម្ពុជា ដោយផ្តោតសំខាន់លើបែបបទនៃការធ្វើរោគវិនិច្ឆ័យ និងការថែទាំ ការព្យាបាល និងការបង្ការជំងឺរាប់ទាំងការតាមដានបញ្ហាសុខភាព ឬជំងឺ ។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកផ្នែកវេជ្ជសាស្ត្រកុមារនេះជាសៀវភៅដែលបានចងក្រងលើកទី២ ដែលមានចំនួន ២ភាគ៖ ភាគទី១ និងភាគទី២ នៅកម្ពុជា ដោយក្រុមការងារបច្ចេកទេសជំនាញ នៃក្រសួងសុខាភិបាល និងមានការចូលរួមពីដៃគូសំខាន់ៗ អ្នកជំនាញ ឯកទេសជំនាញពីផ្នែកពាក់ព័ន្ធទាំងឡាយ រួមទាំងគ្រូពេទ្យព្យាបាល និងគ្រូពេទ្យឯកទេសរោគកុមារបម្រើការងារនៅតាមមន្ទីរពេទ្យគ្រប់លំដាប់ថ្នាក់ មន្ត្រីដែលកំពុងបំពេញការងារនៅការិយាល័យសុខាភិបាលស្រុកប្រតិបត្តិ និងមន្ទីរសុខាភិបាល នៃរដ្ឋបាលរាជធានី ខេត្ត កម្មវិធីជាតិ សមាគមវិជ្ជាជីវៈសុខាភិបាលផ្សេងៗ ក៏ដូចជាអង្គការដៃគូពាក់ព័ន្ធ។

មគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកនេះ ត្រូវបានរៀបចំឡើងសម្រាប់អ្នកវិជ្ជាជីវៈសុខាភិបាល និងអ្នកវិជ្ជាជីវៈពាក់ព័ន្ធ ជាពិសេសអ្នកផ្តល់សេវាសុខភាព រាប់បញ្ចូលទាំង វេជ្ជបណ្ឌិត និងអ្នកប្រកបវិជ្ជាជីវៈសុខាភិបាលផ្សេងទៀត នៅមូលដ្ឋានសុខាភិបាលសាធារណៈ និងឯកជន ក៏ដូចជាសិក្ខាកាម អ្នករៀបចំគោលនយោបាយ អ្នកពាក់ព័ន្ធនានា គណៈវិជ្ជាជីវៈ និងសមាគមវិជ្ជាជីវៈផ្សេងៗ។

ក្រសួងសុខាភិបាលសូមណែនាំដល់អ្នកវិជ្ជាជីវៈសុខាភិបាល និងអ្នកពាក់ព័ន្ធទាំងអស់ ត្រូវចូលរួមអនុវត្តតាមមគ្គុទ្ទេសក៍ព្យាបាលគ្លីនិកនេះ សម្រាប់ប្រតិបត្តិកិច្ចការរបស់ខ្លួន ក្នុងគោលបំណងពង្រឹងប្រសិទ្ធភាព ប្រសិទ្ធផល និងគុណភាព សុវត្ថិភាពក្នុងការថែទាំព្យាបាលអ្នកជំងឺ ក៏ដូចជាការកសាងសមត្ថភាពធនធានមនុស្សក្នុងវិស័យសុខាភិបាល ។

រាជធានីភ្នំពេញ ថ្ងៃ..៣១..ខែធ្នូ ឆ្នាំ ២០២៥

រដ្ឋមន្ត្រីក្រសួងសុខាភិបាល

សាស្ត្រាចារ្យ ឈាង រ៉ា

FOREWORD

Under the leadership of the Royal Government of the 7th Legislature of the National Assembly of the Kingdom of Cambodia, the Ministry of Health pays high attention to the health and well-being of the entire population. The Ministry of Health is strongly committed to ensuring the provision of equitable, safe and quality patient-centered health services for the Cambodian population in line with the Health Strategic Plan 2025-2034 and the Royal Government Roadmap Towards Universal Health Coverage in Cambodia 2024-2035.

This Clinical Practice Guidelines (CPG) for Pediatrics provides national guidance on management protocols of priority health problems related to pediatrics with a focus on diagnosis and care, including curative and preventive care, as well as follow-up of health problems.

This Guidelines, published for the second time in Cambodia in two parts, Part 1 and Part 2; was developed by the Technical Working Group of the Ministry of Health with participation from various stakeholders and individuals, including experts from relevant fields ranging from clinicians and doctors specialized in pediatrics working in hospitals at all levels to district health officers, Provincial Health Departments, national programs, health professional associations, as well as partner organizations.

The Guidelines is intended for use by health professionals and other relevant professionals, especially health care providers, including doctors and other health practitioners in both public and private health facilities as well as trainees, policymakers, relevant individuals, professional councils and professional associations.

The Ministry of Health guides all health professionals and relevant individuals to use this Guidelines in their professional practice with the aim of improving effectiveness, efficiency and quality in patient care and safety, as well as contributing to human resource capacity building.

Phnom Penh, 31 December, 2025

Minister of Health

Prof. CHHEANG RA

ACKNOWLEDGEMENT

The Ministry of Health wishes to extend its profound appreciation to Excellencies, Ladies and Gentlemen, Professors, Doctors, Experts, Officials of the Ministry at all levels as well as partner organization officials and all individuals who have shared their experiences and inputs contributing to the development of this important Clinical Practice Guidelines.

We particularly thank H.E. Prof. **Yit Sunnara**, Secretary of State, Chair and all Vice-chairs and members of the Technical Working Group of Clinical Practice Guidelines for Pediatrics under the overall leadership and guidance of the Steering Committee for National Medical Care and Therapy of the Ministry of Health.

We would also like to express our deep gratitude to all partners involved, including the World Health Organization and other partners, for their technical and financial contributions to the formulation of the guidelines.

This Clinical Practice Guidelines for Pediatrics represent another significant and commendable achievement of the Ministry of Health of the Kingdom of Cambodia.

Phnom Penh, 31 December, 2025

Chair of the Steering Committee for
National Medical Care and Therapy

H.E. Prof. Yit Sunnara

Contents

INTRODUCTION

I. BACKPROUND

The Ministry of Health of Kingdom of Cambodia is committed to improving the health and well-being of all Cambodian population through the provision of quality, safe, acceptable, equitable and affordable healthcare services. Implementing evidence-based, appropriate, and cost-effective health interventions within care packages at various levels of the health system, guided by contextually relevant best practices in clinical practice guidelines (CPGs), can significantly enhance population health.

Clinical Practice Guidelines (CPGs) are essential diagnostic and care tools in achieving UHC by ensuring that healthcare services are provided timely, effectively, safely, continuously and with patient-centeredness. The guidelines provide evidence-based and or up-to-date for health services at different levels of the health system. They ensure that health problems are appropriately diagnosed and clinical decisions are based on the best available evidence and experiences, leading to improved patient diagnosis and care outcomes as well as more efficient use of resources. By adhering to CPGs, healthcare providers can offer consistent, high-quality care that meets national and international standards.

The 1st Clinical Practice Guidelines (CPGs) for Medicine and Pediatrics were published in 1997 and 2013,respectively. They are the only existing CPGs in Cambodia. Since then, many new developments have taken place, especially in the area of laboratory tests, medical imaging, diagnosis tools and treatment options. Regularly reviewing and updating the CPGs offer up-to-date and more evidence-based recommendations for health services and interventions tailored to Cambodia's current and future needs. Updating the clinical practice guidelines aims to enhance both quality and coverage by providing a solid evidence-based foundation for changes in services. This includes the diagnosing, treatments, and support necessary to deliver these services as defined in the essential packages of care under the CPA guidelines.

II. DEVELOPMENT PROCESS

This Clinical Practice Guidelines was formulated by “Technical Working Group of Clinical Practice Guidelines for Pediatrics “of the Ministry of Health through face-to-face and online meeting of the working group and small group meeting and discussions with guidance and endorsements from the Steering Committee for National Medical Care and Therapy of the Ministry of Health mainly through its meeting .The development process of the guidelines was actively participated by various stake holders and individuals, including experts from related fields ranging from clinicians working in hospitals at all levels, district health officers, Provincial Health Department, national institutes, national programs, health professional associations as well as experts and officials partner organizations .

Each health section follows standard format except in few cases. This guidelines contains two parts-Part Iand Part II and Part III with each separate volume presented in its hard copy division and publication.

The guideline covers a variety of topics/diseases/conditions within specialized chapters. The guidelines do not cover the national programs topics/diseases/conditions such as HIV/AIDS, TB, Malaria, Dengue, Schistosomiasis and vaccine preventable diseases as they are treated in National Programs documents,specifically.

III. PURPOSE AND USERS

The main aim of these guidelines is to assist health care providers and practitioners make informed decisions on clinical diagnosing and treatment based on recommended protocols based on systematic review of evidence, experiences and assessment of the benefits and harms of alternative care options. The guidelines is used for health professionals and relevant stakeholders in both public and private sectors, including doctors, related health professionals, trainees and students, policy makers, professional societies, in both public and private health facilities and institutions, including Provincial and district hospitals, private clinic, training and research institutions.

The main end users of the CPG are clinicians, managers and other health professionals practicing in patient care settings in both private and public sectors, particularly at referral hospitals and private clinics to support the delivery of consistently safe, quality and cost effective and equitable health care. They should be harmonized with the CPA guideline, IPC guideline, AMR guideline, Cambodian Hospital Accreditation Standards (CHAS) and Quality Enhancement Monitoring Tool (QEMT) and other MoH guidelines to motivate and facilitate their relevance and use. CPG can also be used by other relevant bodies and people such as in training and research institutions as well as by other organization or institutions as per the relevancy of their mandates.

Chapter I: Critical Care

PEDIATRIC BASIC LIFE SUPPORT

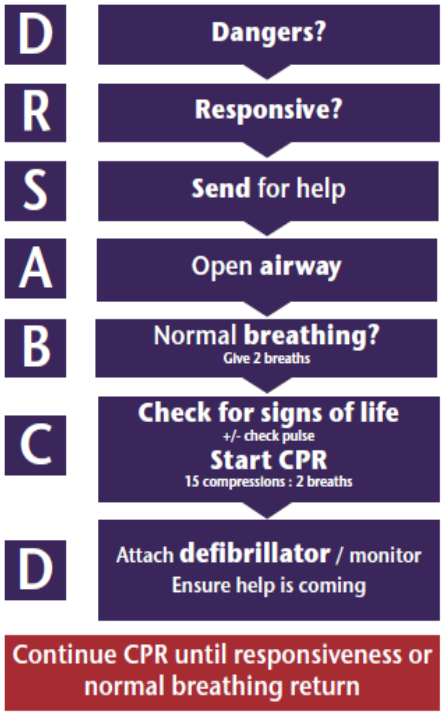
EANG Habsreng, PEN Sotheavy, NGETH Pises

I. Key Facts

Basic Life support (BLS) refers to the type of care that healthcare providers or first responder provides to anyone who is experiencing cardiac arrest, respiratory distress or obstructed airway.

The outcome for children following cardiac arrest is generally poor, therefore early recognition and provide appropriate management as soon as possible is crucial.

II. Steps in Pediatric Basic Life Support: DRS-ABC



1. Dangers?

It is essential that the rescuer does not become a second victim and that the child is removed from continuing danger as quickly as possible.

2. Responsive?

- The simple assessment of responsiveness consists of asking the child loudly "Are you alright?" and gently applying a stimulus such as holding the head and shaking the arm, this will avoid exacerbating a possible neck injury whilst waking a sleeping child.
- Infants and very small children who cannot talk yet and older children who are scared, are unlikely to reply meaningfully but may make some sound or open their eyes to the rescuers voice.

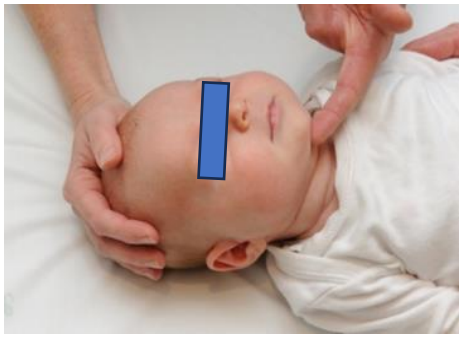
Checking for response

3. **Send for help**

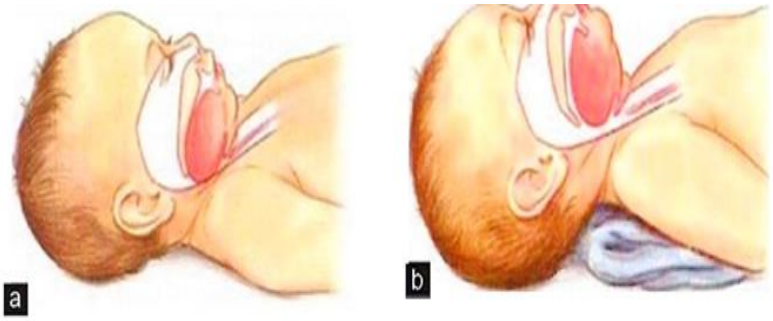
Help should be summoned rapidly. If there is more than one rescuer, one start BLS and another calling for help.

a. Airway: Opening Airway

- When a child is unconscious, all muscles are relaxed. If the infant/child is lying on their back the tongue falls against the back of the throat and obstructs the airway.
- To open the airway
  - Lay infant/child flat on the back on a firm surface
  - Head tilt and chin lift positioning: neutral position in infant, and sniffing position in children (see pictures)
  - Jaw thrust in case of suspect neck injury or the head tilt and chin lift manoeuvre is not possible.

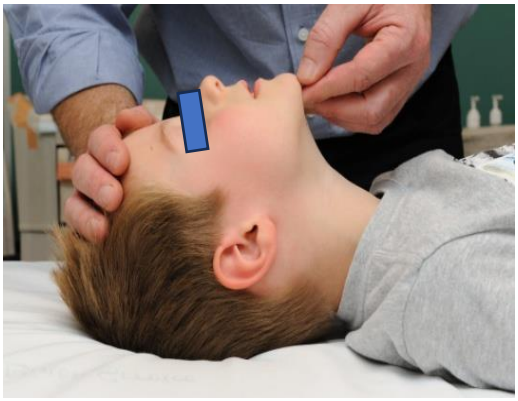


Infant: Neutral position

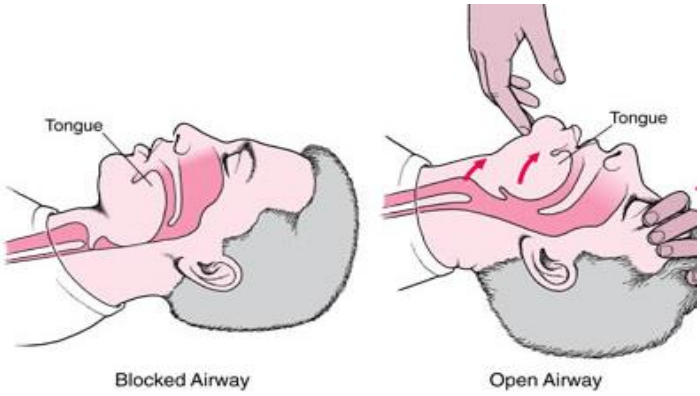


a. Airway is blocked in flexion position

b. Airway is opening in neutral position



Open airway in child: sniffing position

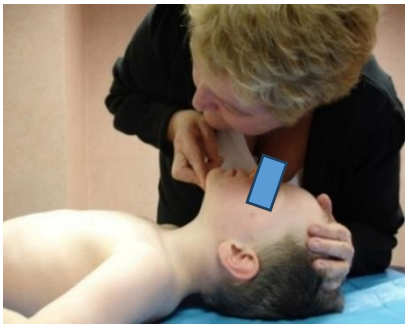


Picture 1: Airway is blocked in neutral position

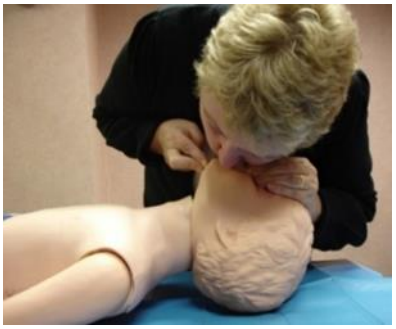
Picture 2: Airway is opening in sniffing position

b. Breathing normally?

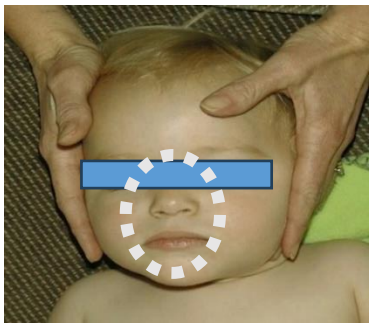
- Once the airway is cleared and open, check for normal breathing for no more than 10 seconds, using the following method.
  - *Look:* for movement of lower chest or upper abdomen
  - *Listen:* for escape of air from nose and mouth
  - *Feel:* for movement of chest and upper abdomen
- If no breathing, gave 2 rescue breaths (mouth to mouth in child or mouth to mouth and nose in infant)
  - *If* breathing normally, turn the child in recovery position
  - *Note* that an occasional gasp or noisy breathing is not considered normal breathing.



Look, listen and feel



Mouth to mouth ventilation (child)

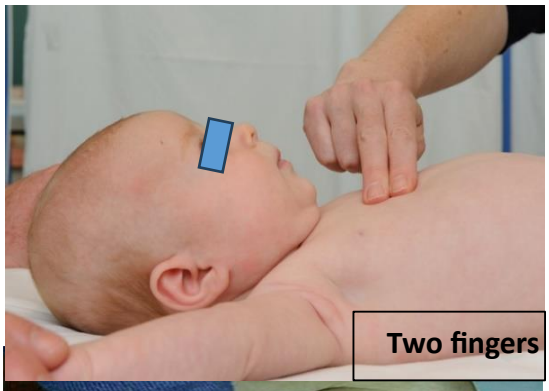


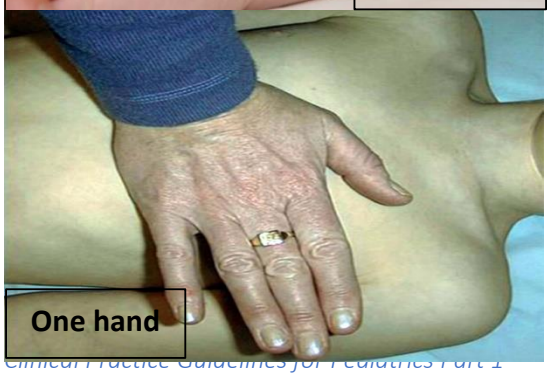
Mouth to mouth and nose

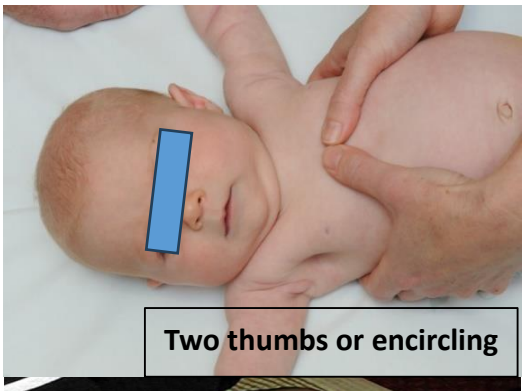
c. Circulation

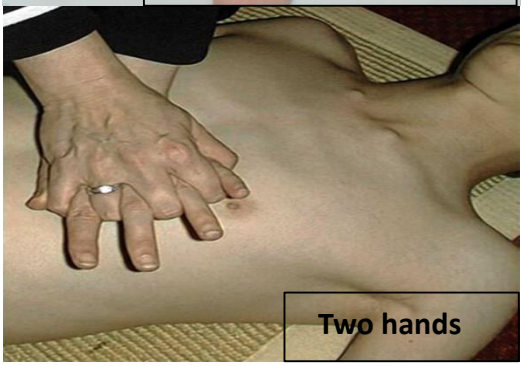
- If there are no signs of life (unconsciousness, no movement, no normal breathing or coughing), check for a pulse (for no more than 10 seconds). In children the carotid pulse can be palpated. In infants the neck is generally short and fat and the carotid pulse may be difficult to identify. Therefore, the brachial pulse or the femoral pulse should be felt.
- Start chest compression if:
  - *Cardiac*(pulseless) arrest: no pulse / no sign of life
  - *Bradycardia* (heart rate < 60/ minute) with a pulse and poor perfusion.

	Infant	child
Pulse check	Brachial or femoral	Carotid
Landmark	Lower half of sternum	Lower half of sternum
Technique	Two fingers or encircling	One hand or 2 hands
Depth of compression	1/3 to ½ of chest depth	1/3 to ½ of chest depth
Rate of compression	100 per minute	100 per minute
Ratio	30:2 (single rescuer) 15:2 (2 rescuers)	30:2 (single rescuer) 15:2 (2 rescuers)









d. High quality of CPR (5 mains components)

Push hard: adequate chest compression depth, at least 1/3 of chest wall.
Push fast: Optimal chest compression rate, 100-120/min or ratio 15:2
Release completely: allow full chest recoil between compression
Minimizing interruption in CPR
Avoid excessive ventilation.

e. Duration of CPR:

Rescuers should minimize interruption of chest compression, and CPR should not be interrupted to check for response or breathing as this is associated with lower survival rates.

If multiple rescuers available, rescuers should be changed at least every 2 minutes to prevent rescuer fatigue and deterioration in chest compression quality.

Rescuers should continue CPR until:
The victim responses or starts breathing normally
It is impossible to continue (exhaustion, the scene becomes unsafe…)
A health professional arrives and takes over the CPR.

4. Defibrillator: Automatic external defibrillator (AED)

An Automatic external defibrillator is a portable device that identifies shockable rhythm that should be treated with defibrillator;

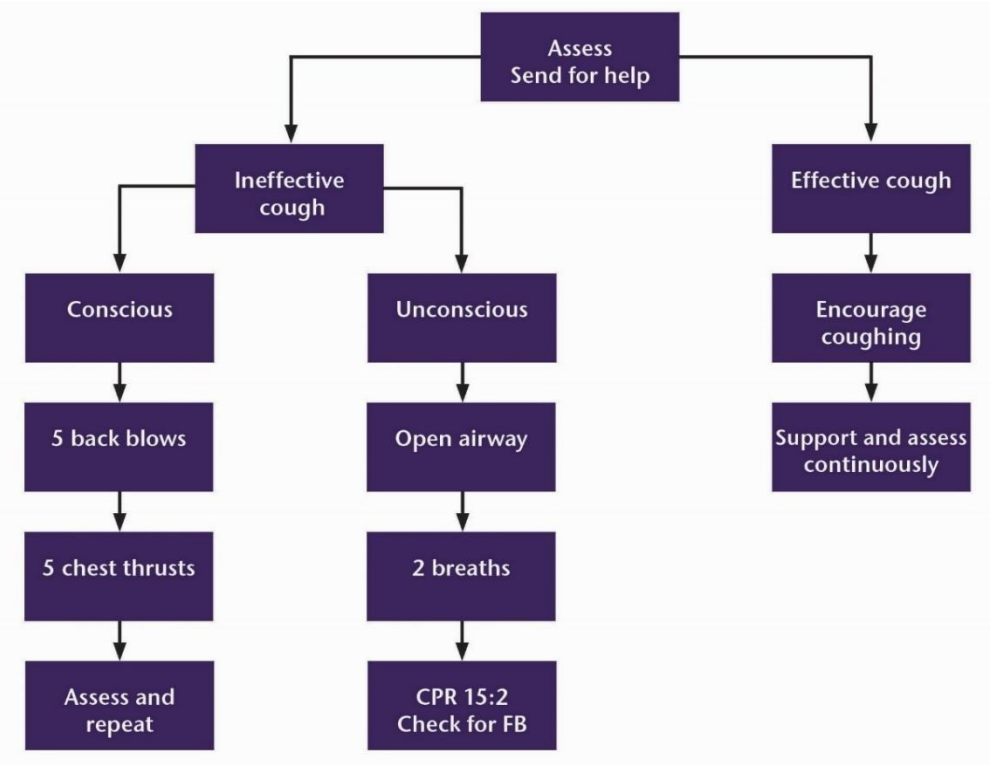
The use of the AED in now included in BLS teaching for adult because early defibrillation is the most effective intervention for the large majority of unpredicted cardiac arrest in adults.

In children and young people, circulatory or respiratory failure cause of cardiac arrest predominate.

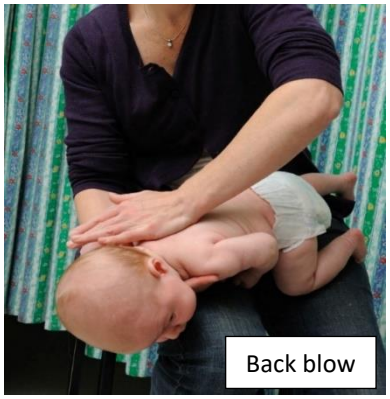
However, in certain circumstances, children may suffer a primary cardiac cause of cardiac arrest, and the use of AED maybe lifesaving.

5. Choking or foreign body airway obstruction (FBAO)

- The vast majority of death from foreign body airway obstruction (FBAO) occur in preschool children.
- The diagnosis may not be clear-cut but should be suspected if the onset of respiratory compromise is sudden and is associated with coughing, gagging, stridor.
- **The sequence of action in chocking child (FB, foreign body)**



- If the child is coughing, encourage coughing. A spontaneous cough is more effective at relieving an obstruction than any externally imposed maneuver.
- An effective cough is recognized by the ability to speak or cry and to take a breath between cough. The child should be continually assessed and not left alone.
- If the cough becomes ineffective – that is quieter or silent and the victim cannot cry, speak or take a breath, or become cyanosed or starts to lose consciousness, then call for help and start the intervention follow the above algorithm.


Back blow


Chest thrust

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1. Advanced Pediatric Life Support (APLS) 6th edition from Australian and New Zealand Resuscitation Council, published in 2016.
2. American Heart Association (AHA) Cardiopulmonary resuscitation (CPR) and Emergency Cardiovascular care (ECC) guideline 2020.
3. Pediatric Clinical Practice Guidelines (CPGs) 2003 written by Dr. Chheng Kheng and Lorntry Patrch.

RECOGNITION OF THE CRITICALLY ILL CHILD

PHY Samnang, SROUR Yina

I. Key Facts

- Earlier recognition and management of potential respiratory, circulatory or central neurological failure will reduce mortality and secondary morbidity. [1]
- A Cross-Sectional Survey in Cambodia, Published June 3, 2010, there were 2,821 children under 5 that the ten most frequently reported diagnoses among young children were mainly common tropical infectious diseases such as acute respiratory infections, diarrhea, dengue, typhoid fever, tuberculosis, malaria and meningitis. [2]
- Four cardinal clinical manifestation that recurrent presented at Pediatric Emergency: Respiratory distress, Alteration of level consciousness, Seizure and Shock. [3,4]

II. Overview

1. Important differences between children and adult [1]

a. Weight

- As most drugs and fluids are given as the dose per kilogram of body weight, it is important to determine a child's weight as soon as possible.
- The Broselow or Sandell tapes use the height (or length) of the child to estimate weight.
  - For Infants < 12 months: Weight (kg) = (age in months + 9)/2
  - For Children aged 1-5 years: Weight (kg) = 2 x (age in years + 5)
  - For Children aged 5-14 years: Weight (kg) = 4 x age in years.

b. Anatomy

- Occiput is relatively large and the neck short
- The tongue is relatively large
- Infants less than 6 months old are primarily nasal breathers
- Epiglottis is horseshoe-shaped, and projects posteriorly at 45°
- The cricoid ring is oval in shape
- The trachea is short and soft.
- Both the upper and lower airways are relatively small
- Diaphragmatic breathing
- Ribs lie more horizontally in infants hard to expansion
- The child's circulating blood volume per kilogram of body weight 70–80 ml/kg
- Lose heat more rapidly and consequently are relatively more prone to hypothermia.

❖ Conclusion: All above were important for early identify and intervention of respiratory distress.

c. Physiology

- Tidal volume varies on body weight (5–7 ml/kg)
- Increased respiratory rate
- Highest cardiac index
- Increased heart rate
- Systolic pressures depend on age

❖ Conclusion: All above were important for early identify and intervention of circulation failure.

2. The goal is to rapidly assess for: [3,4]

- Airway patency,
- Adequacy of gas exchange,
- Provide adequate circulation of blood through the body

3. Pediatric Assessment Triangle: [3,4]

- *Appearance*—interaction, muscle tone, consolability, look/gaze or speech/cry.

- *Work of breathing*—use of accessory muscles of respiration (increased work of breathing) or absent respiratory effort, abnormal breath sounds.
- *Circulation*—abnormal skin color (pallor, cyanosis), bleeding.

4. **Respiratory distress is defined:** [3,4]
   - Increased respiratory rate (tachypnea) and
   - Respiratory efforts (increased work of breathing)
5. **Respiratory Failure:** [3,4]
   - Inadequate to deliver sufficient oxygen to meet demands of the body
   - Inability to eliminate carbon dioxide.
   - Arterial blood gas analysis
     - PaCO2 >50 mmHg (inadequate ventilation)
     - PaO2<60mmHg (inadequate oxygenation)
6. **Primary assessment of airway and breathing:** [1]

a. Airway and breathing:

- Assessment is aimed at deciding whether the airway is:
  - Clear—open and unobstructed.
  - Maintainable—maintained by simple measures like position, suction etc.
  - Not maintainable—needs advanced measures like intubation
- Any audible sound during breathing is suggestive of airway obstruction
  - Stridor, Wheezing, Grunting
- Respiratory rate and Pattern
  - Fast or slow
  - Absent, mean apneic
  - Irregular

Table 1. Normal ranges: Respiratory rate (RR), Heart rate (HR), Blood pressure (BP) [1]

Age	Guide weight(kg)		RR at rest breath per mn 5th–95th centile	HR beats/mn. 5th–95th centile	BP Systolic		
	Boy	Girl			5th centile	50th centile	95th centile
Birth	3.5	3.5	25-50	120-170	65-75	80-90	105
1 month	4.5	4.5					
3 months	6.5	6	25-45	115-160			
6 months	8	7	20-40	110-160			
12 months	9.5	9			70-75	85-95	
18 months	11	10	20-35	100-155			
2 years	12	12	20-30	100-150	70-90	85-100	110
3 years	14	14		90-140			
4 years	16	16		80-135			
5 years	18	18			80-90	90-110	111-120
6 years	21	20		80-130			
7 years	23	22					
8 years	25	25	15-25	70-120			
9 years	28	28					
10 years	31	32					
11 years	35	35					
12 years	43	43	12-24	65-115	90-105	100-120	125-140
14 years	50	50		60-110			

b. Respiratory Effort

- Normal or Increased
- Nasal flaring
- Chest Retraction
- Head position in hyper-extension
- Seesaw respiration
- Inadequate
- Apnea
- Weak cry or Baking Cough

c. Chest Expansion and air-entry:

- Normal or Decrease
- Unequal or Prolonged expiration

d. Inspiratory or expiratory noises

- Stridor—An inspiratory noise while breathing, is a sign of laryngeal or tracheal obstruction.
- Hoarseness
- Grunting—is produced by exhalation against a partially closed glottis. This is a sign of severe respiratory distress and is characteristically seen in infants with pneumonia or pulmonary oedema, raised intracranial pressure, abdominal distension or peritonism.
- Wheezing—indicates lower airway narrowing and is more pronounced in expiration.
- Flaring of the nostrils—is seen especially in infants with respiratory distress.
- Gasping—is a sign of severe hypoxia and may be pre-terminal.
- A silent chest is an extremely worrying sign.

❖ **Exceptions**

There may be absent or decreased evidence of increased effort of breathing in three circumstances:

1) In the infant or child who has had severe respiratory problems for some time, fatigue may occur and the signs of increased effort of breathing will decrease. Exhaustion is a pre-terminal sign.
2) Children with cerebral depression from raised intracranial pressure, poisoning or encephalopathy will have respiratory
   inadequacy without increased effort of breathing. The respiratory inadequacy in this case is caused by decreased respiratory drive.
3) Children who have neuromuscular disease (such as spinal muscular atrophy or muscular dystrophy) may present in respiratory failure without increased effort of breathing.
   The diagnosis of respiratory failure in such children is made by observing the efficacy of breathing, and looking for other signs of respiratory inadequacy. These are discussed in the text [1].

e. Oxygen saturation by Pulse oximetry:

- Normal SpO2 in an infant or child in air at sea level is 97–100%.
- A good plethysmography (pulse) waveform is important to help confirm the accuracy of measurements.

f. Effects of respiratory inadequacy on other organs:

- Heart rate—tachycardia, in fever or anxiety also have a tachycardia. In case of severe or prolong hypoxia, Bradycardia will exist.
- Skin color—Cyanosis.
- Mental status—will be agitated and/or drowsy.

g. Severity of respiratory distress: [3,4]

Table 2: Grade of respiratory distress

Mild	Moderated	Severe	Respiratory failure
- Tachypnea - Dyspnea or shortness of breath	- Tachypnea - Minimal chest wall retractions - Flaring of nasal	- Marked Tachypnea - (> 70 breaths/min) - Apneic episodes/bradypnea/ - irregular breathing - Lower chest wall retractions - Head bobbing (use of sternocleidomastoid muscles) - Cyanosis	- Respiratory distress +cyanosis or CNS* and/or cardiovascular** - signs of hypoxemia

**CNS signs of hypoxemia: restlessness, obtunded sensorium, somnolence, seizures, coma*

*** Cardiovascular signs of hypoxemia: marked tachycardia, bradycardia, hypotension, and cardiac arrest*

7. Primary assessment of circulation:

A. Recognition of potential circulatory failure

a. Heart rate

- Normal rates are shown in Table 1.
- The heart rate initially increases in shock due to catecholamine release and as compensation for decreased stroke volume.
- Bradycardia—is defined as less than 60 beats per minute, was a sign of poor perfusion.

b. Pulse volume: need to comparative palpation of both peripheral and central pulse

- If peripheral pulse absent and central pulse weak—serious signs of shock
- Bounding pulses or too strong—may be caused by an increased cardiac output (e.g., septicemia)

c. Capillary refill time

- cutaneous pressure on the center of the sternum or on a digit for 5 seconds, Figure 1
- Duration of refill was 2 second
- If slow to refill—can indicate poor skin perfusion, but need more indicator such: HR, pulse volume, BP, urine output for right intervention.

d. Blood pressure

- Use of the correct cuff size—accurate blood pressure measurement
- The width of the cuff should be more than 80% of the length of the upper arm and the bladder more than 40% of the arm's circumference. Figure 2.
- Normal rates are shown in Table 1.

B. Effects of circulatory inadequacy on other organs

a. Respiratory system

Respiratory rate increase, without retraction—represented of metabolic acidosis resulting from circulation failure.

b. Skin

- Mottled, cold, pale skin peripherally—sign of poor perfusion (circulation failure).
- Need more indicator above for more accurate.
- Conscious
- Agitation and then drowsiness leading to unconsciousness—caused by poor cerebral perfusion.

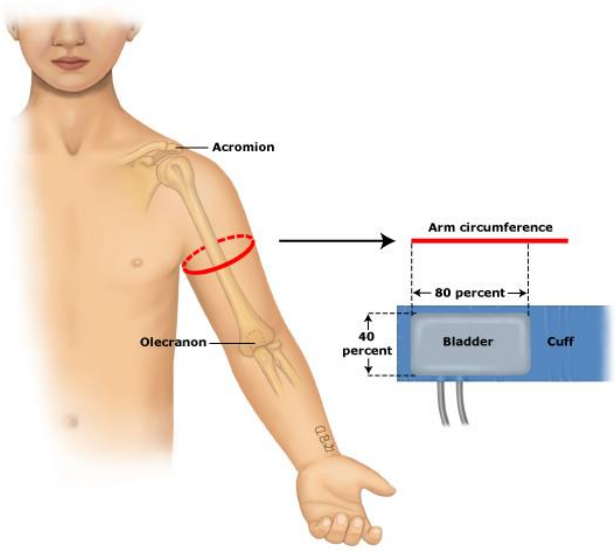


Figure 2: *The width of the cuff should be more than 80% of the length of the upper arm and the bladder more than 40% of the arm's circumference*.

- Urinary output
- less than 1 ml/kg/h in children
- less than 2 ml/kg/h in infants
- A history of reduced wet nappies or urine production should be asked for.

c. Cardiac failure— cause of respiratory inadequacy:

- Cyanosis, not correcting with oxygen therapy
- Tachycardia out of proportion to respiratory difficulty
- Raised jugular venous pressure
- Gallop rhythm/murmur
- Enlarged liver
- Absent femoral pulses.

8. Primary assessment of Disability:

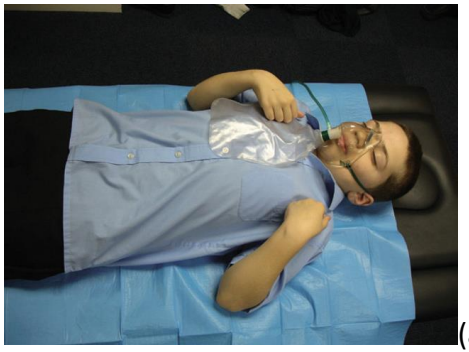
a. Consious level:

- A rapid assessment of conscious level can be made by assigning the patient to one of the categories shown in the box.
- Responds to pain—need to observe the eyes and limbs did
  - Opening eyes to pain
  - Localizing to pain

A	Alert—compare to GCS 15/15
V	Respond to Voice— compare to GCS ~13/15
P	Respond only to Pains— compare to GCS ~10-8/15
U	Unresponsive to all stimuli— compare to GCS ~8/15 or less

b. Posture:

- Hypotonia
- Decorticate (flexed arms, extended legs) — is a sign of serious brain dysfunction (Figure: a)
- Decerebrate (extended arms, extended legs) — is a sign of serious brain dysfunction (Figure: b)

 (a)  (b)

c. Pupils:
- Dilatation, none reactive to light and inequality—which indicate possible serious brain disorders or other cause.

d. Respiratory effects of central neurological failure:
- Recognizable breathing pattern abnormalities with raised intracranial pressure:
- Hyperventilation
  - Cheyne–Stokes breathing
  - Apnea

e. Circulatory effects of central neurological failure:
- Cushing's response–Systemic hypertension with sinus bradycardia indicated of Cerebral herniation, this is a late and pre-terminal sign.

f. Primary assessment of exposure:
- It includes undressing the child for a focused
- Physical examination,
- Looking for evidence of trauma,
- Petechia /purpura and warming if indicated.

III. Primary assessment and resuscitation

- In a severely ill child, a rapid examination of vital functions is required
- The ABC approach should first to perform

1. Air-way:

a. Assess patency by:
- Looking for chest and/or abdominal movement
- Listening for breath sounds
- Feeling for expired air

b. Vocalizations, such as crying or talking, indicate ventilation and some degree of airway patency

c. If there is obvious spontaneous ventilation, note other signs that may suggest upper airway obstruction:
- The presence of stridor
- Evidence of recession

d. If there is no evidence of air movement then chin lift or jaw thrust maneuvers must be carried out. **Reassess the airway after any airway-opening maneuvers**

e. If there continues to be no evidence of air movement then airway patency can be assessed by performing an airway opening maneuvers while giving rescue breaths.

❖ Resuscitation: If the airway is not patent, then this can be secured by:
- A chin lift or jaw thrust the use of an airway adjunct
- Tracheal intubation

2. Breathing:

- If the patency of respiration is distress, classified of severity as table above Table 2.
- Resuscitation:

- Give high-flow oxygen (flow rate 15 l/min) through a mask with a reservoir bag to any child with respiratory difficulty or hypoxia.
- If respiratory effort is weak, this should be supported respiration with bag–valve–mask ventilation or intubation and intermittent positive pressure ventilation.

3. Circulation:

- If the patient has sign of hypoperfusion. The assessment of circulation has been described as above 7.A.
- Resuscitation:
  - In every child with an inadequate circulation:
  - Give high-flow oxygen through either a mask with a reservoir bag or an endotracheal tube if intubation has been necessary for airway control or inadequate breathing.
  - Venous or intraosseous access should be gained and an immediate infusion of crystalloid (20 ml/kg) given. Urgent blood samples, especially blood glucose, may be taken at this point.

4. Disability:

- Any problem, the ABC approach should be performed first.
- Assessment of consciousness was description as above 8.
- Any patient with a decreased conscious level or convulsions must have an initial glucose stick test performed.

a. Resuscitation

- If air-way at high risk, consider intubation to stabilize.
- If hypoglycenia, treat it with a bolus of glucose (2 ml/kg of 10% glucose) followed by an IV infusion of glucose, after taking blood for glucose measurement in the laboratory and a sample for further studies.
- If seizure, treat it with Diazepam Intra-rectal 0.5mg/kg, maximum dose 20mg/dose, can repeat dose after 4hrs.

b. Manage raised intracranial pressure if present

- Head in-line in a 20° head-up position (to help cerebral venous drainage).
- Give hypertonic (3%) saline 3 ml/kg. Mannitol can be used as an alternative (250–500 mg/kg; i.e., 1.25–2.5 ml of 20% solution IV over 15 minutes), provided serum osmolality is not greater than 325 mOsm/l), NSS 0.9% is prefer.
- Consider dexamethasone (only for oedema surrounding a space-occupying lesion) 0.5 mg/kg 6-hourly.

IV. Secondary Assessment

1. Focuse on SAMPLE abbriviation

a. Sign and Symtome:
Respiratory, Cardiovascular, Central Nervous System, Skin, Gastroentestinal problem, etc…

b. Allergy history

- Skin rash, Eczema, Urticaria, etc.…
- Medication, Seafood, etc.…

c. Medication

- Anti-Epileptic, Prednisolone, Immusuppresor drug, etc.…
- Any medication that the child is currently on or has been on should be recorded.

d. Past Medical History

- Congenital heart disease, Operation, Birth Asphyxia, Epilepsia, Asthma, ect…

e. Last Food intake
The last food that the patient was eated before hospitalization.

f. Event of Illness
Duration of the illness.

2. Investigation

- Chest X-ray: in case of respiratory problem, etc.…
- CT-scan or MRI: in case of respiratory or brain problem, etc.…
- Ultrasound: Abdominal, Heart, etc.…
- Blood test: Full blood count, Urea and electrolytes, Arterial blood gas, Lactate, Procalcitonin, CRP, ERS, Band neutrophil,
- Liver function test: AST, ALT, Albumine, etc…
- Coagulation profile: PT, aPTT, Bleeding time, etc.…
- Blood culture.
- Urine analysis and urine culture
- Toxicology
- Respiratory Virus Screening.

3. Identify

A. Respiratory type:

a. Upper airway obstruction:

- Acute laryngitis, laryngotracheitis, diphtheria,
- foreign body aspiration.
- Epiglottitis, Croup

b. Lower airway obstruction:

- Bronchiolitis, Bronchitis, Pneumonia.
- Lung tissue disease: large pleural effusion, pneumothorax, tumors, Hemopneumothorax and flail chest.

c. Disordered control of breathing:

- Impaired consciousness, raised intracranial pressure, intracranial bleeding, poisoning.
- Acidosis, salicylate intoxication.
- Acute paralytic poliomyelitis, Guillain-Barre syndrome, organophosphate poisoning, snake bite, diaphragmatic paralysis.

B. Circulatory type:

- Hypovolemic shock: bleeding, severe dehydration, Severe burn.
- Distributive (e.g. septic, anaphylactic) shock
- Obstructive shock: Pneumothorax, Pleurisies, Tamponade.
- Cardiogenic shock: Endocarditis, Myocarditis, Pericarditis.

V. Acute treatment

1. Ensure adequate oxygenation: Administer 100% oxygen non-rebreather facemask if hypoxia is present.

2. Assess and maintain a patent airway: Consider intubation and assisted ventilation if there are concerns about hypoventilation or inability to maintain airway reflexes.

3. Evaluate for hemodynamic compromise: Secure IV access early, consider intra-osseous access if venous access is difficult. Administer fluid resuscitation if there are signs of shock e.g., tachycardia, prolonged capillary refill time, cool peripheries. Give IV crystalloids of 20ml/kg boluses and watch for response. If there is suspicion of cardiogenic shock, give fluids cautiously and consider early inotropic support.

a. Correct rapidly reversible, potentially life-threatening derangements. This includes:

- Hypoglycemia: IV dextrose 10% 4–5ml/kg or dextrose 25% 1–2ml/kg
- Hyponatremia: IV 3% NaCl 2ml/kg over 30 minutes
- Hyperkalemia: IV insulin 0.1units/kg + IV dextrose 50% 2ml/kg and/or sodium polystyrene sulphonate (kayexalate) PR/oral 0.5–1g/kg
- Hypocalcemia: IV 10% Calcium chloride 0.2ml/kg over ten minutes)

b. Early antibiotic therapy if sepsis is suspected. Example: Ceftriaxone with dose 100mg/kg/day, Gentamycin 5mg/kg/day. In case severe sepsis or septic shock, Meropenem with dose 20-40mg/kg/dose q 8hrs, Vancomycin with dose 60mg/kg/day q 6 hrs.

c. Transfer patient to an appropriate care facility after initial stabilization.

VI. Monitoring

1. The goals of monitoring are:

- Early detection of worsening/complications
- Assessment of response to therapy
- Rapid documentation of clinical state

2. Monitoring Protocol:

- Rate, rhythm and depth of respiration.
- Heart rate
- Blood pressure
- Temperature
- Presence/absence of cyanosis
- Use of accessory muscles, flaring of nose and chest wall retractions, and the degree of distress.
- Air entry in both lungs. In case an endotracheal tube has been passed, check its position and patency and need for suction.
- Signs of exhaustion such as somnolence, confusion, and seizures.
- Non-invasive monitoring: Oxygen saturation (pulse oximetry) and if available End tidal CO2 (EtCO2).
- Arterial blood gas (ABG). This must be interpreted together with the clinical data of the patient.

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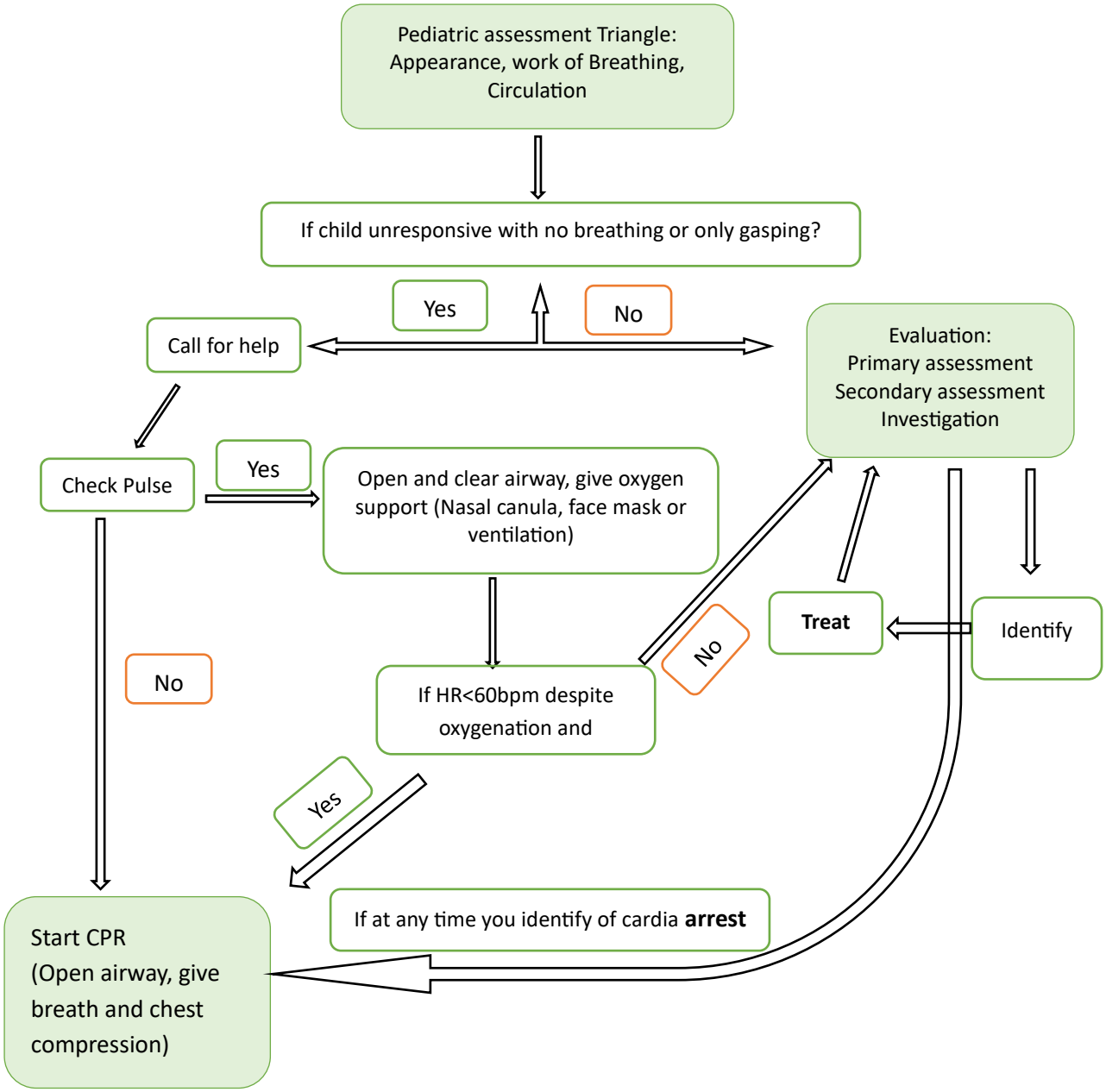
Recognition Critical Ill Child Algorithm



MANAGEMENT OF CARDIAC ARREST

EANG Habsreng, PEN Sotheavy, NGETH Pises

I. Key Facts

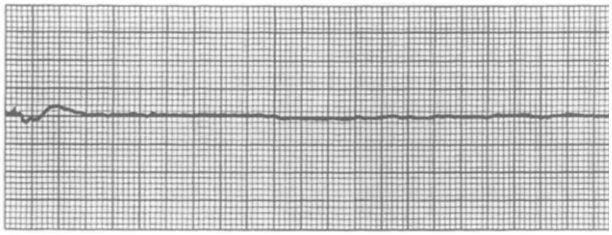
- Unlike in adults, cardiopulmonary arrest in children is less likely to be a primary cardiac even. [1]
- Cardiac arrest in children is the result of asphyxia in a majority of the cases. Early onset of effective, high-quality CPR can improve survival. [1]

II. Introduction

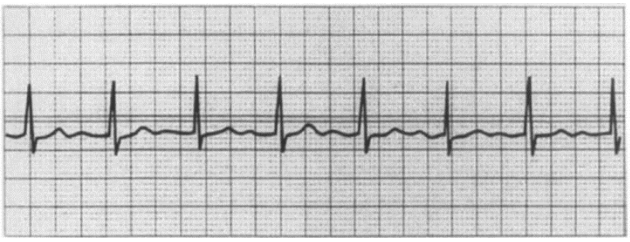
Cardiac arrest has occurred when there is no effective cardiac output. Before any specific treatment is started, effective basic life support (BLS) must be established (see BLS guideline).

There are 4 cardiac arrest rhythms which are divided into 2 groups [1,2,3]

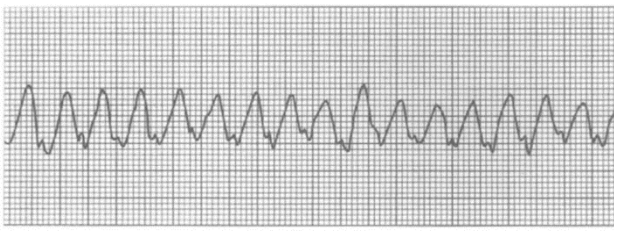
1. Non-shockable: do not require defibrillation
   - Asystole (most common cardiac arrest rhythm)
   - Pulseless electrical activity (PEA)
2. Shockable: require defibrillation
   - Ventricular fibrillation (VF)
   - Pulseless ventricular tachycardia (pVT)



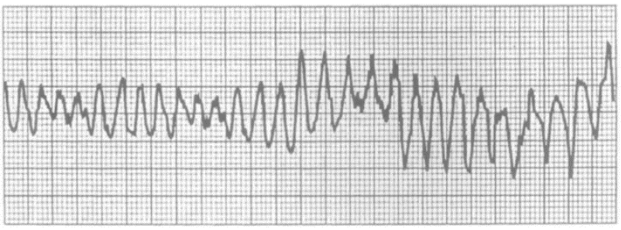
Asystole



Pulseless electrical activity (PEA)



Ventricular tachycardia (VT)



Ventricular fibrillation (VF)

III. Sequence of actions in cardiac arrest

1. **Start basic life support (see pediatric BLS guideline)**
2. **Oxygenate, ventilate, and start chest compression**
   - Provide ventilation initially by bag and mask with high oxygen concentration. Ensure a patent airway by using an airway maneuver as described in the pediatric basic life support guideline.
   - Ensure that ventilation remains effective when continuous chest compressions are started.
   - If airway cannot be well secured, intubation should be performed. This will both control the airway and enable chest compression to be given continuously, thus improving coronary perfusion pressure.

- When performing CPR in infants and children with an advanced airway (intubated), ventilate at the rate of about 1 breath every 2 to 3 second (20-30/min). [2]

3. **Attach to monitor or defibrillator** assess the cardiac rhythm to identify shockable or non-shockable rhythm.

A. Non-shockable rhythm (Asystole/PEA): more common finding in children.

B. Continuous perform high quality CPR (see pediatric BLS guideline)

- Give Adrenaline
- If venous or intraosseous (IO) access has been established, give Adrenaline 0.1 ml/kg of 1:10 000 solution (1 ampoule of adrenaline mix with NSS 9 ml)
- If circulatory access is not present, and cannot be obtained quickly, but the patient has a tracheal tube in place, consider giving Adrenaline 1 ml/kg of 1:10 000 solution via the tracheal tube.
- Give Adrenaline every 3-5 minutes (usually every 4 minutes)
- Continue CPR, only pausing briefly every 2 min to check for rhythm change

a. Consider and correct reversible causes (4H 4T) during CPR:

- Hypoxia
- Hypovolemia
- Hyper/hypokalemia
- Hypothermia
- Tension pneumothorax
- Toxic/therapeutic disturbance
- Tamponade (cardiac)
- Thromboembolism

b. Consider the use of other medications such as alkalizing agents (Sodium Bicarbonate 1mmol/kg) IV slowly in case of:

- prolonged resuscitation
- known or suspected hyperkaliemia
- Tricyclics antidepressant overdose

❖ **Note that:**

- Bicarbonate must not be given in the same intravenous line as calcium because precipitation will occur.
- Sodium bicarbonate inactivates Adrenaline and dopamine, so the line must be flushed with saline if these drugs are subsequently given.
- Bicarbonate must not give by intratracheal route

C. Shockable rhythm (VF/VT): less common in pediatric cardiac arrest.

a. Continue CPR until a defibrillator is available.

b. Defibrillate the heart: Give first shock of 4J/kg (asynchronized)

c. Resume CPR:

- Without reassessing the rhythm or feeling for a pulse, resume CPR immediately, starting with chest compression.
- Continue CPR for 2 min, then pause briefly to check the monitor:
  - If still VF/VT, give a second shock of 4J/kg
  - Without reassessing the rhythm or feeling for a pulse, resume CPR immediately, starting with chest compression. Consider about reversible causes (4H 4T).
- Give Adrenaline 0.1 ml/kg (1:10 000) IV or IO after the 2nd shock, once chest compressions have resumed.
- Repeat Adrenaline every 3-5 minutes until ROSC.
- Give Amiodarone 5 mg/kg after 3rd shock only (1).
- Continue giving shocks every 2 min, continuing compressions and minimizing the breaks in chest compression as much as possible.

- Note: After each 2 min of uninterrupted CPR, pause briefly to assess the rhythm.
  - If still VF/VT: Continue CPR with the shockable (VF/VT) sequence.
  - If asystole: Continue CPR and switch to the non-shockable (asystole or PEA) sequence as above.
  - If organized electrical activity is seen, check for signs of life and a pulse:
    - If there is ROSC, continue post-resuscitation care.
    - If there is no pulse (or a pulse rate of < 60/min), and there are no other signs of life, continue CPR and continue as for the non-shockable sequence above.

IV. When to stop resuscitation [1]

Resuscitation efforts are unlikely to be successful and cessation can be considered if there is no return of spontaneous circulation at any time with up to 20 minutes of cumulative life support and in the absence of recurring or refractory VF/VT. Exceptions are patients with a history of poisoning or hypothermia in whom prolonged attempts may occasionally be successful.

V. Parental presence [1]

Family members should be offered the opportunity to be present during the resuscitation of their child. The presence of parents at the child's side during resuscitation enables them to gain realistic understanding of the efforts made to save their child and they may show less anxiety and depression afterward.

❖ **Important points:**

- A staff member must be with the parents to support and explain the events to them.
- The team leader, not the parents, decides when it is appropriate to stop the resuscitation. If the presence of the parents is impeding the progress of the resuscitation, they should be asked to leave.

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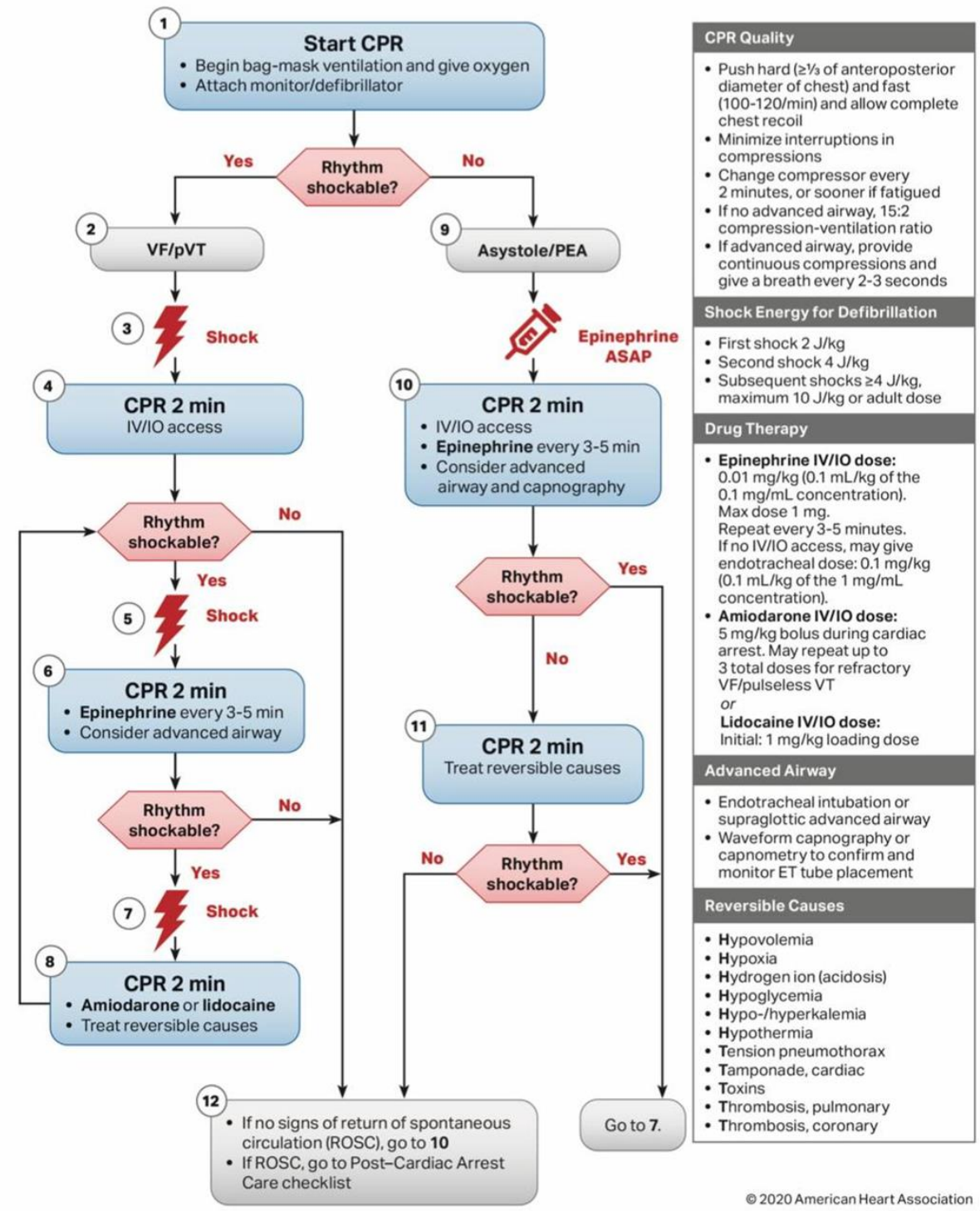
Pediatric Cardiac Arrest Algorithm.



CHOKING

MOM Sathya, KHUN Leangchhun, IV Malene, YAY Chantana

I. Key Facts

- Choking is one of the leading causes of unintentional death in infants, who require a different rescue procedure than adults. [1]
- Choking is a true medical emergency that required fast, appropriate action by anyone available. [2]
- Choking prevents breathing and can be partial or complete.
- Children aged 6months to 4 years are at high risk.
- One U.S. child ***chokes to death*** approximately every five days; and 75 percent of choking deaths occur in children under the age of 3 years
- Approximately 95% of deaths from choking occur in the home environment.
- In a survey in Jayavarman VII hospital during 2 years period from 1st January 2017 to 31th December 2018, 20 cases of suffocation in children under 15 years were identified. The majority of the children concerned are less than 5 years old (10 cases or 50%). [3]

II. Overview

1. Definition

Choking (foreign body airway obstruction (FBAO) is the mechanical obstruction of the flow of air from the environment into the lungs that can be cause by obstruction due to ingestion of food, objects, small toys, vomit. [4]

2. Causes

- Physical obstruction of the airway by a foreign body (food, toys, household objects). In one study, peanuts were the most common obstruction
- The tongue of an unconscious person falling to the back of the throat.
- blood or vomit collects in the throat. [4,5]

3. Pathophysiology

After foreign body aspiration occurs, the foreign body can settle into 3 anatomic sites, the larynx, trachea, or bronchus.

- Of aspirated foreign bodies, 80-90% become lodged in the bronchi.
- Several papers have demonstrated equal frequency of right and left bronchial foreign bodies in children.
- In adults, bronchial foreign bodies tend to be lodged in the right main bronchus because of its lesser angle of convergence compared with the left bronchus and because of the location of the carina left of the midline.
- Larger objects tend to become lodged in the larynx or trachea.

4. Risk factors

- Nonfood factors: coin, balloons, balls, marbles, batteries, small toys, bottle or pen caps, safety pin.
- Food factors: hard candy, hot dogs, peanut, grapes, carrots, corn, sticky food. [10,11]

III. Signs and Symptoms

1. If an infant is choking, more attention must be paid to an infant's behavior.

High pitched or wheezing sounds when breathing in

- Difficult breathing.
- Weak cry, weak cough, or both.
- Clutching at the throat with one or both hands. [5]

2. Clinical features based on impaction location:

- Impaction in larynx or trachea:

- Sudden and catastrophic event Coughing,
- choking ± vomiting
- Severe respiratory distress
- Foreign bodies inhaled
- Stridor
- Cyanosis
- Altered mental state
- Drooling and voice changes
- Total obstruction will rapidly progress to unconsciousness and cardiorespiratory arrest
- May be present in a child in cardiorespiratory arrest who is impossible to ventilate.

- Impaction in main bronchus:
  - Witnessed episode of choking, coughing or wheezing while eating or playing (many are unwitnessed)
  - Tachypnoea and respiratory distress
  - Cyanosis
  - Persistent wheeze (may be focal and partially respond to bronchodilators)
  - Persistent cough
  - Fever
  - Hemoptysis
  - Shortness of breath
  - Recurrent or persistent consolidation
  - May be asymptomatic after initial event before developing complications (pneumonia, abscess, bronchiectasis etc.)
- Impaction lower than main bronchus: Often asymptomatic after initial event, or may have symptoms as for main bronchus FB.

IV. Diagnosis

- The normality of the clinical and radiological examination, the absence of functional signs, do not make it possible to formally eliminate the presence of an intra-bronchial foreign body.
- Indeed, in the case of confirmed foreign-bronchial foreign bodies, according to the data of the literature, in 10 to 25% of cases the child is asymptomatic and the clinical examination normal, and in 12 to 42% of cases the chest x-ray is normal.
- The establishment of the diagnosis is based solely on the identification of the penetration syndrome during interrogation and the completion of bronchoscopy.

1. Imaging:

a. X ray of the chest (for radio dense objects):

- High-kilovolt anteroposterior and lateral radiographs of the airway are the tests of choice in patients in whom laryngeal foreign bodies are suspected.
- Position: posteroanterior and lateral radiographs are an adjunct to the history and physical examination in patients in whom foreign body aspirations are suspected.
- Lateral decubitus chest films may be helpful in children in whom the dependent lung remains inflated with bronchial obstruction. Typically, the dependent lung collapses.
- Chest radiographs (inspiratory and expiratory films) demonstrate atelectasis on inspiration and hyperinflation on expiration with a foreign body obstruction the bronchus.

b. CT scan indicated for radiolucent foreign body and being able to provide more accurate three-dimensional localization of the foreign body. And being able to differentiate tissue densities, allowing for better visualization of inflammation, abscesses, and granuloma that are frequently secondary clues to a retained foreign body.

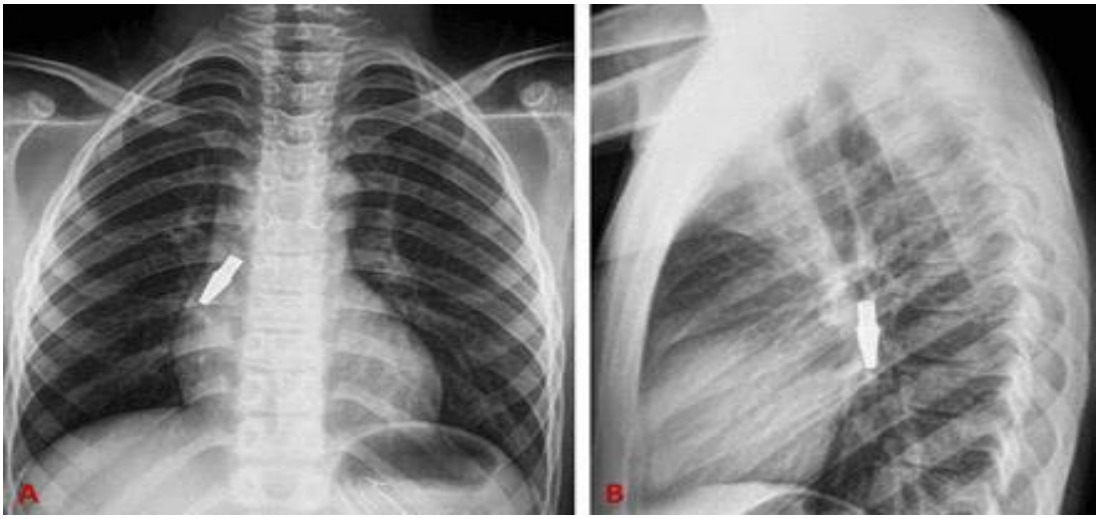


Image 1: *pen cap in the right main bronchus.* [7]

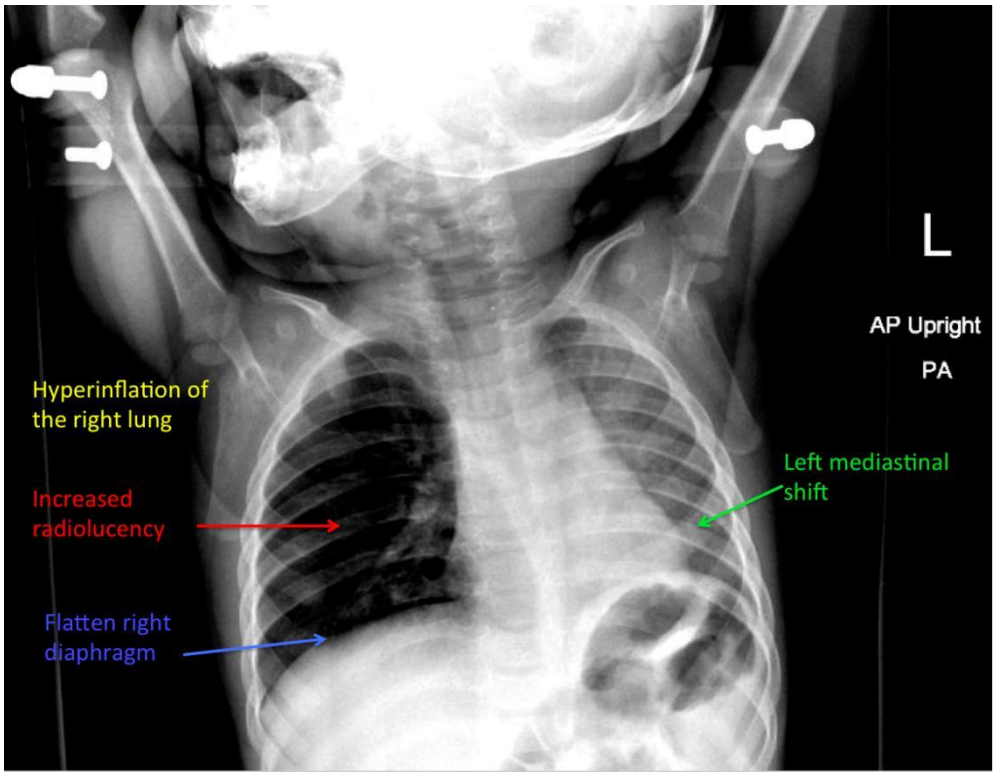


Image 2: *food stuck in the right main bronchus with indirect sign* [8]

2. **Laboratory test**: not necessary
3. **Differential diagnosis**
   - Acute epiglottitis – sitting forward, drooling, toxic looking, temperature.
   - Croup– coryzal symptoms, cough associated, improved with steroids/ adrenaline nebulizer.
   - Laryngomalacia– present from an early age, improves with age.
   - Whooping cough– unimmunized child, cough associated, coryzal symptoms may have associated temperature. [9]

V. Complications

The most significant complication of choking is the risk of death from asphyxiation and follow by neurological sequela, pneumonia, sore throat, laryngitis. [11]

VI. Treatment and management

1. What to do if a person starts to choke?

Ask" **are you choking?"**

- In partial airway obstruction: the person is able to answer you by speaking.
- In complete airway obstruction: the person is unable to answer.

If the person is coughing forcefully and not turning a bluish color, stay with the person and encourage him or her to cough until the obstruction is cleared.

Do not give the person any to drink

Do abdominal thrush for adults and children older than 1year (Heimlich maneuver). [12]

a. Mofenson maneuver:

It is used for the babies younger than 1year of age.

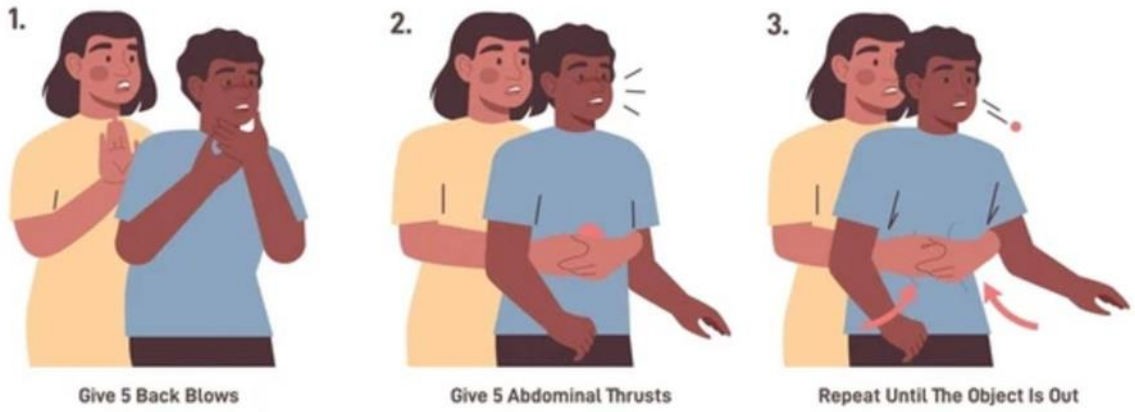
- Lay the infant on your arm or thigh in a head down position,
- Give 5 blows to the infant's back with heel of Hand,
- If obstruction persists, turn infant over and give 5 chest thrusts with 2 fingers, one
- finger breadth below nipple level in midline,
- If obstruction persists, check infant's mouth for any obstruction which can be removed,
- If necessary, repeat sequence with back slaps again. [13]

1. Remove the object with your finger only if you can see it

2. Place the infant stomach-down across your forearm and give five quick, forceful blows on infant's back with heel of your hand

3. Place two fingers in the middle of infant's breastbone and give five quick downward thrusts.

b. Heimlich maneuver:



1) Try to cough foreign object.
2) Make a fist and place it just above belly button.
3) You can also lean over a table edge or chair to add force.

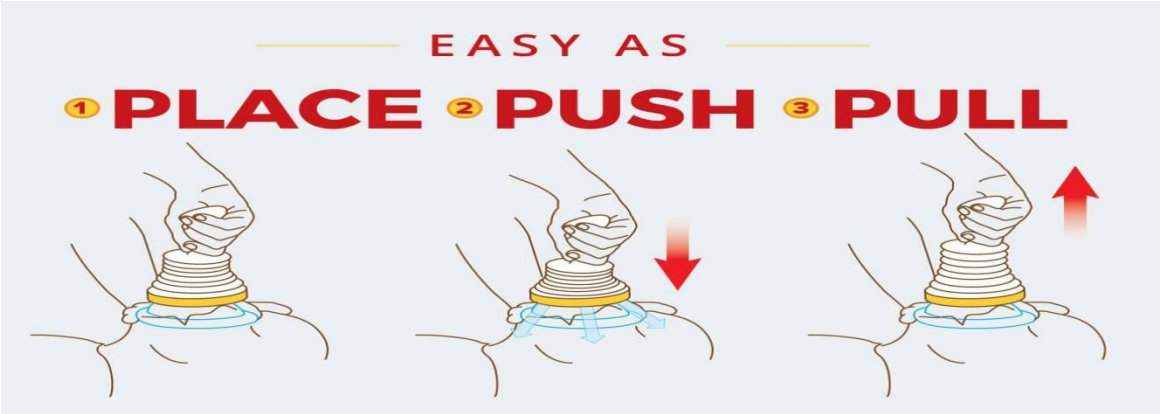
c. How to perform abdominal thrush? (for infants over one year)

- Lean the person forward slightly and stand behind him or her. Make a first with one hand. Put your arms around the person and grasp your fist with your other hand in the midline just below the ribs. Make a quick, hard movement inward and upward in an attempt to assist the person in coughing up the object. This maneuver should be repeated until the person is able to breath.
- The American Red Cross recommends [12]

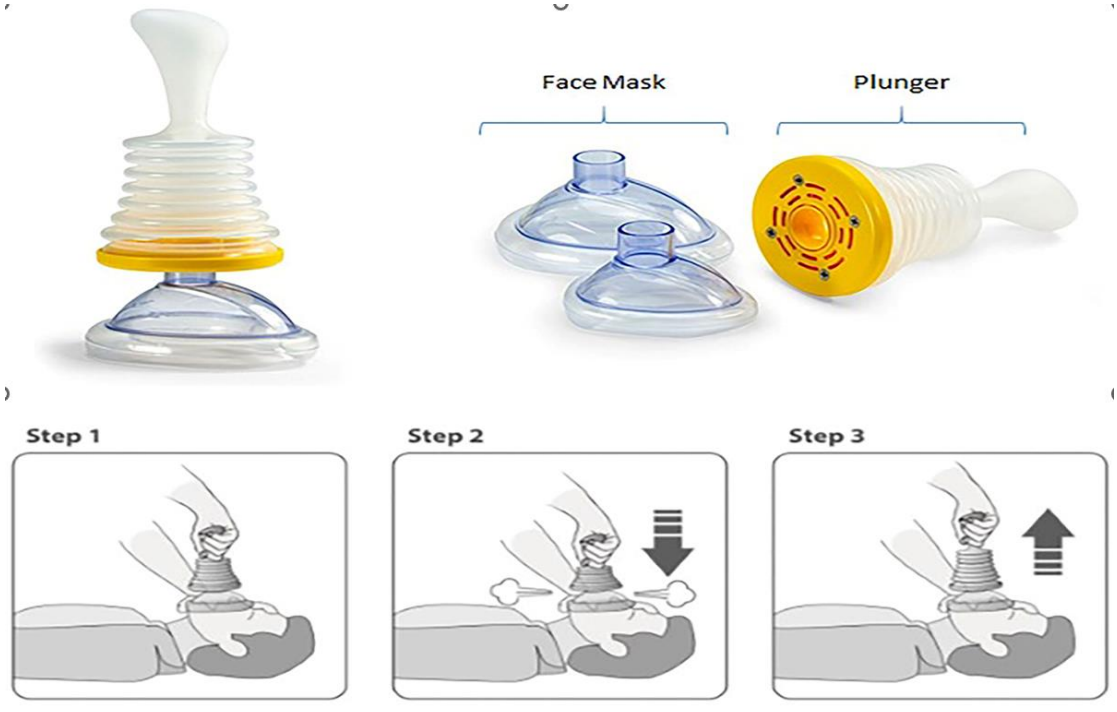
1) Give five back blows
2) Give five abdominal thrusts
3) Alternate between five blows and five thrusts until the blockage is dislodged.

- If the person loses consciousness, gently lay him or her on their back on the floor. To clear the airway, kneel next to the person and put the heel of your hand against the middle of the abdomen, just below the ribs. Place your other hand on top and press inward and upward five times with both hands. If the airway clears and the person is still unresponsive, begin cardiopulmonary resuscitation (CPR).
- CPR involves both chest compression and artificial respiration. These actions are often enough to dislodge the item sufficiently for air to pass it, allowing gaseous exchange into the lungs.

1. **Anti choking device:** success rate of 94% in removing choking objects since 2014. [14]



1) Place the face mask over the mouth and nose of the choking victim, using your hand to create a seal.
2) Press down to expel air through the sides of the device.
3) While maintaining a seal between the facemask and the victim's face. Pull up
4) forcefully on the device to create suction and dislodge the airway obstruction.



2. **Appropriate mode of transportation to the reference center:**
   Any child suspected of having inhaled a foreign body (on the basis of a penetration syndrome) must be referred without delay to a specialized center:
   - Transport in sitting position
   - If the child is dyspneic or if doubt about an epiglottitis the transport must be medicalized and able to intubate the child immediately if necessary (SMUR pediatric)
   - By warning the reception team of the arrival of the child.
3. **At hospital:**
   a. *Airway: open the airway.*
   b. *Breathing:* support breathing using bag-valve-mask ventilation until definitive airway is established (i.e., endotracheal intubation). Monitor oxygenation and end tidal CO2 (after intubation).
   c. *Circulation:* assess circulation, establish intravenous (IV) access, chest compressions if necessary
   d. *Endotracheal intubation*
   - Premedication:
     - Atropine: prevent intubation-induced bradycardia and post hypoxia
       Dose: 0,01mg/kg (MAX:1A=0,6mg)
     - Midazolam: (benzodiazepine) for sedative with anticonvulsant effect more potency than Diazepam. Dose:0,1-0,3mg/kg
     - Ketamine: analgesic agent and mild respiratory suppression good for sedation and pain management. Dose:1-3mg/kg
   - Endotracheal tube size (ETT):

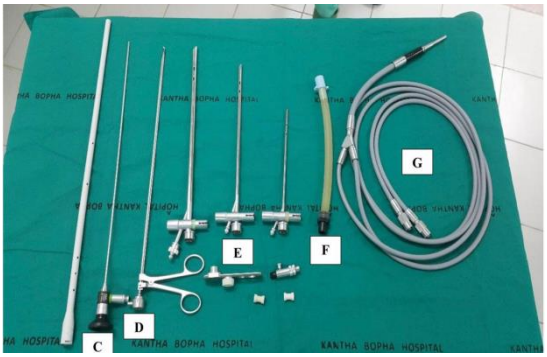
Table 1. *Neonatal tube size*

Weight (g)	Gestational age (weeks)	Tube size (mm)	Oral tube length (mm)
<1,000	<28	2,5	7
1,000-2,000	28-34	3,0	8
2,000-3,000	34-38	3,5	9
>3,000	>38	3,5-4,0	10

Table 2. *Infant tube size*

Age	ETT size	ETT length (oral)
1month – 1year	3,5mm – 4mm	10-11mm
1 year – 10years	Uncuffed ETT size (mm) = (age in years/4) + 4. Cuffed ETT size (mm ID) = (age in years/4) + 3.	ETT X 3
>10 year	7mm – 7,5mm	ETT X 3

   - Always confirm with chest auscultation for (bilateral breath sound) and chest x-ray.
   e. *Laryngoscopy* for foreign body that can be directly visualized
   f. *Bronchoscopy* rigid (after resuscitated the patient) is indicated if clinical suspicion of foreign body aspiration (history of possible aspiration, focal abnormal lung exam or abnormal chest radiography).
   Following the removal of the foreign body, beta-adrenergic nebulization treatments followed by chest physiotherapy are recommended to help clear related mucus or treated bronchospasm.



A: *monitor,* ***B:*** *source of light,* ***C:*** *optical stem,* ***D:*** *extractor forceps* ***E:*** *trocar for bronchoscopy with different caliber* ***F:*** *connector between apparel of bronchoscopy with ventilation machine*
G: *optical cable.*

VII. Prevention and education

- Cook and prepare food to the right shape, size, and texture
- Avoid small, sticky, or hard foods that are hard to chew and swallow.
- Meals and snack time:
  - Have your child sit up while eating (no lying down, crawling, or walking).
  - Have your child sit in a high chair or other safe place.
  - Avoid letting your child eat in the car or stroller.
  - Keep mealtimes calm. Avoid distractions, disruptions, and rushing when eating.
- Avoid small toy (then their mouth). [15]

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EMERGENCY MANAGEMENT OF SHOCK

RITH Ravin, MENG Chhay, SROUR Yina, KIM Ang

I. Key Facts

In Low and Middle Income countries, the prevalence of shock ranged from 1.5% in a pediatric hospital population to 44.3% in critically ill children and the mortality estimates ranged between 3.9-33.3%. [1] The early use of the recommended Pediatric Advanced Life Support (PALS) guidelines for the management of shock is associated with decreased mortality (8.69% vs 15.01%, respectively) and decreased functional morbidity (1.24% vs 4.23%, respectively). [2]

The most common cause of shock in pediatric patients is hypovolemia followed by septic shock [3]. The overall incidence of sepsis and septic shock appears to have increased from 3.7% to 4.4%, although mortality has declined 10.9% over the same period by early recognition and intervention. [4]

II. Overview

1. Definition [3]

Shock is an acute, life-threatening syndrome of circulatory dysfunction resulting in inadequate delivery of oxygen and other nutrients to meet tissue metabolic demands. This is in turn leads to anaerobic metabolism and cellular acidosis, culminating in loss of normal cellular function, cell death, organ dysfunction, and eventually death, if not recognized and appropriately treated.

2. Types and Causes [3]

- Hypovolemic: results from decreased preload from extravascular fluid loss or intravascular fluid loss. Example: Hemorrhagic, Gastroenteritis, Stomal loss, Intussusception, Volvulus, Peritonitis, Burn.
- Distributive: results from a decrease in systemic vascular resistance, with abnormal distribution of blood flow within the microcirculation and inadequate tissue perfusion. Example: Septicemia, Anaphylaxis, Vasodilating drugs, Spinal cord injury.
- Cardiogenic: results from pump failure, manifested physiologically as decreased systolic function and depressed cardiac output. Example: Arrythmias, Heart failure (cardiomyopathy, myocarditis), Valvular disease, Myocardial contusion.
- Obstructive: result when blood flow is physically obstructed. Example: Congenital cardiac (Coarctation, Hypoplastic left heart, aortic stenosis), Tension/hemopneumothorax, Flail chest, Cardiac tamponade, Pulmonary embolism.
- Dissociative: the circulating blood volume is adequate but the hemoglobin molecule is unable to give up the oxygen to the tissues (Profound anemia, Carbon oxide poisoning, Methemoglobinemia).

3. Risk factors [3]

- Immunocompromised
- Severe malnutrition
- Diabetes mellitus
- Chronic liver or renal disease
- Heart disease.

4. Physiopathology [3]

Shock results from an acute failure of circulatory function. Inadequate amounts of nutrients, especially oxygen, are delivered to body tissues and there is inadequate removal of tissue waste products. A series of compensatory mechanisms are activated to cope with the initial shock state which results in clinical manifestations. Untreated, shock states can rapidly deteriorate into failure of multiple organ systems and eventually irreversible shock. Recognition of pre-shock states is important so early goal-directed therapy can be

instituted. Shock is a progressive state which can be divided into three phases: compensated, uncompensated and irreversible.

a. **Compensated shock:** normal systolic blood pressure, tachycardia, decreased tissue perfusion (initially, prolonged capillary refill advancing to decreased pulses, cool skin, and decreased urine output as shock progresses)
b. **Uncompensated shock (Hypotensive shock):** decreased systolic blood pressure, narrow blood pressure, worsening tachycardia and tissue perfusion, evidence of inadequate end-organ perfusion (oliguria and altered mental status)
c. **Irreversible shock:** without timely recognition and treatment, irreversible shock occurs and is marked by coma, acute kidney injury, liver failure, cardiovascular collapse, and death.

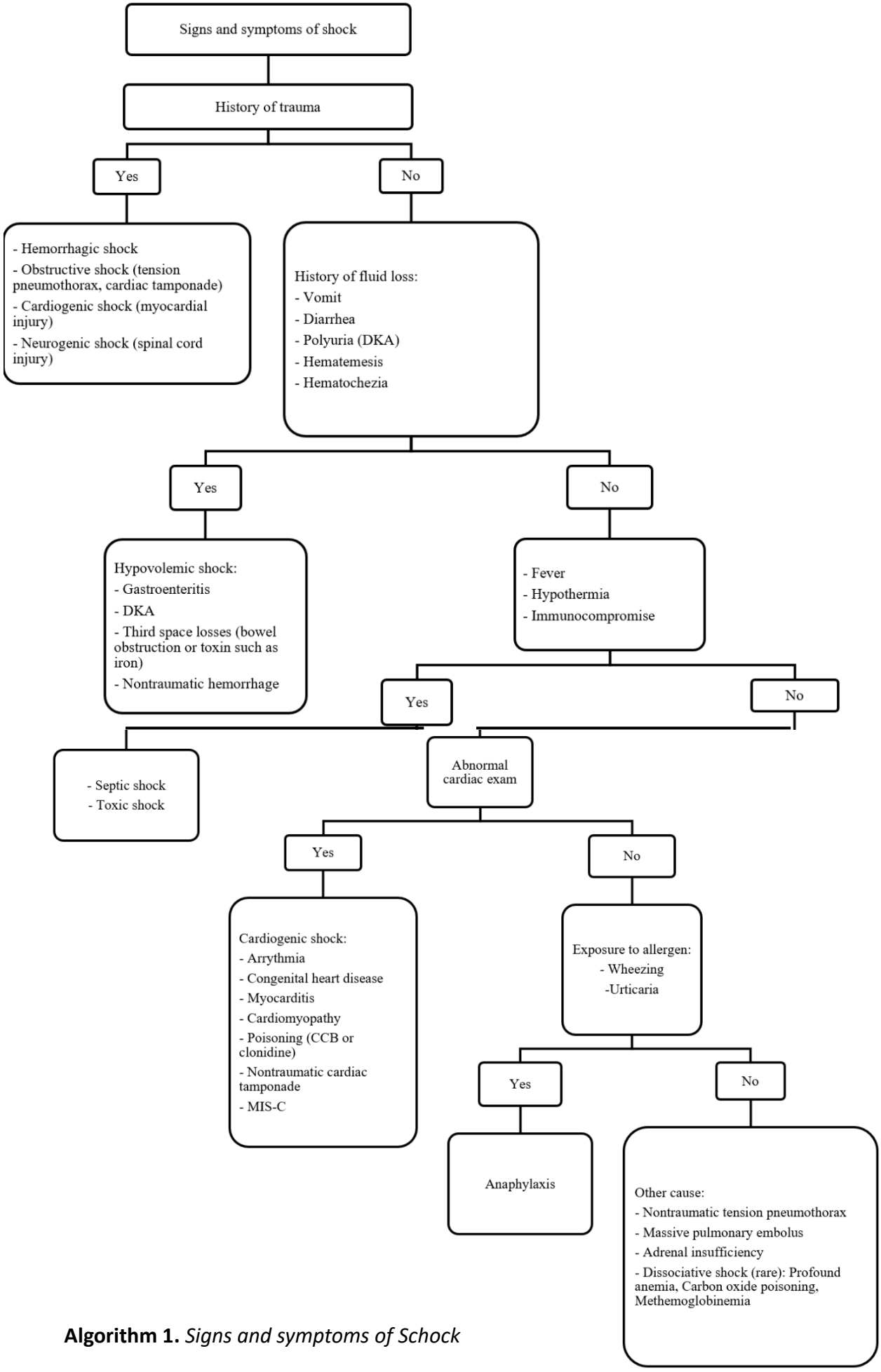
III. Signs and symptoms [5]

1. General signs of hypoperfusion

- General appearance: sick-looking, lethargy
- Altered mental status: agitation, confused or coma
- Cardiovascular: tachycardia, hypotension (Term neonates (0 to 28 days): <60 mmHg, Infants (1 to 12 months): <70 mmHg, Children (1 to 10 years): <70 mmHg + (child's age in years x 2), Children >10 years: <90 mmHg), weak peripheral pulse, cool extremities, CRT > 2 seconds, hepatomegaly, jugular venous distension, murmur, gallop
- Respiratory: tachypnea, crackled, wheezing, decreased air entry
- Skin: pallor, cyanosis, purpura, ecchymosis, infected wound or urticaria
- Decreased urine (oliguria which is defines as a urine output < 1mL/kg/h in infant and < 0,5mL/kg/h in children) or no urine output.

2. Specific key features of the child in shock [3]

- Hypovolemic shock:
  - History of vomiting and/or diarrhea point to gastroenteritis, volvulus, intussusception, ruptured appendix …
  - Burn
  - Dengue hemorrhage fever (National guideline of Dengue fever),
  - Polyuria and the presence of acidotic breathing and a very high blood glucose points to diabetes ketoacidosis.
- Hemorrhagic shock: History of major trauma points to blood loss (solid organ injury from blunt abdominal trauma or pelvic fracture).
- Obstructive shock: Immediate history of major trauma points to tension pneumothorax, hemothorax, cardiac tamponade.
- Septic shock: Presence of fever, hypothermia and/or rash, or immune compromised
- Anaphylactic shock: Presence of urticaria, angioneurotic oedema or history of allergen exposure.
- Cardiogenic shock:
  - Cyanosis unresponsive to oxygen or a grey color with signs of heart failure in a baby under 4–6 weeks points to duct-dependent congenital heart disease. The presence of heart failure in an older infant or child points to cardiomyopathy or myocarditis,
  - Severe tachycardia and an abnormal rhythm on the ECG points to arrythmia,
  - Worsening clinical condition with fluid resuscitation are suggestive of cardiogenic shock.



Algorithm 1. *Signs and symptoms of Schock*

IV. Diagnosis

1. Investigation:

Table1. *Investigation*

Routine laboratory test:	- Complete blood count and blood film, Blood group and cross-match - Blood glucose level, Electrolytes, Ionized calcium - Blood urea nitrogen, Creatinine, Liver Function Test - Coagulation profile, Disseminated Intravascular Coagulation screen (Fibrinogen, D-dimer) - Arterial or venous blood gases, Serum lactate - Urinalysis
Hypovolemic shock	- Dengue NS1Ag, IgM or IgG in case of suspect of DHF - X-ray (Chest, Plain abdomen, limbs…) - Point-of-care Ultrasound - CT-scan
Septic shock	- C-reactive protein or Procalcitonin - Serum cortisol, - Cultures blood, urine, respiratory secretions, CSF - Chest X-ray, whole abdomen ultrasound
Anaphylactic shock	- IgE, Allergy test
Cardiogenic shock	- Chest X-ray, EKG, Heart Ultrasound

2. Differential diagnosis [6]

- Hypoglycemia
- Acute pancreatitis
- Acute kidney injury
- Adrenal crisis
- Acute respiratory distress syndrome
- Salicylate toxicity.

V. Complications

- Anoxic ischemic encephalopathy
- Renal failure
- Gastro-intestinal ulceration
- Multiorgan failure
- Disseminated intravascular clotting
- Brain death.

VI. Management

1. **Clinical and physiologic indicators** that should be targeted during therapy (with goals in parentheses) include: [7]
   - Blood pressure (systolic pressure at least 5th percentile for age: 60 mmHg <1 month of age, 70 mmHg + [2 x age in years] in children 1 month to 10 years of age, 90 mmHg in children 10 years of age or older)
   - Quality of central and peripheral pulses (strong, distal pulses equal to central pulses)
   - Skin perfusion (warm, with capillary refill <2 seconds)
   - Mental status (normal mental status)

- Urine output (≥1 mL/kg per hour once effective circulating volume is restored).

a. Airway [3]

- Airway opening maneuvers
- Airway adjuncts
- Urgent induction of anesthesia and intubation to secure the airway.
- For the shock due to blunt trauma, patients should have a rigid cervical collar in place and full spinal immobilization until a spinal fracture can be ruled out.

b. Breathing

- Adequate airway: administer 100% supplemental oxygen at a high flow rate via a face mask or, if respiratory distress is present, via high flow nasal cannula or noninvasive continuous positive airway pressure (CPAP).
- If the patient is in respiratory failure, consider intubating and providing mechanical ventilation.
- The goal is to maintain an oxygen saturation of 94 to 98%.

c. Circulation [3]

- Insert 2 widebore IV cannula, if possible, immediately proceed to IO access if peripheral venous access is difficult, perform blood work including microbiological cultures.
- Begins with boluses of up to 20 ml/kg crystalloid over 5–10 minutes, titrated to reversing hypotension, increasing urine output (>1 ml/kg/h), and attaining normal capillary refill, peripheral pulses and level of consciousness.
- Be cautious in those with primary cardiogenic shock and in those with signs of raised intracranial pressure (ICP): fluid bolus (5–10 ml/kg) to optimize preload.
- If more than 2-3 volumes of crystalloid have been infused into a patient at risk for hemorrhage (e.g. from trauma), administer blood or packed red blood cells (PRBCs).
- Intubation and ventilation should be sought in patients who have received more than 40 ml/kg fluid with signs of ongoing shock.

2. Emergency intervention in obstructive shock

- Tension pneumo- or hemothorax: Chest tube placement (needle thoracostomy may temporarily relieve tension pneumothorax)
- Cardiac tamponade: Pericardiocentesis
- Pulmonary embolus: Antithrombotic therapy and, in selected patients, thrombo-embolectomy

3. Hypovolemic shock

- Children with hypovolemic shock should receive 20 mL/kg per bolus of isotonic crystalloid, such as normal saline or Lactated Ringer solution, infused over 5 to 10 minutes and repeated, as needed, up to three times (total of 60 mL/kg) in patients without improvement and no signs of fluid overload (e.g. decreased oxygenation, crackles, gallop rhythm, and/or hepatomegaly).
- Additional therapies, transfusion of packed red blood cells should be infused in 10 mL/kg in patients with hypovolemic shock from hemorrhage, may be required depending upon the response to fluid administration.
- For children with hemorrhagic shock, the source of bleeding must be identified and controlled (external hemorrhage in children such as direct compression, use of vascular pressure points, hemostatic gauze, and tourniquets).
- During initial fluid therapy, abnormalities in blood glucose, electrolyte, and calcium measurements should be identified and treatment initiated.
- Refractory shock: In most children with hypovolemic shock, rapid improvement occurs with initial fluid administration. Children who have not improved after receiving a total of 60 mL/kg of isotonic fluid should be evaluated for other causes of shock (e.g. septic shock, heart failure from myocarditis, spinal cord injury).

- Vasoactive medications such as epinephrine or norepinephrine have no place in the treatment of isolated hypovolemic shock.

4. Management of anaphylaxis [8]

- The first and most important therapy in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis.
- Airway:
  - Immediate intubation if evidence of impending airway obstruction from angioedema.
  - Delay may lead to complete obstruction => Cricothyrotomy may be necessary.
- IM epinephrine (1 mg/mL preparation):
  - Epinephrine 0.01 mg/kg should be injected IM in the mid-outer thigh.
  - For large children (>50 kg), the maximum is 0.5 mg per dose.
  - If there is no response or the response is inadequate, the injection can be repeated in 5 to 15 minutes (or more frequently).
  - If Epinephrine is injected promptly IM, patients respond to 1, 2, or, at most, 3 injections.
  - If signs of poor perfusion are present or symptoms are not responding to Epinephrine injections, prepare IV Epinephrine for infusion, place patient in recumbent position and elevate lower extremities, normal saline rapid bolus 20 mL/kg. Re-evaluate and repeat fluid boluses (20 mL/kg), as needed.
- Albuterol: For bronchospasm resistant to IM epinephrine, give albuterol 2.5 mg inhaled via nebulizer.
- H1 antihistamine: Consider giving Diphenhydramine 1 mg/kg (maximum 50 mg IV, over 5 minutes) or Cetirizine (children aged 6 months to 5 years can receive 2.5 mg IV, those 6 to 11 years of age can receive 5 or 10 mg IV, over 2 minutes).
- H2 antihistamine: Consider giving Famotidine 0.25 mg/kg (maximum 20 mg) IV, over at least 2 minutes.
- Glucocorticoid – Consider giving Methylprednisolone 1 mg/kg (maximum 125 mg) IV.

5. Management of septic shock [3]

- Give a fluid bolus of crystalloids and reassess for signs of improvement.
- Ensure that an antibiotic has been given as soon as possible, preferably after doing a blood culture.
- A 3rd generation cephalosporin (cefotaxime or ceftriaxone), is usually used, but an anti-staphylococcal antibiotic (vancomycin or clindamycin) should be considered if there is possible toxic shock syndrome.
- There are some specific considerations:
  - Under 3 months old: add amoxicillin to cover Listeria.
  - Use cefotaxime (not ceftriaxone) in premature or jaundiced infants, in hypo-albuminemia and if calcium infusion is being used.
  - If hospital acquired or neutropenic, consider tazobactam.
  - If previous culture of resistant organism, give appropriate antibiotic (MRSA: add vancomycin; ESBL: meropenem).
  - If vascular access device has been used for more than 48 hours add vancomycin.
- Inotrope infusion: when a 3rd fluid bolus is required, start inotropes [9, 10]
  - Epinephrine or norepinephrine is recommended as a first-line vasoactive agent for fluid-refractory pediatric septic shock over dopamine.
  - Typically, epinephrine is the preferred inotrope for patients with sepsis-induced myocardial dysfunction, although dopamine may be substituted if epinephrine is not available.

- And norepinephrine is used in patients with signs of low systemic vascular resistance or vasodilation.
- If abnormal perfusion, poor myocardial contractility, or hypotension persist despite escalating doses of epinephrine, options include:
  - Systemic vascular resistance is normal or low – Addition of norepinephrine is suggested to provide additional vasoconstriction.
  - High systemic vascular resistance – If there is evidence of high systemic vascular resistance (either by clinical exam findings or direct hemodynamic measures), then dobutamine or milrinone is suggested because of their inotropic properties and afterload reduction.
- For persistent vasomotor dilation despite adequate fluid resuscitation, vasopressin if available, may also provide additional vasopressor effect through a none catecholamine pathway.
- For an epinephrine infusion, the initial starting dose is 0.05 to 0.1 mcg/kg/minute; titrate to response up to 1.5 mcg/kg/minute. We typically add a second vasopressor if patients have not responded to an epinephrine dose of 1.5 mcg/kg/minute [11].
- For a norepinephrine infusion, the initial dose starting dose is 0.05 to 0.1 mcg/kg/minute; titrate to desired effect up to 2 mcg/kg/minute [12].
- For dopamine infusion, the initial dose starting dose is 5 mcg/kg/minute; titrate to desired effect up to 20 mcg/kg/minute [13].
- For dobutamine infusion, the initial: 0.5 to 1 mcg/kg/minute; titrate gradually every few minutes until desired response achieved; usual range: 2 to 20 mcg/kg/minute. [14]
- For milrinone, start with 50 mcg/kg administered over 10 to 60 minutes then 0.25 to 0.75 mcg/kg/minute titrate to effect [13].
- For Vasopressin 0.17 to 8 milliunits/kg/minute (0.01 to 0.48 units/kg/hour) [15]
- Because of an increase in mortality with delay in time to inotrope use, it is now recommended that peripheral inotropes can be used whilst central access (or IO) is being attained.

- Hydrocortisone is given [9, 10, 16]
  - In patients at risk for absolute adrenal insufficiency due to purpura fulminans, recent or chronic treatment with corticosteroids, hypothalamic or pituitary abnormalities, or other causes of congenital or acquired adrenal insufficiency
  - When high doses of inotropes are needed or the shock state does not respond to inotrope therapy
  - Hydrocortisone 50 to 100 mg/m2 or 1 to 2 mg/kg (maximum 100mg) as an initial dose followed by 50 to 100 mg/m2 or 1 to 2 mg/kg (maximum 100 mg/day) either given continuously or divided and given every four to six hours.

6. Cardiogenic shock [3]

- Fluid should be administered slowly and in boluses of 5 to 10 mL/kg.
- Emergency treatment of duct-dependent congenital heart disease in newborn: IV infusion of Dinoprostone (PGE2), this will usually reopen and keep the arterial duct patent, which will help in stabilizing the patient before definitive surgical intervention.
  - Cyanotic well and non-acidotic: start at 10–15 ng/kg/min.
  - Acidotic or unwell with suspected duct-dependent lesion: start at 20 ng/kg/min.
  - If no response within first hour, increase to up to 50 nanograms/kg/min.

- Emergency treatment of cardiomyopathy or myocarditis:

    - In those presenting in shock and suspected to have myocarditis or cardiomyopathy, aggressive fluid resuscitation needs to be avoided and inotropes need to be used.
    - Adrenaline is usually the preferred inotrope and can be used both centrally and peripherally.
    - Dobutamine is the initial agent of choice in cardiogenic shock with low cardiac output and maintained blood pressure (starts at 5 to 20 mcg/kg/min) [17].
    - Consider a diuretic, if the child is not shocked, to offload the heart, such as IV furosemide 0.5–1 mg/kg.
    - Urgent cardiology advice should be sought
    - Consider early transfer to a pediatric cardiac center as these children can be extremely difficult to manage.
- If a tachyarrhythmia is identified as the cause of shock, up to three synchronous electric shocks at 1.0, 2.0 and 2.0 J/kg should be given.

7. Correct acidosis

- Adjust ventilation setting if respiratory acidosis
- Maintain arterial pH ≥ 7.25
- If pH is < 7.15 in decompensated shock and the ventilation is adequate, give IV Sodium Bicarbonate [17]
    - (Desired Bicarbonate - Measured Bicarbonate) x Weight(kg) x 0.6 (max: 1mEq/kg or 50 mEq per dose).
    - If acid base status is no available, IV or IO: 0.5 to 1 mEq/kg/dose over 5 to 15 minutes; maximum dose: 50 mEq/dose. [14]

8. Treat hypoglycemia and hypocalcemia

- Hypoglycemia [18]
    - Children with shock are at risk for hypoglycemia; rapid blood glucose should be measured as IV access is obtained.
    - If the bedside value is low (<70 mg/dL [3.89 mmol/L]) in symptomatic patients
    - Infants and children up to 12 years: 2.5 to 5 mL/kg of 10% dextrose solution (D10W), or 1 to 2 mL/kg of 25% dextrose (D25W).
    - Adolescents ≥12 years: 1 to 2 mL/kg of D25W
    - Maximum single dose is 25 g (10% dextrose: 100 mg/mL; 25% dextrose: 250 mg/mL.)
    - Moderately permissive hyperglycemia strategy target blood glucose 140 to 180 mg/dL (7.7 to 10 mmol/L).
- Hypocalcemia [16, 19]
    - Children with shock are at risk for hypocalcemia, serum ionized calcium should be measured as IV access is obtained.
    - For patients with a serum ionized calcium <1.1 mmol/L (4.8 mg/dL)
    - Calcium gluconate 10%, 50 mg/kg (0.5 mL/kg), maximum dose 2 g (20 mL) by slow IV or IO infusion over five minutes.

9. Treat disseminated intravascular coagulation [6, 20]

- Patients with septic shock frequently have disseminated intravascular coagulopathy that may warrant treatment. Thus, baseline measures of clotting status should be routinely obtained in children with septic shock.
- Platelets, fresh frozen plasma, and/or cryoprecipitate should be provided to patients with disseminated intravascular coagulopathy and significant bleeding.
- A reasonable guide for the judicious use of blood components in the setting of significant bleeding includes maintaining platelet counts >50,000 per mm^3 and fibrinogen concentration >100 mg/dL (1 mol/L).

- Fresh frozen plasma provides both procoagulant and anticoagulant proteins and is administered every 12 to 24 hours at a dose of 10 to 15 mL/kg per infusion.
- Cryoprecipitate has higher concentrations of factor VIII and fibrinogen and can be
- Cryoprecipitate has higher concentrations of factor VIII and fibrinogen and can be used to correct hypofibrinogenemia. It is administered every six hours as needed at a dose of 10 mL/kg per infusion.

VII. Monitoring

- All patients with shock should be admit in ICU.
- Upon admission, they should be on hourly monitor blood pressure, heart rate,
- saturation monitoring and strict input-output (I/O) charting.
- Urinary catheterization is needed to quantify output and for initial urine cultures.
- Arterial line should be inserted for invasive BP monitoring
- Central venous pressure can be trended via central venous access
- Nasogastric tube and empty stomach to decrease risk of aspiration
- Mixed venous saturations and serum lactate levels may be useful to gauge end
- organ oxygen deficit
- Serum cortisol levels should be taken before hydrocortisone treatment.

Initial shock management in children – *See Table 2*

❖ Abbreviation:

ICU: intensive care unit; HR: heart rate; BP: blood pressure; HFNC: high-flow oxygen by nasal cannula; NIV: noninvasive ventilation; IV: intravenous; IO: intraosseous; US: ultrasound; ECHO: echocardiography; PT: prothrombin time; INR: international normalized ratio; PTT partial thromboplastin time; ECG: electrocardiography; e-FAST: extended focused assessment with sonography for trauma.

❖ A trial of HFNC or NIV, such as continuous positive airway pressure ventilation or bi-level positive airway pressure ventilation, may avoid the need for endotracheal intubation in selected patients. Patients with hemodynamic instability should receive appropriate interventions to treat shock prior to or during intubation. Refer to UpToDate content on HFNC, NIV, and rapid sequence intubation in children.

❖ Ancillary studies are determined by patient presentation and suspected type or types of shock present. Other laboratory and ancillary studies may also be indicated based upon the suspected underlying condition that is causing shock.

❖ Fluid volume should be calculated based upon ideal body weight (e.g. 50th percentile for age).

❖ When performed by trained and experienced physicians, bedside ECHO can provide rapid evidence of myocardial dysfunction, including dysfunction due to obstructive shock.

❖ Patients with signs of fluid overload who continue to receive fluid boluses warrant close monitoring for respiratory and cardiac failure. The clinician should have a low threshold for endotracheal intubation and mechanical ventilation to treat pulmonary edema in these patients.

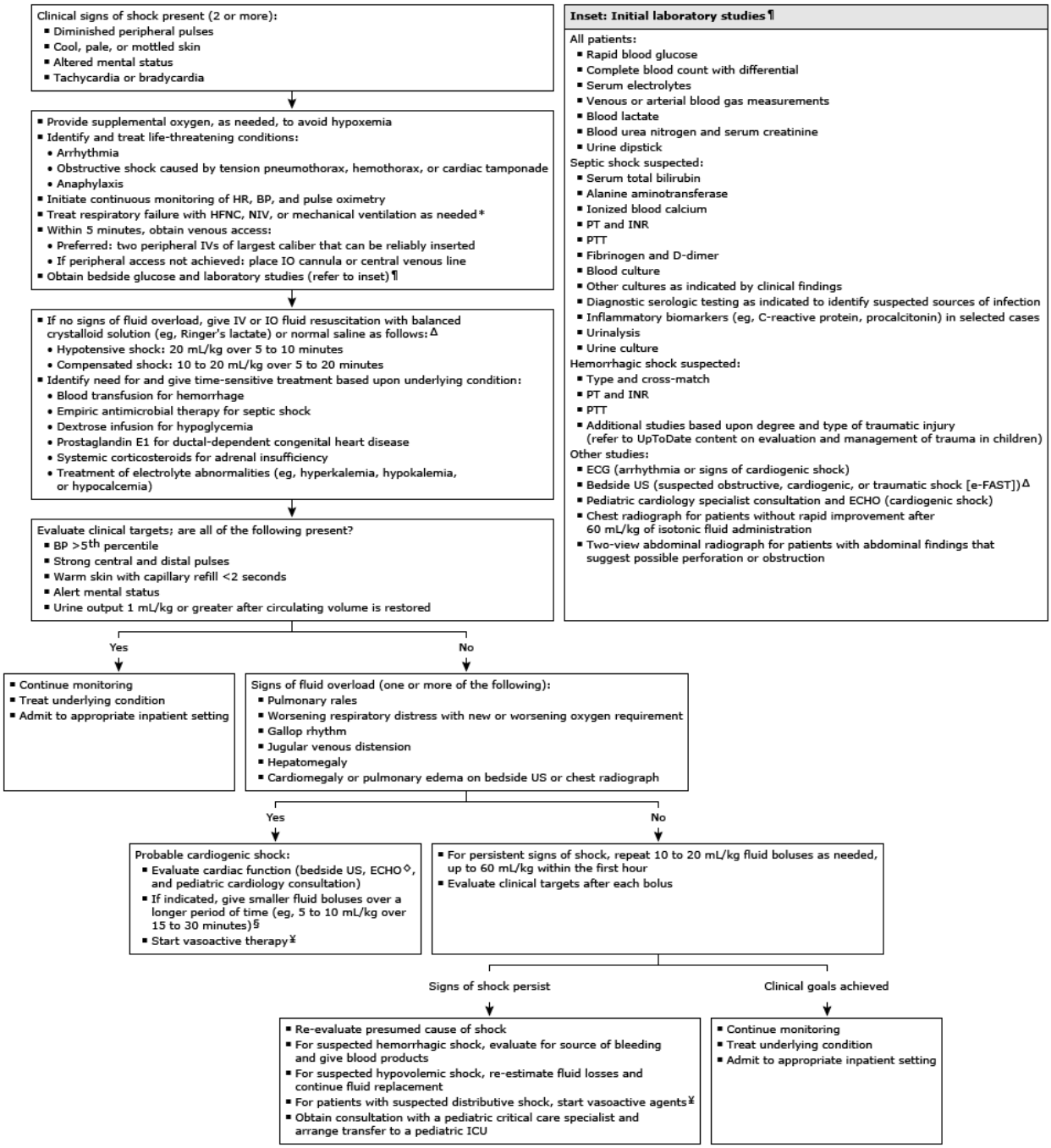
❖ Suggested vasoactive therapy depends upon type of shock and clinical findings; refer to UpToDate topics and graphics on management of shock in children.

Initial resuscitation of children with septic shock [9] – *See Table 3*

❖ ICU: intensive care unit; IV: intravenous; BP: blood pressure; ECHO: echocardiography. A clinical diagnosis of severe sepsis or septic shock is made in children who have signs of suspected or proven infection, inadequate tissue perfusion, and two or more age-based criteria for the systemic inflammatory response syndrome (SIRS). The SIRS is present when a child has an abnormality of temperature (fever or hypothermia) or age-specific abnormality of the white blood cell count and one of the following: tachycardia, bradycardia, respiratory distress, or pulmonary condition requiring mechanical

ventilation. Systematic screening is recommended to assist with early recognition. Refer to UpToDate content on signs and symptoms of SIRS and recognition of sepsis and septic shock.

Table 2. *Initial shock management in children*

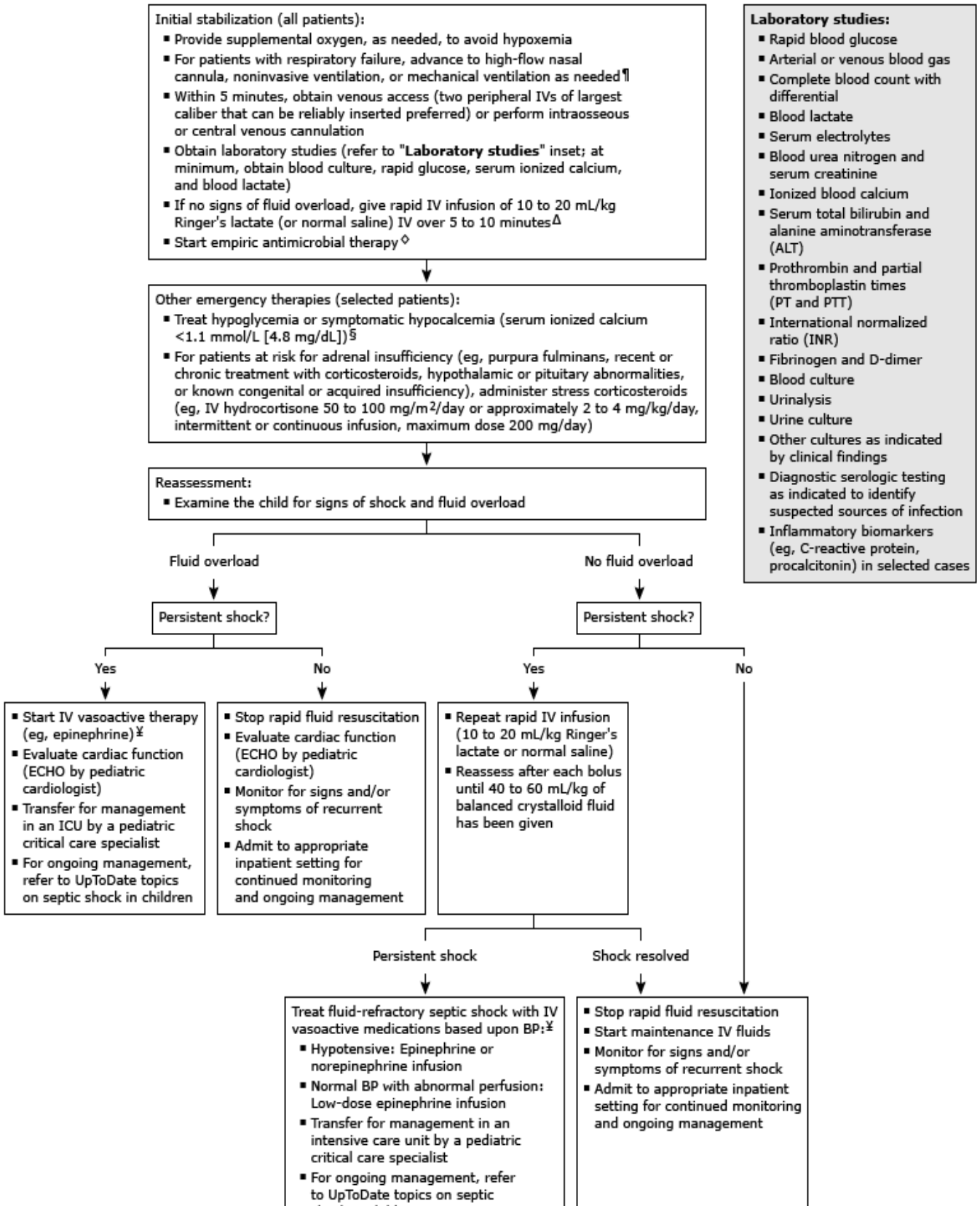


- A trial of noninvasive ventilation, such as continuous positive airway pressure ventilation or bi-level positive airway pressure ventilation, may avoid the need for endotracheal intubation in selected patients. Patients with hemodynamic instability should receive appropriate interventions to achieve hemodynamic stability prior to or during intubation. When performing rapid sequence intubation in children with septic shock, ketamine, if available and not contraindicated (i.e. patients younger than three months of age or with psychosis), is suggested for sedation. Etomidate is not recommended unless ketamine is not available or contraindicated. Infants younger than 3 months may receive IV fentanyl 1 to 2 mcg/kg slowly.
- Fluid volume should be calculated based upon ideal body weight (e.g. 50th percentile for age). If the patient develops signs of fluid overload (e.g. rales, worsening respiratory distress, new or worsening oxygen requirement, gallop rhythm, hepatomegaly, or has cardiomegaly or

pulmonary edema on chest radiograph), the fluid bolus should be omitted or reduced (e.g. 5 to 10 mL/kg given over 15 minutes).

- ❖ Consultation with an expert in pediatric infectious disease is strongly encouraged for all children with septic shock. Empiric antimicrobial treatment should consist of broad-spectrum antibiotics and, for susceptible patients, antifungal and antiviral agents. Refer to UpToDate topics on recognition and initial resuscitation of septic shock in children for specific regimens.
- ❖ For recommended dosing and administration of dextrose or calcium infusion, refer to UpToDate topics on hypoglycemia or hypocalcemia.
- ❖ For recommended dosing and administration of vasoactive infusions in children, refer to UpToDate topics on initial resuscitation of septic shock in children.

Table 3. *Initial resuscitation of children with septic shock*



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CHILDREN AND INFANT WITH SEIZURES

TEN Raksmey, CHEA Pao, KHUN Leangchhun, YAY Chantana

I. Key Facts [1]

- Seizures are a common occurrence in children.
- Seizures in children and infants can occur with or without fever.
- Febrile seizures are the most common seizure disorder and most common neurological disorder in childhood.
- Febrile seizures occur in children between six months and six years of age.
- Neonatal seizures occur in ~1.5% of neonates, febrile seizures in 2-4% of young children, epilepsy in up to 1% of children and adolescents.
- Population-based estimates suggest that every year 25,000–40,000 children in the United States experience a first unprovoked seizure.

II. Overview

1. Definition [6]

We should know the definition of the words related to 'Seizures': Convulsion, Epilepsy; Infant age, Children.

- Seizure is a paroxysmal involuntary disturbance of brain function that may manifest as impaired conscious level, abnormal motor activity, behavioral abnormalities, sensory disturbance, or autonomic dysfunction.
- Convulsion is a generalized seizure with increased tone and tonic-clonic movements of the body.
- Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate seizures.
- Infants: 1 month to 1 year
- Children: < 18 years old.

2. Etiology [5,6], divides in 2 categories:

a. Provoked:

- Fever: The most common cause of seizures in Children is a fever, also known as a febrile seizure
- Infection: Infection can cause seizures, especially in newborns and infants
- Head injury: Brain injuries can cause seizure including those sustained at birth.
- Blood sugar: High or Low blood sugar levels can cause seizures.
- Blood pressure: Very high blood pressure can cause seizure
- Medication: Some medications can cause seizures.
- Drugs: Illegal drugs like cocaine and amphetamines can cause seizures.

b. Unprovoked:

- Genetic conditions: Genetics conditions can cause seizures.
- Brain lesions: Lesion in the brain can cause seizures.
- Rasmussen syndrome: A rare condition that causes seizures and progressive neurologic deterioration.

3. Risk Factors [6]

- Seizure in Childhood: High fever
- Brain: Infection, Tumor
- Head injuries
- Age
- Family History
- Malformation of the brain (Include Blood vessels in the brain Stroke and other vascular disease.

4. **Physiopathology** [9]
   - It consists 4 keys points about pediatric seizure pathophysiology:
     - Excitatory/Inhibitory Imbalance: The most fundamental mechanism is disruption in the balance between excitatory neurotransmitters (like glutamate) and inhibitory neurotransmitters (like GABA), resulting in excessive neuronal excitation.
     - Hyperexcitability and Hypersynchrony: Neurons become hyperexcitable, meaning they are more prone to firing action potentials, and hypersynchronous, firing together in large groups, leading to the characteristic electrical discharges seen in seizures.
     - Brain development Factors: The developing brain in children is particularly susceptible to seizures due to ongoing maturation and potential vulnerabilities in neuronal networks.
     - Genetic predisposition: Many childhood epilepsy syndromes are linked to genetic mutation that affects ion channel function, neurotransmitter balance, or neuronal connectivity, increasing seizure susceptibility.
   - There are many types of seizures in children: [8]
     - Focal, meaning the seizure activity begins in the one part of the brain and may spread from there.
     - Generalized, meaning the seizure affects all part of the brain at once
     - Infantile spasms, a type of seizure that begins during the first year of life.
     - Status Epilepticus, which involve convulsion of more than five minute.
     - Febrile seizure, which occur within 24 hours of a fever for children six months and five years of age.

III. Signs and Symptoms [5,6]

Divide in to 2 types:

1. **Non-motor seizures:**
   - Change of consciousness (awareness) during the seizure, or between seizures
   - Becoming unresponsive
   - Staring into space
   - Become vague, disorientated or confused
   - Numbness or tingling sensation
   - Hallucinations (seeing, hearing or feeling things that are not there)
   - Problem with thinking.
2. **Motor seizures:**
   - Stiffening movements (Known as the 'Tonic' phase- this may cause a person to fall.
   - Jerking movements (Known as the 'Clonic' phase)
   - Switching between stiffening and jerking (known as 'tonico-clonic')
   - Floppiness and loss of muscle tone (known as 'Atonic') -this may also cause a person fall.
   - Tremor or shaking or strange posture
   - Sudden nod of the head
   - Repetitive movements, such as lip smacking or chewing.

IV. Diagnosis [5,6,7]

1. **Clinic evaluation:**
   - Seizure-onset, frequency, duration, progression,
   - Seizure-Description, Video evaluation, Type
   - Present illness-other symptom of disease
   - Past history-seizures
   - Development history
   - Family History

- General Physical Examination-all systems of body
- Neurological Examination -abnormal findings

2. **Laboratory**:
   - CBC, CRP
   - ICT malaria test (Immunochromatographic)
   - Serum Glucose
   - Electrolyte, Calcium and BUN(Metabolic)
   - CSF examination and microbiology
3. **Imaging**
   - X-Ray Chest (Infection)
   - Neuro-imaging: CT/MRI Brain
   - EEG (to find out Epilepsy)
4. **Differential diagnosis**:
   - Breath-holding spells
   - PNES (Psychological non epileptic Seizure, Pseudo-seizure)
   - Parasomnia (sleep disorder)
   - Syncope
   - Tics
   - Movement disorder
   - Gratification disorder.

V. Management

1. **Goals** of seizure Management: [7]
   - Rapid stabilization of cardio-respiratory function
   - Termination of clinical and electrical seizures activity
   - Treatment of Life-threatening precipitants
   - Recognition and minimization of adverse physiologic consequences.
2. **Seizures** at Hospital: [4]
   - Check ABC (Airway, Breathing, Circulation)
   - High flow O2
   - Attach monitoring
   - Check blood Glucose (<3mmol/l need Treatment)
   - Using Medication
3. **Medication** [6,7]

   a. 1st line Treatment: Benzodiazepine is recommended:
   - Diazepam: 0.05mg/kg (max 5mg) IV/IO, 0.3mg/kg(max10mg) IR
   - Lorazepam: 0.1mg/kg (max4mg) IV or IO
   - Midazolam: 0.1mg/kg (max5mg) IV/IM, 0.2mg/kg (max10mg) IN

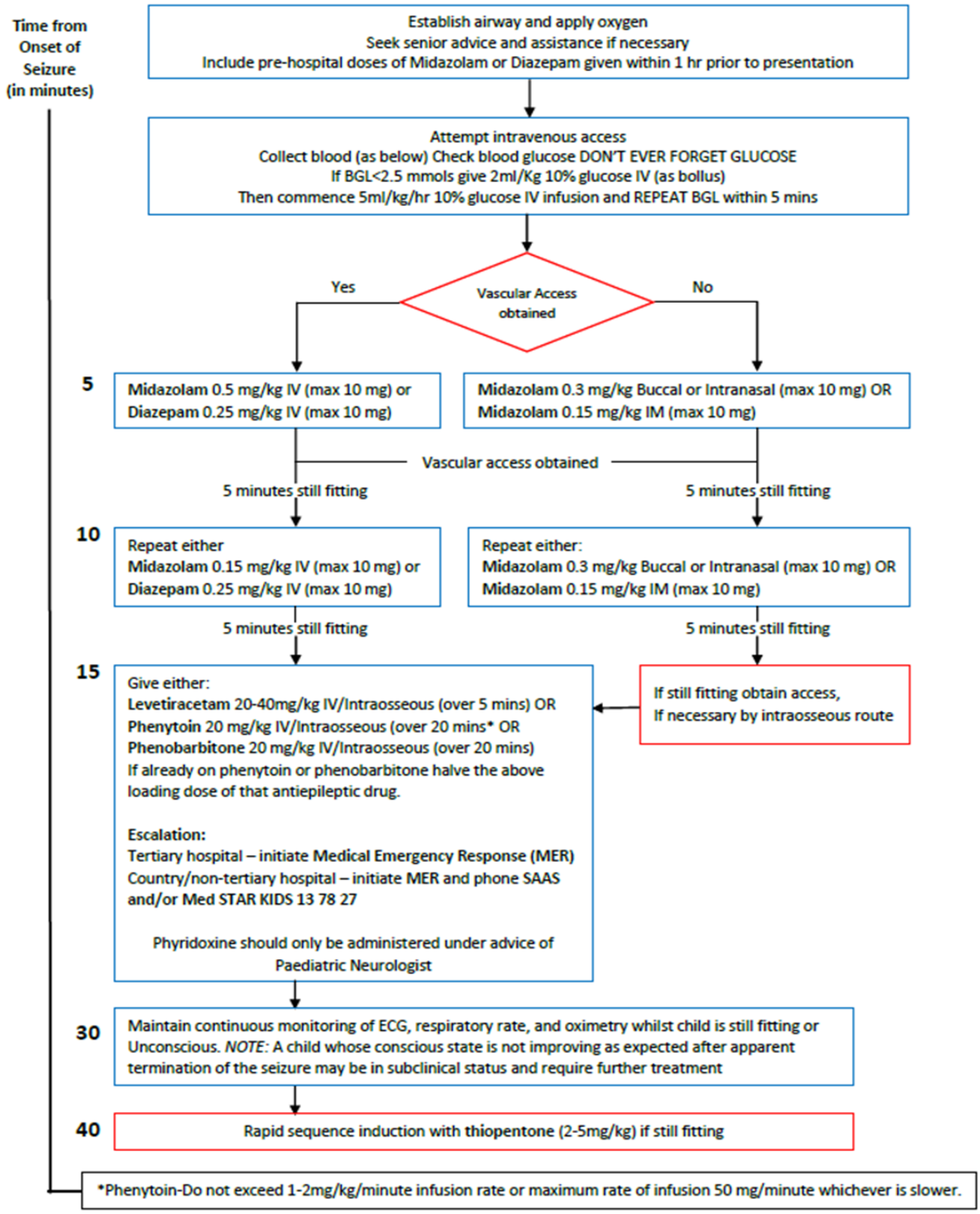
   b. 2nd line treatment:
   - Phenobarbital: 10-20mg/kg (max 40mg/kg) IV/PO
   - Fosphenytoin: 15-20 PE/kg (max 1gm) (IM/IV/IO)
   - Levetiracetam (Keppra): 10-20mg/kg (max 60mg/kg) IV/PO.

VI. Prevention and Education [7]

While having seizures at home: 10 first aids step:
- Stay calm
- Look around
- Note the time
- Stay with them
- Cushion their head
- Don’t hold them down
- Don’t put anything in their mouth

- Check the time again. If a convulsive, seizure doesn't stop after 5 minutes or they have another seizure without recovering fully from the first seizure (Status epilepticus)
- After the seizure has stopped, put them into the recovery position.
- Stay with them until they are fully recovered.

Acute hospital management of seizure algorithm: [10]



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COMA IN CHILDREN

CHREA Makara, CHEA Pao, KHUN Leangchhun, YAY Chantana

I. Key Facts

- Coma is an alteration of consciousness in which a person appears to be asleep, cannot be aroused, and shows no awareness of the environment. [1]
- It is representing and acute life-threatening, emergency, requiring prompt intervention for preservation of life and brain function.
- It most commonly appears in ICU department.
- GCS (Glasgow coma scale) is a state of prolonged unconsciousness; It's an important role to evaluation the level of coma and prognostic in acute phase.
- The severity of coma is depending on theirs causes: traumatic and non-traumatic.
- Traumatic and non-traumatic causes of coma have roughly equal annual incidences of approximately 30 per 100,000 children each. [4]
- Non-traumatic causes are more frequent in infancy and early childhood.

II. Overview

1. Definition

We need to know these terms:

- Consciousness is a combination of arousal which is wakefulness or alertness and awareness.
- Coma, a state of "unarousable unresponsiveness," is the most profound degree to which arousal and consciousness are impaired [1] or a condition in which a patient is in a state of deep unconsciousness and cannot be awakened, caused especially by severe injury or illness.
- Delirium is a disturbance of consciousness with reduced ability to focus, sustain, or shift attention or state of agitation characterized by irritability, disorientation, fearful responses and sensory misperception.
- Lethargy: lethargy, obtundation, and stupor refer to states in which arousal is partially impaired. Patients in these states have some difficulty maintaining attention during an examination, tend to fall asleep when not stimulated, and poorly to questions and commands.
- Brain death: death by neurologic criteria requires that a patient has suffered a catastrophic brain injury that results in a permanent loss of consciousness and of all brainstem reflexes. Brain death in children most commonly occurs as a result of trauma and anoxic encephalopathy. [5]

2. Etiology

- Coma can be categorized as:
  - Traumatic brain injury (TBI) and
  - Non-traumatic.
- Common non-traumatic causes of coma include. [2,3]
  - Infections: Meningitis, encephalitis, hypertension encephalopathy, sepsis.
  - Accidental and intentional poisonings and overdoses: paracetamol toxic, sedation drugs, Rey syndrome….

- Metabolic disorders: (e.g. Hypoglycemia, hypo/hypernatremia, diabetic ketoacidosis, inborn errors of metabolism.
- Seizures and epilepsy in children
- Near drowning: submersion injury
- Intracranial hemorrhage due to vascular malformation or tumors.
- Hypoxic-ischemic injury, which can result from any of the above mechanisms or from cardiopulmonary arrest. (e.g. arrhythmia, underlying congenital heart disease, foreign body aspiration, acute respiratory failure).

3. Risk factors

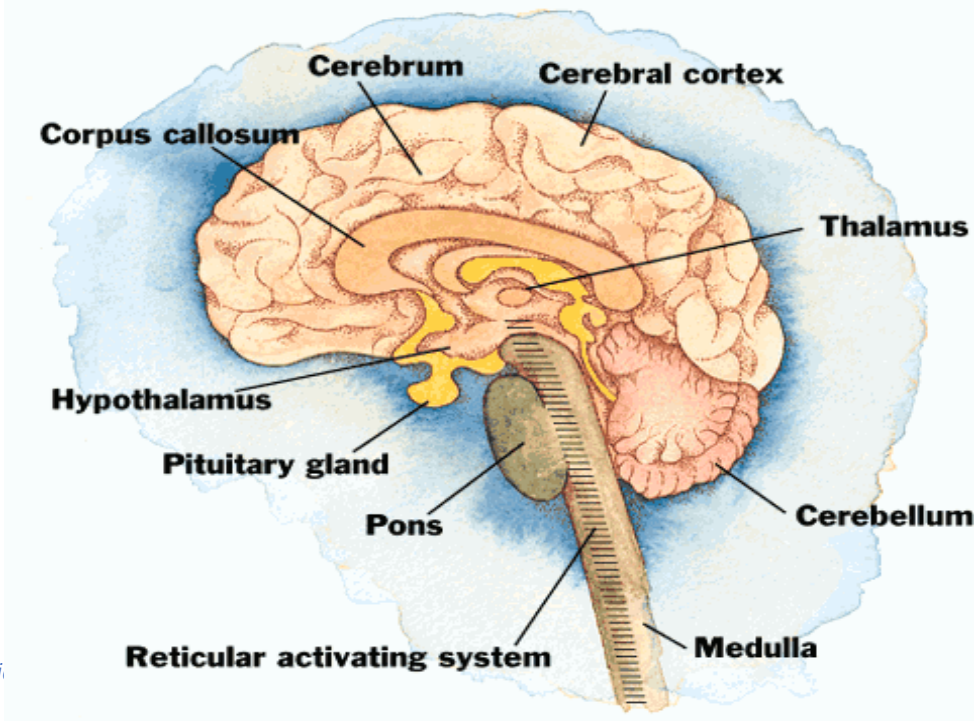
- A severe head injury
- Hemorrhage or ischemic
- Seizures
- Infection
- Brain tumors/infection or hypoxic for a long time.
- Metabolic abnormalities
- Liver failure or kidney failure.

4. Physiopathology

- Arousal depends on intact communication between the ascending reticular activating system (ARAS) and its targets in the hypothalamus, thalamus, and
- cerebral cortex.
- The ARAS is a loosely organized network of neurons within the brainstem whose major function is to modulate arousal in response to signals from the environment. Awareness is based on an even more widely distributed network of connections between cortical and subcortical structures.
- Two mechanisms in coma: [6]

a. A diffuse brain hypoxic: brain damage due to interruptions in perfusion to the brain. (e.g. Infection, toxics, metabolism, anoxic, epilepsy, profound hypotension or cardiac arrest).

b. Direct lesion: results from dysfunction of the ascending reticular activating system or in both cerebral hemispheres (ARAS). E.g. Brainstem lesion or intracranial hemorrhage.



III. Clinical Features

1. General and physical examination

a. Assessing vital signs and the ABCs (airway, breathing [ventilation and oxygenation], and circulation) are crucial for initial stabilization but may also provide clues about the underlying etiology:

- Temperature:
  - Fever suggests infection but is also seen with inflammatory disorders.
  - Hypothermia can occur with infection in infants but is more often due to drug intoxication, environmental exposure, or hypothyroidism.
- Heart rate:
  - Tachycardia can occur with fever, pain, hypovolemia, cardiomyopathy, tachyarrhythmia, and status epilepticus.
  - Bradycardia occurs with hypoxemia and hypothermia, and with increased ICP as part of the Cushing triad (bradycardia, hypertension, irregular respirations).
- Respiratory:
  - Tachypnea can be seen with pain, hypoxia, metabolic acidosis (kussmaul's breathing) or hyper ventilation.
  - Slow, irregular, or periodic respirations occur with sedative intoxication, and injury.
- Blood pressure:
  - Hypotension suggests hypovolemic, septic, or cardiogenic shock, intoxication, adrenal insufficiency or cerebral hypoperfusion and coma.
  - Hypertension may directly cause encephalopathy or due to pain, agitation, toxic, increased ICP.
- Skin: The skin appearance provides useful information
  - Mottling and delayed capillary refill suggest a shock state.
  - Bruising suggests traumatic injury including abusive head trauma.
  - Petechial and purpuric rashes may be suggestive of meningococcal infection.
  - Jaundice may suggest hepatic encephalopathy.
  - A cherry-red appearance is suggestive of carbon monoxide poisoning.

b. Neurologic examination (detail as below)

- Pupil responsivity
- ICP: Intracranial presser
- Brainstem reflexes: pupillary responses to light, extraocular movements, and corneal reflexes
- Motor responses
- Eye movements
- Level of consciousness: Glasgow Coma Scale
  - The pupillary examination is often abnormal in children who present with stupor and coma.
    - Anisocoria suggests a brainstem insult or a supratentorial lesion that is causing compression of the oculomotor nerve or nucleus within the brainstem.
    - Small, reactive pupils can be seen with metabolic disorders and certain intoxications.
    - Bilaterally fixed pupils that are either mid-position or dilated can be seen with severe afferent defects but are most often seen with brainstem insults that disrupt both the sympathetic and parasympathetic control of the eyes.
    - Sympathomimetic and anticholinergic drugs also cause dilated pupils.
  - Intra cranial pressure:
    - A history of preceding headache, double vision, or nausea suggests increased intracranial pressure (ICP) or
    - Cushing triad: bradycardia, hypertension, irregular respirations.
  - Brainstem reflexes:

- The corneal reflex tests also known as the blink reflex or eyelid reflex is an involuntary blinking of the eyelids elicited by stimulation of the cornea. absence of corneal reflex its mean prolongs deep coma or brain death.
- The gag reflex also known as the pharyngeal reflex, is an involuntary reflex involving bilateral pharyngeal muscle contraction and elevation of the soft palate. It is essential to evaluate the medullary brainstem, as it plays a role in declaring brain death.

- Motor responses:
  - Refers to the well-defined muscular reaction that occurs in response to a stimulus.
  - Decerebrate posturing includes extension and internal rotation of the arms and legs.
  - Decorticate posturing produces adduction and flexion at the elbows, wrists, and fingers, with leg extension and rotation.
  - Classically, decerebrate posturing implies brainstem involvement from a compressive or destructive process, while decorticate posturing implies a more rostral and potentially less dire insult.
- Eye movements: persistent conjugate eye deviation to one side may suggest injury to the ipsilateral cerebral hemisphere or ongoing seizure activity problem from the contralateral hemisphere.
  - Doll's eye reflex or Oculocephalic reflex: a test of brain function that is performed in comatose patients by elevating the head roughly 30 degrees and rapidly rotating the head from side to side with the eyes kept open. When comatose patients have possible cervical spine injury, this reflex should not be tested.
  - Caloric reflex or Oculovestibular reflex: ice cold water is used to irrigate the ear canal and should produce a slow conjugate deviation toward the irrigated side. An absent or asymmetric response indicates brainstem dysfunction.
- The Glasgow Coma Scale (GCS): refer to degree of level coma severity according to three categories of responsiveness: eye opening, motor, and verbal responses.
  The Glasgow Coma Scale (GCS) is scored between 3 and 15. (Total: 15/15)
  - Score ≤8 severe brain injury.
  - Score between 9 to 12: moderate injury.
  - Score ≥13 or higher: mild injury.

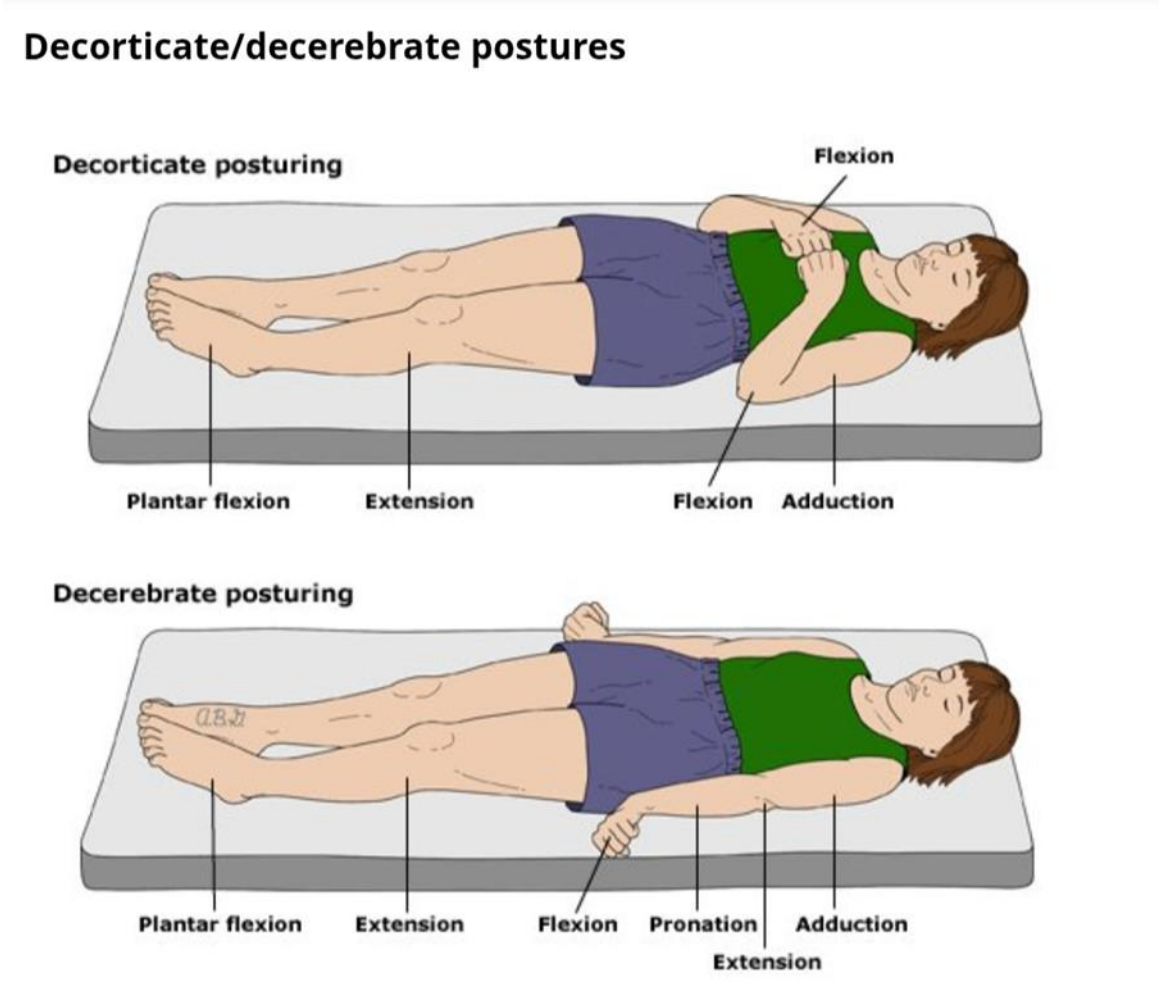
GLASGOW COMA SCALE

Activity	Score	Child/Adult	Score	Infant
Eye opening	4	Spontaneous	4	Spontaneous
	3	To speech	3	To speech/sound
	2	To pain	2	To painful stimuli
	1	None	1	None
Verbal	5	Oriented	5	Coos/babbles
	4	Confused	4	Irritable cry
	3	Inappropriate	3	Cries to pain
	2	Incomprehensible	2	Moans to pain
	1	None	1	None
Motor	6	Obeys commands	6	Normal spontaneous movement
	5	Localizes to pain	5	Withdraws to touch
	4	Withdraws to pain	4	Withdraws to pain
	3	Abnormal flexion	3	Abnormal flexion (decorticate)
	2	Abnormal extension	2	Abnormal extension (decerebrate)
	1	None	1	None (flaccid)

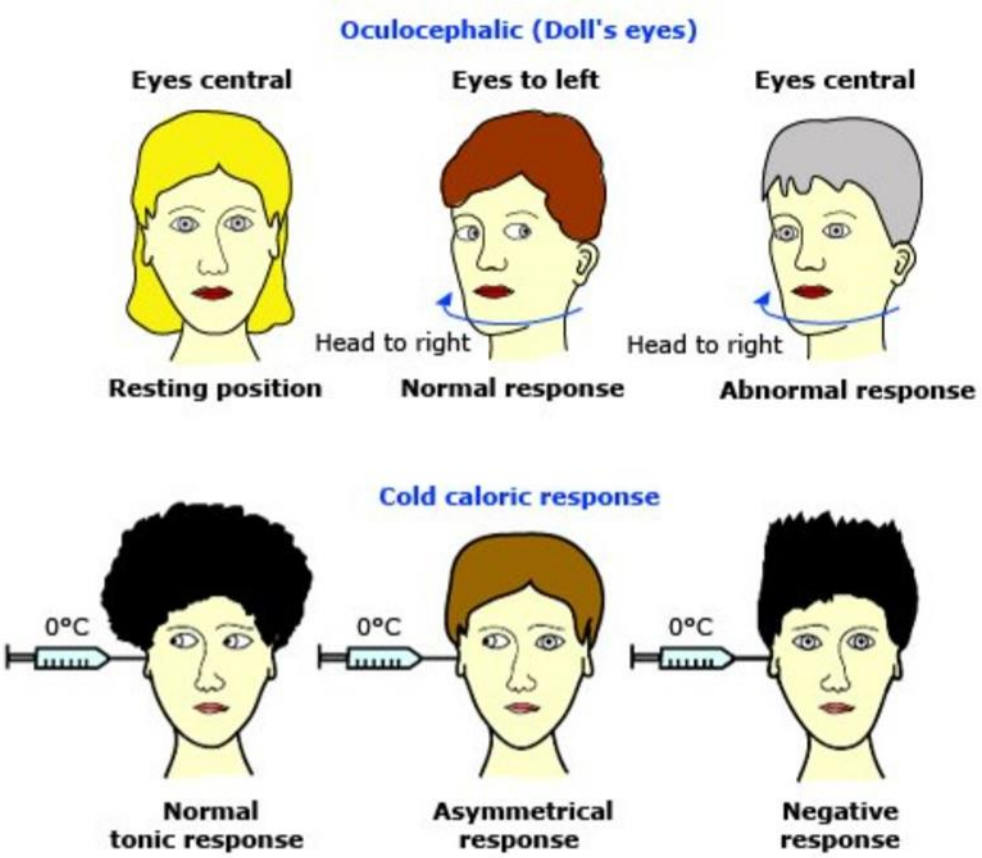
Adapted from Hunt EA, Nelson-McMillan K, McNamara L. The Johns Hopkins Children's Center Kids Kard, 2016.

2. Additional examination

- Fundoscopy
  - Papilledema suggests increased ICP of more than several hours duration.
  - Retinal hemorrhages are most commonly associated with abusive head trauma in infants. [9]
- Meningismus
  - Meningeal irritation or inflammation suggesting meningitis is demonstrated by passive resistance to neck flexion (nuchal rigidity), involuntary knee flexion with forced hip flexion (Kernig sign), or involuntary hip and knee flexion with forced neck flexion (Brudzinski sign). [10]



Oculocephalic and caloric response



- **Oculocephalic (doll's eyes) response:** This test should not be performed if a cervical spine injury is suspected. Observe the motion of the eyes while passively moving the head. In a comatose patient, conjugate movement of the eyes in the direction opposite to the head movement is expected. An absent or asymmetric response in an unconscious patient implies brainstem dysfunction.
- **Caloric response:** After visually checking that the tympanic membrane is intact, ice cold water is used to irrigate the ear canal and should produce a slow conjugate deviation toward the irrigated side. An absent or asymmetric response indicates brainstem dysfunction. Intact eye deviation with nystagmus suggests that the patient may not be in coma.

Adapted from: Bateman DE. Neurologic assessment of coma. J Neurol Neurosurg Psychiatry 2001; 71 Suppl 1:13.

IV. Diagnosis

1. History

- The etiology may be apparent from the history, such as when coma results from the expected progression or complication of a known illness or injury.
- Examples include a child who presents after a drowning injury or a child with diabetes presenting with hypoglycemic coma or with cerebral edema from diabetic ketoacidosis.
- The history of symptoms leading up to coma may also provide clues. Coma of abrupt and unexplained onset suggests intracranial hemorrhage, seizure, trauma, or intoxication. A gradual deterioration of mental status suggests an infectious process, metabolic abnormality, or slowly expanding intracranial mass lesion.
- A history of preceding headache, double vision, or nausea suggests increased intracranial pressure (ICP). Inborn errors of metabolism may also present with slowly evolving coma or recurrent episodic coma. [7]
- A history from the caregiver that is vague or inconsistent with the examination may engender suspicion for non-accidental trauma [8].

2. Laboratory testing

All patients presenting with altered consciousness should undergo a rapid bedside test for blood glucose and basic laboratory testing, including:

- serum electrolytes
- CBC (complete blood count)
- blood sugar
- renal function tests
- liver function tests
- arterial or venous blood gas
- blood and urine cultures or
- urine analysis
- screening blood and urine for drugs toxins.

3. Imaging

a. Computed tomography (CT):

- It is the best initial neuroimaging test for evaluating a child in unexplained coma.
- CT quickly detects pathology in need of immediate surgical intervention, including
- hydrocephalus, herniation, and mass lesions due to infection, neoplasia, hemorrhage, and edema.
- CT should be performed immediately when the examination suggests increased intracranial pressure (ICP, papilledema, bulging fontanelle in infants, or bradycardia with hypertension) or a trans tentorial herniation syndrome.

b. Magnetic resonance imaging (MRI)

- MRI provides greater structural detail and is more sensitive for early evidence of encephalitis, infarction, diffuse axonal injury from head injury, petechial hemorrhages, cerebral venous thrombosis, and demyelination.

- When initial testing (CT, laboratory studies) does not provide a definitive diagnosis, MRI can be helpful.
- MRI may also offer information regarding prognosis in patients with anoxic or traumatic coma.

c. Electroencephalogram: EEG should be performed in children with coma of unknown etiology.

d. Lumbar puncture (LP)

- Urgent evaluation of cerebrospinal fluid (CSF) is required when there is suspected
- infection of the central nervous system (CNS).
- Lumbar puncture procedure cannot do in cases:
  - Signs of impending herniation
  - Prolonged or focal seizures
  - Focal neurological signs
  - GCS < 13
  - Coagulation disorders
  - Localizes infection or
  - Rejection from family.

Table 5. ***Cerebrospinal fluid findings***

	Opening Pressure (cmH2O)	Glucose (mg/dL)	Protein (mg/dL)	White Blood Cell Count	Differential
Normal	5-20	>50 or 2/3 serum glucose	<50	<5	No differential
Bacterial	Elevated	<50	elevated	>500	Neutrophilic predominance
Viral	Normal	Normal	Normal or slightly elevated		Lymphocytic predominance
Fungal or tuberculosis	Elevated	Normal or low	Elevated	<1000	Lymphocytic predominance
Autoimmune	Normal	Normal	Elevated	<500	Lymphocytic predominance

4. Differential diagnosis

Conditions mistaken for coma:

a. Locked-in syndrome:

- Complete paralysis.
- Patients with acute lesions of the brainstem, particularly the pons, may be unable to move or speak while retaining awareness.
- Other causes of severe motor paralysis (e.g. Guillain-Barré syndrome, botulism) may also cause a similar condition.

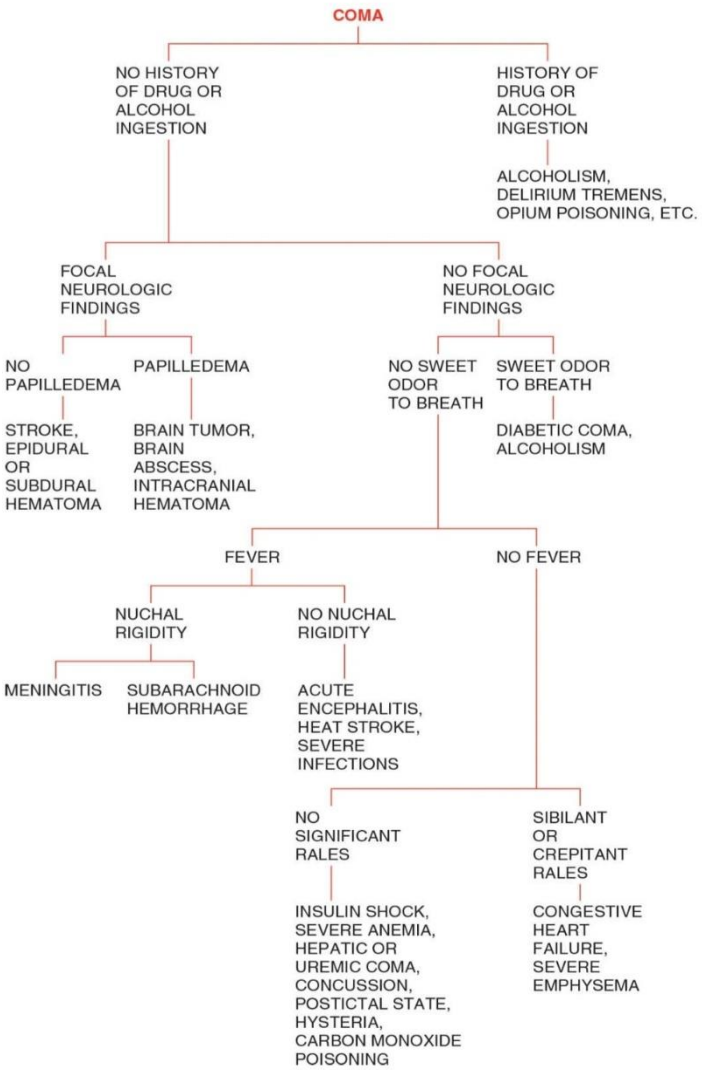
b. Akinetic mutism:

- Or abulia may be produced by lesions in the portions of the frontal lobes responsible for initiating movement.
- The patient retains awareness and often tracks movements with the eyes but rarely initiates other movements or obeys commands. Tone, reflexes, and postural reflexes usually remain intact.

c. Catatonia: Is a group of symptoms that usually involve a lack of movement, communication and also can include agitation, confusion and restlessness.

d. Delirium/Lethargy or brain death (see the definition in overview).

Algorithmic diagnosis of symptoms and signs of Coma



V. Complications and prognosis

1. Possible complications

- Bedsores
- Urinary tract infection
- Psychological: anxiety, depression
- Blood clots in legs and other problem may develop.
- Encephalopathy or sever cerebral palsy.

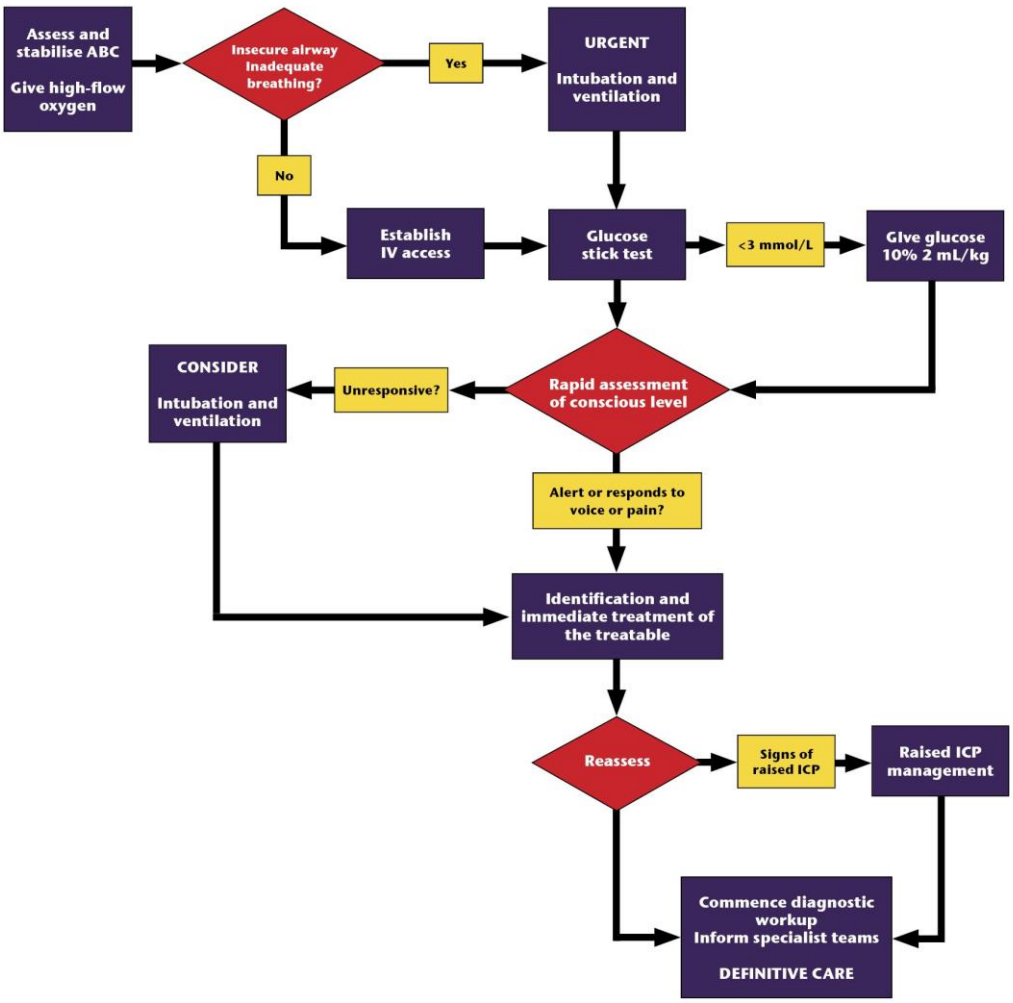
2. Prognosis

- Outlook for recovery comas can last from days to weeks while come severe cases have lasted several years.
- Recovery from coma depends on causes, duration and depth of coma.
- For children presenting with stupor or coma due to poisoning or overdose (accidental or intentional) not complicated by secondary anoxic brain injury, the prognosis is generally good. With appropriate supportive care, most children make a full recovery.
- For children with acute hypoxic-ischemic injury (e.g. following cardiac arrest or drowning), outcomes are generally poor.
- Coma from traumatic brain injury far better than those with coma from other structural causes.

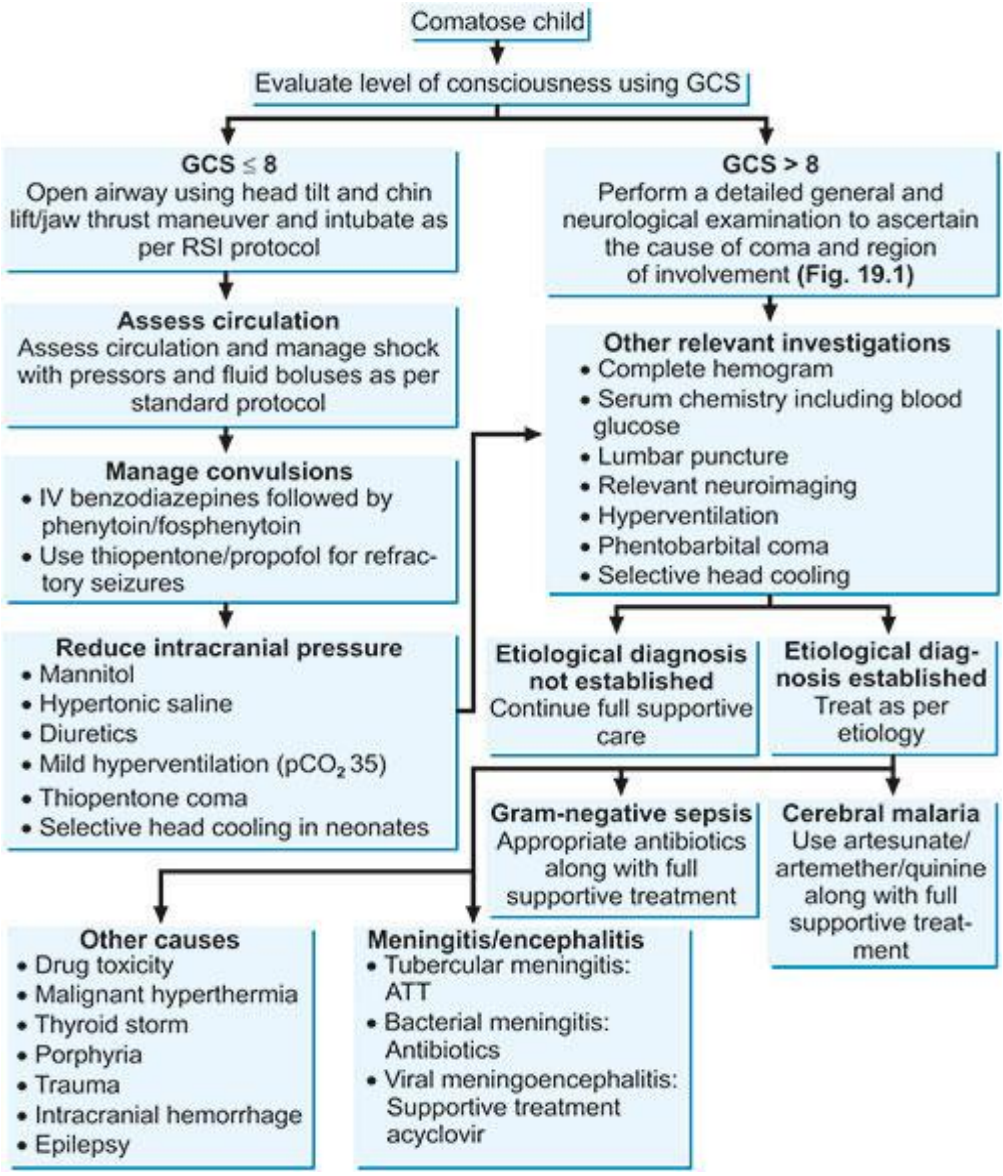
VI. Treatment

Early treatment of coma is generally supportive until a definitive diagnosis is made.
An important goal of early treatment is to limit brain injury.

1. **Rapid assessment and initial stabilization:** knowing the right approach can save lives
   - ABC VS CAB:
     - ABC (Airway, Breathing, Circulation):
       - A: clear the airway
       - B: check if the person is breathing
       - C: ensure circulation (pulse)
     - CAB (Circulation, Airway, Breathing)
       - C: start chest compressions
       - A: open the airways
       - B: give breaths
     - CAB: is the preferred method for CPR focusing on fast compressions to keep the blood flowing!
   - Intubate if GCS ≤8 or respiratory failure
   - Stabilize cervical spine
   - Supplement O2
   - IV access
   - Hypotension: fluid vs vasopressors
   - Check blood as to find sever hypoventilation
   - Check glucose level, hematocrit.
2. **Focused clinical evaluation to assess depth of coma,** See the figurations as detail in below.



Algorithms: Decreased conscious level from APLS Australia.
(APLS: Advance Pediatric life support)



- About Mannitol (Osmotic agent) is not safe in pediatric especially with fluid, electrolyte imbalances and can damage to renal failure.
- RSI: Rapid Sequence Intubation.

3. Emergency management of causes and complications

- Glucose: hypoglycemia may result in seizures coma and brain damage so should be treated immediately with 2.5ml/kg of 10 % dextrose solution.
- To reduced Intracranial pressure:
  - Position: elevation of the head from 15-30 degrees.
  - Rapid treatment of hypoxia, hypo ventilation, and hypotension.
  - May need intubation/mechanical ventilation.
  - Anti-seizure medication: seizures frequently occur in children with elevated ICP and require emergency treatment.
  - Pain control: (paracetamol: 15mg/kg/dose q6h, or morphine 0,1mg-0,3mg/kg/dose
  - Sedation and muscle relaxation
  - Hypertonic saline:

        - Initial IV bolus of 5 mL/kg of 3% saline. This dose may be repeated, hourly, as needed until the serum sodium reaches 160 mEq/L.
        - Continuous infusion of 3% saline at rates of 0.5 to 1.5 mL/kg/h adjusted for maintain ICP <20 mmHg may also be used after the ICP is controlled by hypertonic saline boluses. [11]
    - Drain placement or operation if need.
    - Mannitol and Steroid is not recommended in traumatic brain injury but
    - In case spinal cord injury: high dose methylprednisolone (30mg/kg/ IV bolus then infusion of 5.4mg/kg/h for 23h) should be within 8h of onset injury. [12]
- Infection:
    - Empiric antibiotic and antiviral therapy is recommended.
    - If bacterial meningitis (e.g. ceftriaxone 100 mg/kg per day in one or two divided doses, maximum dose 4 g per day, sometime need vancomycin 60 mg/kg per day in four divided doses).
    - Viral encephalitis: acyclovir 30 to 60 mg/kg per day in three divided doses (very severe with herpes simplex virus.
    - Blood cultures and lumbar puncture (LP) should be obtained, prior to starting antibiotics if possible.
    - Antimicrobial therapy should be continued until infectious conditions have been excluded.
- Seizure:
    - Ongoing seizures (status epilepticus) are treated as an emergency.
    - If have available:
        - Phenobarbital 5-20 mg/kg/day (po).
        - Diazepam: 0.5 mg/kg/dose (IR); 0.3 mg/kg/dose IV.
        - Midazolam: 0.1- 0.3 mg/kg/dose IV
        - Ketamine: 1-3 mg/kg/dose IV
        - Sometime need neuro muscular blockers but risk myopathy. (e.g. Vecuronium)
- Acid-base and electrolytes imbalance:
    - Electrolyte imbalance and acidosis may cause or be a complication of coma and may increase the risk of neurologic injury.
    - Intervention is generally not necessary to correct mild to moderate hypernatremia in the management of children with severe traumatic or hypoxic-ischemic brain injury.
    - Hypernatremia commonly occurs in patients treated with hypertonic saline for management of intracranial hypertension; moderate hypernatremia is a goal of therapy in this setting.
- Antidotes:
    - Antidote use is recommended only in the setting of known or strongly suspected drug overdose.
    - Examples: Naloxone in case morphine overdose or acetylcysteine with acetaminophen overdose while flumazenil is an effective antidote for benzodiazepine overdose, such overdoses alone are rarely life-threatening and may be managed with supportive airway measures.
        - Naloxone: 0.01 mg/kg IV, IM or S/C, can repeated if necessary.
        - Acetylcysteine: loading dose 140 mg/kg PO then use maintenance dose
        - 70 mg/kg PO every 4h for total of 17 doses. (repeat if emesis occurs).
        - Flumazenil: 0,01 mg/kg IV may repeat if need.
- Agitation: sedative agents should be administered because agitation may increase ICP, interfere with respiratory support, work of breathing during patient needs mechanical ventilation and increase the risk of injury.
- Temperature control:

- Fever should be treated aggressively with antipyretics and/or cooling blankets.
- Hyperthermia (>38.5°C) can contribute to brain damage in cases of ischemia.
- This can cause worsening intracranial hypertension in patients with elevated ICP and further contribute to secondary brain injury following acute traumatic or anoxic brain injury.

- Tumors, intracranial hemorrhage: operation as soon as possible.

VII. Prevention and education

- Anti-H2 or IPP (Proton pump inhibitors) to prevent gastritis.
- Nutrition support in patients with coma or severe cerebral palsy; sometime need PEG tube feeding. (PE.G.Percutaneous Endoscopic Gastrostomy).
- Chang positions every 6h to prevent bedsore.
- Infection control for health care providers with coma in children is a role important to escape from nosocomial infection. (Most commonly are urine tube, gastric tube, aspiration, IV lines, breathing machines or direct contact).
- Educational psychologists support for patients and their families.

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PEDIATRIC ACUTE RESPIRATORY DISTRESS SYNDROME

PREAP Mengmarady, LEAN Kimsreng, KIM Ang

I. Key Facts

Pediatric ARDS (PARDS) is diagnosed by the presence of hypoxia and new chest infiltration occurring within seven days of a known insult.

The incidence of ARDS is certainly lower in the pediatric population as compared to adults. The incidence in the pediatric population is reported between 2.2 and 12.8 per 100,000 person-years. From the critical care perspective, ALI/ARDS accounts for 2.2% to 2.6% of pediatric intensive care unit (PICU) admissions, 8.3% of those receiving mechanical ventilation for more than 24 hours, and PICU and hospital mortality ranging between 18% and 32.8%.

II. Overview

1. Definition: [1, 3]

- Age: Perinatal lung diseases are excluded.
- Onset: Within 7 days of pulmonary or no pulmonary insult.
- Origin of pulmonary edema: it should be noncardiogenic pulmonary edema and not fully explainable by fluid overload.
- Chest imaging: Showing new-onset unilateral or bilateral pulmonary opacities excluding atelectasis or effusion. The opacities are representative of acute parenchymal lung disease.
- Definition of hypoxemia: oxygenation index (OI) = (FiO2 x mean airway pressure x 100)/PaO2 or oxygenation saturation index (OSI) = (FiO2 x mean airway pressure x 100)/saturated oxygen (SpO2) to quantify the degree of hypoxemia and to determine the severity of ARDS in patients with invasive mechanical ventilation. A PaO2/FiO2 ratio of ≤300 or a SpO2/FiO2 ratio of ≤264 is used to diagnose PARDS for patients with non-invasive, full-face mask ventilation with a minimum continuous positive airway pressure of 5 cm H2O. A recent paper compared the OI and PaO2/FiO2 scores in evaluating PARDS requiring mechanical ventilation and found significant differences between the two scores in the severity grading of patients with PARDS. Both scores were consistent in designating patients with severe PARDS but the OI score was more accurate when combined with the prognostic factors.
- Special populations: Patients with cyanotic heart disease, chronic lung disease and left ventricular dysfunction are also included if the acute deterioration and new infiltrates are not explained by the underlying diseases.

2. Physiopathology:

This course of ARDS pathophysiology was previously described in 3 histopathologic stages, including exudative, proliferative, and fibrotic phases. The timing of these stages is variable, and in fact, evidence suggests the beginning of resolution and fibrotic phase early in the course of ARDS.

At the clinical level, respiratory distress occurs secondary to surfactant depletion, alveolar edema, cellular debris within the alveoli, and increased airway resistance.

The net effect is impairment in oxygenation. A widened interstitial space between the alveolus and the vascular endothelium decreases oxygen-diffusing capacity. Collapsed alveoli result in either low ventilation-perfusion (V/Q) units or a right-to-left pulmonary shunt.

3. **Etiology:**

ARDS occurs as a consequence of diverse pulmonary and no pulmonary etiologies.
The most common conditions associated with ARDS are sepsis and infectious pneumonia (bacterial and viral).
Other more common etiologies include bronchiolitis, aspiration pneumonia, aspiration of gastric contents, major trauma, pulmonary contusion, burns, inhalational injury, massive transfusions, or transfusion-related acute lung injury.
Other causes include acute pancreatitis, fat embolism, envenomation, drowning or submersion injuries, drug reaction, malignancy, and lung transplantation.

III. Diagnosis

1. **Physical examination** [1]

The onset of ARDS can be as rapid as a few hours, but it can have a gradual onset with evolution of clinical features over 1 to 5 days. The evolution of clinical signs depends on the type, acuity, and severity of the initial insult.
As lungs undergo changes during the first exudative stage of the disease, tachypnea is typically noted as the initial physical finding.
Respiratory distress, agitation, and hypoxemia could be other initial clinical features at this stage. Crackles may be audible throughout the lung fields, signifying pulmonary edema coinciding with infiltration on chest radiographs. Concomitant fever may reflect the underlying process causing ARDS (e.g. pneumonia, sepsis) or may reflect massive cytokine release.
Although these are nonspecific features and can be seen with any other respiratory or even systemic illness.
Hypoxemia might be evident by high oxygen requirement, higher CPAP or PEEP, and elevated alveolar-arterial (A-a) oxygen gradient. A-a gradient can be calculated from the equation below for sea level, assuming 100% humidification at the alveolar level.

2. **Chest** r**adiography** may be useful beyond its use as part of the diagnostic criteria
3. **Computed tomography (CT) of the chest,** although not routinely performed, may be helpful in differentiating between atelectasis and consolidation.
4. **Ultrasonography** is an easy method of further assessing pleural effusions and differentiating between transudative and exudative fluid.
5. **Echocardiography** may help exclude cardiogenic edema and would provide information regarding cardiac contractility, intraventricular volume, pulmonary hypertension, and other potential anatomic abnormalities.
6. **Oxygenation Assessment:**

The degree of hypoxemia is evaluated using the PaO2/FiO2 ratio.

- Mild ARDS: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg
- Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg
- Severe ARDS: PaO2/FiO2 ≤ 100 mmHg

There are no specific guidelines for other laboratory workup.

IV. Management

The main management goals are anchored around treating the underlying cause, maintaining adequate oxygenation as well as avoiding secondary lung injury and extra pulmonary complications. [1,2,4]
The management of PARDS is challenging as there is no definitive guideline or conclusive clinical evidence to optimize the treatment regimen.

- Noninvasive ventilation
- Conventional mechanical ventilation (CMV)

- High-frequency oscillatory ventilation (HFOV)
- Prone positioning
- Use of neuromuscular blocking agents (NMB)
- Surfactant Therapy
- Nitric Oxide Therapy
- Liquid Ventilation
- Extracorporeal Life Support
- Steroid Therapy
- Diet and Activity
- Fluid management.

V. Complications

Complications of ARDS may include barotrauma (volutrauma), nosocomial infection, atelectasis, pulmonary embolism, pulmonary fibrosis and ventilator-associated pneumonia.
Dysfunction of other organ systems may also be observed, including right ventricular dysfunction, pulmonary hypertension, gastrointestinal complications (stress ulcer and bacterial translocation), hypoxic brain damage, deep vein thrombosis, myocardial dysfunction, acute kidney failure, fluid retention, catabolic malnutrition and electrolyte abnormalities.

VI. Prognosis

The overall prognosis of ARDS is poor, with high relative mortality rates of approximately 40%.
Long-term sequalae in ARDS survivors include prolonged pulmonary dysfunction, neuromuscular weakness, nutritional deficits, anxiety, depression and post-traumatic stress disorders.

VII. Prevention

All children with chronic lung disease should receive:

- influenza vaccines
- pneumococcal vaccines
- (RSV) specific vaccines as indicated.

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DROWNING

SOK La, HENG lainghuoy; KHUN Leangchhun; YAY Chantana; IV Malene

I. Key Facts

- Drowning remains a significant worldwide public health concern, ranking as the third leading cause of unintentional injury death and accounting for 7% of all injury-related death. It is major cause of disability and death, particularly in children. At least one third of survivor sustain moderate-to-severe neurologic sequelae. [1]
- Drowning usually occurs silently and rapidly, but it is due to hypoxia, which can damage multiple organs, particularly the brain. Thus, the greatest priority in the resuscitation process is to address and correct hypoxia quickly. [2]
- Initial assessment should include ensuring adequate airway patency, breathing, circulation and consciousness (the ABCs), check if there are any injuries, especially after diving or accidental fall. Facial, head and cervical spine injury are common. [3]

II. Overview

1. Definition [4]

- Drowning: The process of experiencing respiratory impairment from submersion or immersion in liquid.
- Fatal drowning: A drowning event with a fatal outcome.
- Non-fatal drowning: A drowning event in which the process of respiratory impairment is stopped before death, and the victim survives. The World Health Organization has proposed a framework to further classify non-fatal drowning based on the severity of respiratory impairment immediately after the drowning process has stopped.
    - Mild impairment: Breathing, involuntary distressed coughing and fully alert
    - Moderate impairment: Difficulty breathing and/or disoriented but conscious
    - Severe impairment: Not breathing and/or unconscious

2. Causes:

The most common causes of drowning include [5]

- An inability to swim
- Panic in the water
- Leaving children unattended near bodies of water
- Leaving babies unattended, even for a short period of time, in bath tube
- Concussion, seizure, or heart attack while in water
- Falling through thin ice
- Alcohol consumption while swimming or on a boat
- Suicide attempt.

3. Risk factors for drowning include [9]

- Head trauma
- Seizure
- Cardiac arrhinia
- Hypoglycemia
- Alcohol and drug use
- Suicide
- Panic attack

- Myocardial infarction
- Depression
- Poor judgment
- Scuba diving
- Natural disaster.

4. **Physiopathology** [5,6], See Figure 1.

The processes of the drowning, When the victim suffers from submersion or immersion in liquid, victim's airway lies below the liquid's surface, an involuntary period of laryngospasm is triggered by the presence of liquid in the oropharynx. The period of laryngospasm, these victims do not aspirate any appreciable fluid, previously referred to as "dry drowning" (approximately 10-15% of individuals maintain tight laryngospasm until cardiac arrest occurs and inspiratory efforts have ceased). They can no longer hold their initial breath in air, causing oxygen depletion and carbon dioxide retention. As the oxygen tension in blood drops further, laryngospasm releases, and the victim gasps, hyperventilates, possibly aspirating variable amounts of liquid in to the lung “wet drowning”. This leads to further hypoxemia.

When a person suffers from submersion or immersion in a liquid medium, vital tissues may become hypoxic and acidotic which may result in cardiac dysrhythmias (progressing from tachycardia, bradycardia, pulseless electrical activity, and asystole). Aspirated fluid can lead to surfactant washout and dysfunction, increased permeability of the alveolar-capillary membrane, decreased lung compliance, and ventilation/perfusion ratio mismatching. This can result from minor to no respiratory complaints to fulminant non-cardiogenic pulmonary edema, with a clinical picture similar to acute respiratory distress syndrome (ARDS).

Determination of the water that the victim was immersed is importance in non-fatal drowning. Volume or serum (electrolyte) changes only occur when a significant volume of fluid is aspirated (fluid aspiration of at least 11 mL/kg is required for alterations in blood volume to occur, and aspiration of more than 22 mL/kg is required before significant electrolyte changes develop, and ingestion of large volumes of freshwater to stomach is the likely cause of clinically significant electrolyte disturbances, such as hyponatremia). If the fluid was obviously contaminated (sewage), as those patients are highly prone to pulmonary infection (Pneumonia).

The two major sequelae of drowning are to the CNS and cardiac system. Within 2 minutes most victims lose consciousness and within 4-6 minutes will develop irreversible brain injury. Global CNS hypoperfusion induces releases of excitotoxic neurotransmitters, free radicals, and lipid peroxidation. Cerebral edema followed by autonomic instability often results followed by ST-segment changes, indicating stress-related myocardial damage. The hypoxemia also induces ventricular arrhythmias and severe pulmonary hypertension.

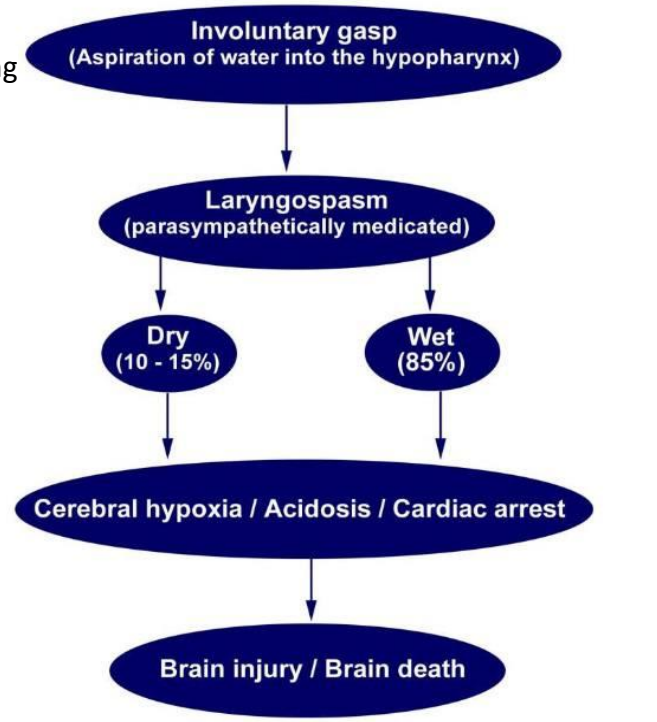
III. Signs and symptoms [7,8]

1. **History:**

- Mechanism and duration of submersion
- Type (e.g. saltwater, freshwater, sewage) and temperature of water
- Time of institution of CPR
- Time of first spontaneous breath
- Time to return of spontaneous of cardiac output
- Vomiting

- Likelihood of associated trauma, other precipitants (arrhythmia, myocardial infection, seizure, nonaccidental injury, ets.).
- All aspect of the drowning episode should be determined including the circumstances around the actual submersion.

Figure1.
Physiologic of drowning



Dry refers to drowning secondary to airway.
Wet refers to drowning secondary to aspiration as well as passive collection of fluid into the airway.

2. Physical examination:

The clinical presentation of people who experience submersion injuries vary widely. A drowning victim may be classified into 1 of the following 4 groups:

a. Asymptomatic:

b. Symptomatic:

- Altered vital signs (e.g. hypothermia, tachycardia or bradycardia)
- Anxious appearance
- Tachypnea, dyspnea, or hypoxia: If dyspnea occurs, no matter how slight, the patient is considered symptomatic
- Metabolic acidosis (may exist in asymptomatic patients as well)
- Altered level of consciousness, neurologic deficit
- Cough
- Wheezing
- Hypothermia
- Vomiting, diarrhea, or both

c. Cardiopulmonary arrest:

- Apnea
- Asystole (55%), ventricular tachycardia/fibrillation (29%), bradycardia (16%)
- Immersion syndrome

d. Obviously dead:

- Normothermia with asystole
- Apnea
- Rigor mortis
- Dependent lividity
- No apparent CNS function

IV. Diagnosis

1. Laboratory test [8]

- Obtain continuous pulse oximetry.
- Obtain arterial blood gas (ABG): analysis is probably the most reliable clinical parameter in patients who are asymptomatic or mildly symptomatic.
- Obtain blood for a rapid glucose determination
- Complete blood count (CBC)
- Electrolyte levels, lactate level, and coagulation profile, if indicated. Collect urine for urinalysis, if indicated. Measure liver enzymes.
- Consider a blood alcohol level and urine toxicology screen for use of drugs.
- Cardiac troponin I testing may be useful as a marker to predict children who have an elevated risk of not surviving to hospital discharge.
- Renal function test.

2. Imagery services and another test [4]

- Radiography: Chest radiography may detect evidence of aspiration, pulmonary edema, or segmental atelectasis suggesting the presence of foreign bodies (e.g. silt or sand aspiration). It may also be used for evaluation of endotracheal (ET) tube placement. Extremity, abdominal, or pelvic imaging may be used if clinically indicated.
- Computed tomography: is indicated in individuals with a history of possible cervical trauma or with neck pain or if doubt exists about the circumstances surrounding the submersion injury.
- Electrocardiography: should be performed in patients with significant tachycardia, bradycardia, or underlying cardiac disease. Consider ECG if the patient has arrhythmias or if arrhythmias are suspected.
- Catheter monitoring: arterial and central venous catheters may be useful in monitoring cardiac output and related hemodynamic parameters. Pulmonary artery catheters are less frequently used, yet may prove useful in patients with unstable cardiovascular status or in those who require multiple inotropic and vasoactive medication requirements.
- Intracranial pressure monitoring: is used in patients with traumatic brain injury or mass lesions (e.g. hematomas).
- Urinary catheterization for ongoing urine output measurement may be warranted.

V. Complications [8]

- Pulmonary: pulmonary edema, pneumonia, pneumatocele
- Cardiac: heart arrest, bradycardia, myocardial infarction
- Neurological: stroke, cerebral hypoxia, cerebral edema
- Renal: Renal failure
- Metabolic acidosis, hyperkaliemia

- Bowel mucosal necrosis (GI bleeding)
- DIC (dissemination intravascular coagulation)
- Liver failure
- Sepsis, septicemia.

VI. Treatment [8,9,10,11]

The children who are asymptomatic and alert require no investigation and consider discharge when:

- Observed 8 hours from the time of drowning
- Normal respiratory examination
- SpO2 ≥ 95%
- Education about water safety provide
- No ongoing safety concerns

Consider consultation with local pediatric team when:

- Increased respiratory effort
- SaO2<95%
- Abnormal lung examination
- Underlying medical condition

Consider transfer to emergency when:

- Persisting alteration conscience state
- Raspatory compromise requiring assister ventilation
- Ongoing hypoxia

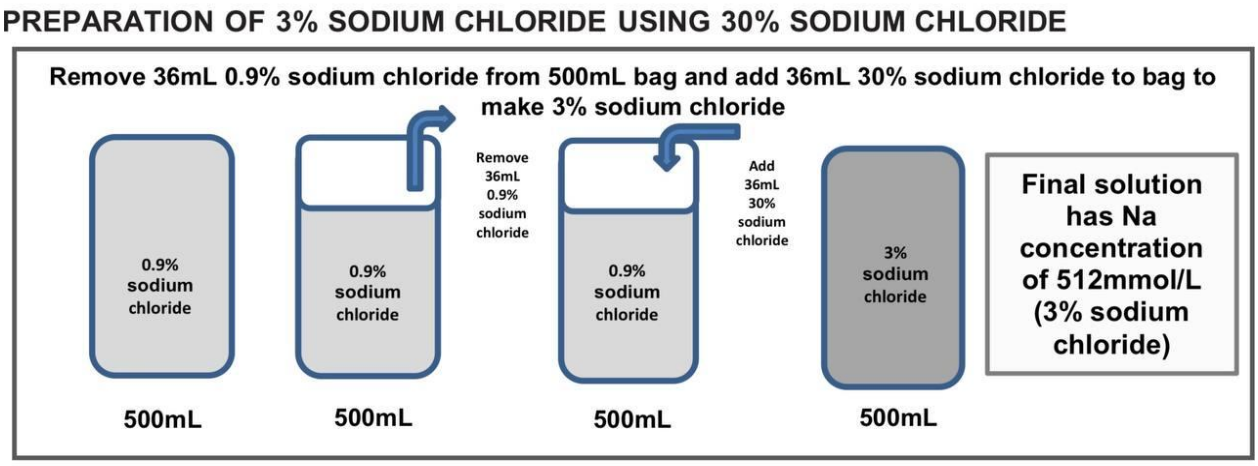
❖ *Emergency management:*

Key principles of management are maintaining adequate oxygenation, preventing aspiration and stabilizing body temperature.

- Start Basic Life Support at the scene (see basic life support CPG)
- Remember the cervical spine may be injury
- Initial resuscitation must be focussing rapid restoring oxygenation, ventilation, and adequate circulation. The air way should be clear of vomiting or foreign material.
- Spontaneously breathing children should initially be placed in the lateral decubitus position. Vomiting is common in drowning victims and aspiration of gastric contents is a major complication.
- Hypoxemia: if hypoxemia persists or signs of ventilation failure, the positive pressure NIV via CAPA (continuous position airway pressure) can improve oxygenation or decreases ventilation-perfusion mismatch. NIV has been used successfully to manage hypoxia but carefully monitored for hypotension and increases intrathoracic pressure.
- Hypothermia: Hypothermia is a common complication of drowning, remove wet clothes and dry child and forced air warming blankets (if core temperature < 34oC)
- Pneumonia: antibiotic should be reserved for the case of pulmonary infection (fever, leukocytosis, radiographic infiltration that develops two to three days after drowning)
- Coma: in a drowning patient who remains comatose, aspects of treatment include the following:
    - Avoid hypoxemia, hypercarbia, hypotension, pain, urinary retention, or agitation, as these can raise intracranial pressure or worsen cerebral oxygenation.
    - The head of the bed should be elevated to 30 degrees

- Reduce intracranial pressure: head of bed elevation, hyperventilation, administration of hypertonic saline 3% or intravenous 20% mannitol (1.5-2g/kg of a 20% solution as single dose infusion IV over 30-60mn).

Figure 2. *Preparation of hypertonic saline 3%*



- Prolonged hyperventilation should be avoided because it causes cerebral vasoconstriction, decreases cerebral blood flow, and worsens cerebral ischemia.
- Anticonvulsants for seizure activity, Sedation should be provided to reduce patient-ventilator desynchrony
- Avoid hyperthermia since it increases cerebral metabolic demand.
- Diuretics can be used to avoid hypervolemia and to treat elevated intracranial pressure.

- Hypotension: administer intravenous crystalloid, initiate a vasopressor (norepinephrine, dose initial 0.05-0.1mcg/kg/min IV infusion, maximum1-2mcg/kg/min) infusion If hypotension is refractory.
- Bronchospasm: Salbutamol inhalation 0.05-0.15mg/kg/dose of solution 2.5mg/2.5ml, Salbutamol IV initial dose 5mgg/kg for 5min follow by maintenance dose 0.1-0.3mcg/kg/min, Salbutamol oral 0.15mg/kg/dose 6 hourly. We use in case of dry drowning.

❖ Outcome: Duration of submersion is the most critical factor in determining outcome; the rate of death or severe neurologic injury is just 10 percent when submerged less than five minutes. The following factors at presentation have been associated with a poor prognosis (4):

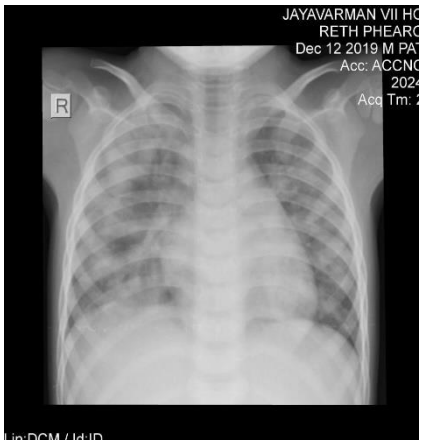
- Duration of submersion >5 minutes (most critical factor)
- Time to effective basic life support >10 minutes
- Resuscitation duration >25 minutes
- Age >14 years
- Glasgow coma scale <5
- Persistent apnea and requirement of cardiopulmonary resuscitation in the emergency department
- Arterial blood pH <7.1 upon presentation.

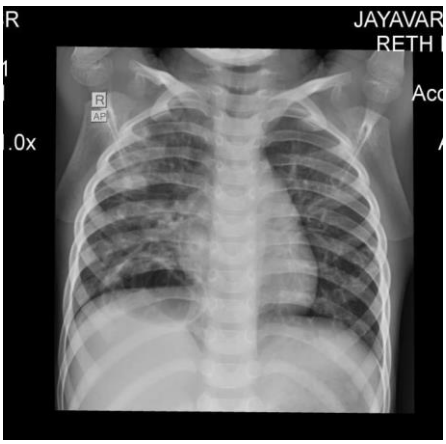
VII. Prevention and education [2]

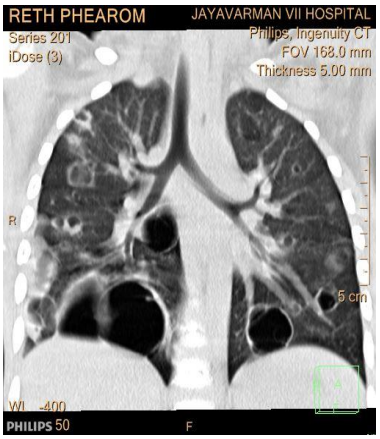
Drowning can happen to anyone any time there is access to water [CDC], we can prevent drowning:

- Learn basic swimming and water safety and water skills
- Build fences that fully enclose pools
- Supervise closely
- Wear a life jacket
- Learn CPR
- Know the risk of natural water
- Avoid alcohol
- Use the buddy system
- Take additional precautions for medical conditions, consider the effects of medication
- Don't hyperventilation or hold your breath for a long time.

Figure 3. *Case clinic of the patient pneumonia and septicemia by pseudomonas pseudomallei post drowning (pond)*



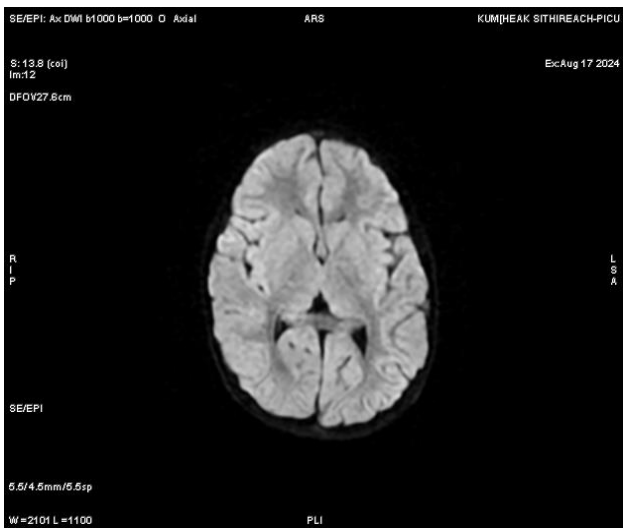


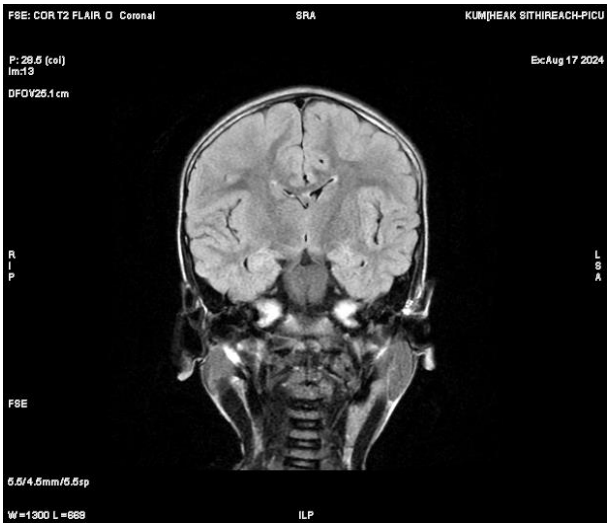


CxR at Day 4 post drowning: Pneumonia + septicemia by pseudomonas pseudomallei

CxR and CT lung at Day 25 post

Figure 4. *Case clinic of the patient brain edema post drowning*





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POISONING

OUK Chamrong, HINH Sally, EANG Habsreng

I. Key Facts

- Poisoning is a significant public health issue for children.[2]
- Commonly in children younger than six years of age and intentional ingestions and recreational drug use in older children and adolescents.[1]
- Each year in the United States, approximately 886,000 to 1 million poison exposures among children younger than six years of age are reported to the American Association of Poison Control Centers (AAPCC).[2]
- Approximately 121,000 to 134,000 exposures are reported for children 6 to 12 years and 166,000 to 177,000 exposures for teenagers 13 to 19 years.[2]
- According to the latest WHO data published in 2020 Poisonings Deaths in Cambodia reached 77 or 0.09% of total deaths. The age adjusted Death Rate is 0.50 per 100,000 of population ranks Cambodia #96 in the world.[3]

II. Overview

1. Definition

Poisoning is the harmful effect that occurs when a toxic substance is swallowed, is inhaled, or comes in contact with the skin, eyes, or mucous membranes, such as those of the mouth or nose.[4]

2. Types of exposes

- Ingestion
- Ocular (eyes) exposure
- Topical (skin) exposure
- Inhalation
- Envenomation (i.e. Snake bite)
- Transplacental.

III. Sign and symptoms

The clinical presentation of poisoning varies depending upon the ingested substance and can range from asymptomatic to critically ill.[1]

- Multiorgan system dysfunction
- Altered mental status
- Respiratory or cardiac compromise
- Unexplained metabolic acidosis
- Seizures
- Puzzling clinical picture.

1. Signs and Symptoms

sudden unexplained illness in the previous healthy child [5]

Signs and Symptoms		
Vital Signs	- Hypothermia - Hyperpyrexia - Bradypnea - Tachypnea - Bradycardia	- Tachycardia - Hypotension - Hypertension - Hypoxia
Neuromuscular	- Nervous system instability - Depression and excitation - Ataxia - Chvostek/trousseau signs - Drowsy or Coma - Delirium, psychosis	- Miosis - Mydriasis - Nystagmus - Paralysis - Seizures

Signs and Symptoms		
Cardiovascular	- Hypoperfusion - Cardiac arrhythmia - Wide QRS complex	
Electrolytes	- Anion gap metabolic acidosis - Electrolytes disturbances	- Hypoglycemia - Serum osmol gap
Skin	- Cyanosis unresponsive to oxygen	- Flushing - Jaundice
Odors	- Acetone - Alcohol - Bitter almond - Oil of wintergreen	- Hydrocarbons - Pear - Violets - Garlic
Radiology	- Small opacity on radiography	

2. Toxidromes [6]

Toxidromes	
Sympathomimetic	- Agitation - Diaphoresis - Fever - Mydriasis - Tachycardia
Cholinergic	- Defecation - Urination - Miosis, muscle fasciculations, muscle weakness - Bronchorrhea, bradycardia, bronchospasm - Emesis - Lacrimation - Salivation
Anticholinergic	- Blind as a bat—*Mydriasis* - Dry as a bone—*Dry skin* - Hot as a hade—*Fever* - Red as a beet—*Red* - Mad as a hatter—*Central nervous system simulation* - Decrease gastrointestinal mobility—*Decrease bowel sounds* - Urinary retention—*Full bladder*
Opioid	- Respiratory depression - Miosis - Coma - Bradycardia

IV. Diagnosis

1. History

Important Historical Questions Regarding a Possible Toxic Exposure [6]

- What was the substance?
- What was the specific name of the product?
- What was the formulation of the substance?
- How much of the substance was involved?
- How much does the child weigh?

a. Exposure history:

- Obtain history from witnesses and/or close contacts. Route, timing, and number of exposures, prior treatments or decontamination efforts.

b. Substance identification and quantity ingested:

- Attempt to identify exact name of substance(s) ingested, including: product name, active ingredients, possible contaminants, expiration date, concentration, and dose.
- Attempt to estimate the missing volume of liquid or the number of missing pills from a container. Poison control can assist with pill identification.

c. Environmental information: accessible items in the house or garage; open containers; spilled tablets; household members taking medications, visitors to the house, herbs, or other complementary medicines.

2. Laboratory investigation

Investigations are done for either specific purposes, to identify occult overdoses, or specific tests to determine the presence or level of a known ingesting.

a. Screening

- 12 lead Electrocardiogram (ECG)
  - Wide QRS (sodium channel blockade)
  - Long QT (potassium channel blockade, anti-psychotic overdose)
  - Heart blocks (calcium channel and beta blockers/calcium channel poisoning
- Serum Paracetamol level (4 hours)
- Blood glucose level (BGL).

b. Specific:

Drug levels if available: Paracetamol (in known ingestion), Iron, Alcohols, Lithium, Salicylate, Theophylline, Anti-epileptics…

c. Other adjunctive tests as indicated

- Blood gas:
  - High anion gap metabolic acidosis: Tricyclic antidepressants, Salicylates (late), Iron, Toxic alcohol, Metformin
  - Respiratory alkalosis: Salicylates
  - Respiratory acidosis: Sedatives.
- Abdominal X-ray: for confirmation of lithium, iron or other heavy metal ingestion (small opacity on radiography).
- Blood tests:
  - Liver Function Tests (delayed paracetamol)
  - Urea Electrolytes and Creatinine (UEC)
  - International Normalized Ratio (INR) (Warfarin, delayed paracetamol)
- Urine Toxicology Screens: (if available)
  - Basic screens include amphetamines, cocaine, opiates, phencyclidine (PCP), and tetrahydrocannabinol (THC).
  - Positive results are presumptive only; must be confirmed by gas chromatography /mass spectrometry.

3. Differential diagnosis

- Head injury
- CNS infection (meningitis, encephalitis...)
- Hypo or hyperthermia
- Ictal and post-ictal
- Metabolic Disorders
  - Hypo or hyperglycemia
  - Hyper or hyponatremia
  - Acute renal failure

V. Treatment

The general approach to all poisonings should follow the **RRSIDEAD** format:[7]
R Resuscitation, **R** Risk Assessment, **S** Supportive Care, **I** Investigations, **D** Decontamination **E** Enhanced Elimination, **A** Antidotes, **D** Disposition.
All so access flow chart below in **Figure.1**

1. Resuscitation

a. Initial Diagnosis and Treatment (ABCD) [8,9,10,11]
To the child suspected poisoning; the first step is prompt recognition and intervention in life- threatening condition follow to **APLS**, **PALS** and **ACLS**.

- Airway: Monitor and maintain an open airway at all times.
  - Is the airway open?
  - Can the airway be kept open manually?
  - Is an advanced airway required?
- Breathing: Look, Listen and feel.
  - Is breathing too fast or too slow?
  - Is there increased respiratory effort?
  - Is an advanced airway required?
- Circulation: Assess pulse, capillary refill time, BP, rhythm
  - Evaluate rhythm and pulse
  - Defibrillation/cardioversion
  - Obtain IV/IO access
  - Give rhythm-specific medications
  - Give IV/IO fluids if needed
- Disability: Neurologic assessments include the
  - AVPU (alert, voice, pain, unresponsive),
  - Glasgow Coma Scale (GCS), and
  - Posture and pupillary.

b. Secondary Diagnosis and Treatment
This includes a focused history and physical examination involving the individual, family, and any witnesses as relevant. Follow the **SPAM**

- **S**igns and Symptoms: Examine patient from head to toe with full neurological exam: Consciousness/delirium, Agitation, anxiety, depression, Fever, Breathing, Appetite, Nausea/vomiting, Diarrhea (bloody), Skin color (sweating, bulla or rashes).
- **P**ast medical history:
  - Complicated birth history
  - Hospitalizations
  - Surgeries
- **A**llergies
  - Any drug or environmental allergies
  - Any exposure to allergens or toxins
- **M**edications
  - What medications is the child taking (prescribed and OTC)?
  - Could child have taken any inappropriate medication or substance?

2. Risk assessment

The following **five factors** will provide an accurate prediction of clinical course, potential complications and time coarse of poisoning to direct management.

a. Agents
b. Dose
c. Time of ingestion: Use the latest possible time if uncertain
d. Patient factors:

- Weight
- Comorbidities that may affect prognosis:
  - Heart disease complicating calcium channel overdose
  - Morbid obesity affecting airway patency

e. Clinical *status* (features and progress)

- Agents commonly affect the autonomic, central nervous system (CNS) and neuromuscular systems and may produce a recognizable 'toxidrome'
- Does the clinical presentation of the patient fit with the predictable profile of the overdose?

3. Supportive care

Supportive care is tailored to the risk assessment and may involve:

- IV hydration
- Control of agitation and seizures with titrated benzodiazepines
- Ensuring normo-glycaemia
- Bladder care (especially monitoring for urinary retention).
- Keep normal temperature

4. Investigation (Review to Diagnostic and workup above)

5. Decontamination

a. Eye: Copious irrigation with saline. Instillation of local anesthetic eye drops and sedation may be required.[14]

b. Skin: Remove clothes, rinse with copious water, then soap and water.[14]

c. Gastrointestinal: Start with cautious. [1,5,7,12,13,14]

- Emesis has no role in the hospital setting
- Activated Charcoal has a very limited role in treatment, but if perform:
  - The Single dose is 1 g/kg, with a maximum dose of 100 g.
  - For adolescents or adult give: 50-100g.
  - Most effective when used within first hour after ingestion but can be given after first hour.
  - Should be given PO to an awake and alert patient. Nasogastric (NG) tube, if a patient is intubated due to risk of aspiration.
  - Substances not absorbed by charcoal: Iron, alcohols, lithium
  - Contraindications: Unprotected airway, caustic ingestion, disrupted gastrointestinal tract, concern for aspiration.
- Gastric Lavage has a very limited role in treatment and less benefit. If perform, it requires intubation for airway protection and should not be used without consultation. [1,7,14]
  - Use a 22 to 24F-gauge orogastric tube (36 to 40F in adult).
  - Position the patient on the left side with the head down 20 degrees.
  - Pass lubricated tube down the esophagus a distance equal to that be-
  - tween chin and xiphoid process.
  - Confirm tube position by insufflation of air.
  - Gently lavage with 10 mL/kg (200 mL in adult) of warm tap water.
  - Continue until returned fluid is clear.
  - Consider administration of activated charcoal via orogastric tube before removal.
- Whole Bowel Irrigation (WBI) has a limited role in treatment. [1,5,7,13,14]
  - Indicated for evacuation of substances not bound to activated Charcoal.
  - Use a polyethylene glycol electrolyte solution preparation to irrigate the bowel.
  - Recommended rates:
    - 9 months to 6 years (500 mL/hr.),
    - 6 to 12 years (1000 mL/hr.),

- more than 12 years (1500 to 2000 mL/hr).
- Often will need two NG tubes and pumps to maintain these rates.
- Infusion for 4 to 6 hours is usually required to achieve a clear effluent.

- Contraindications to the use of WBI include the presence of ileus, bowel obstruction, bowel perforation, hemodynamic instability, and unprotected airway.

6. Enhance elimination [1]

- Multiple-dose activated charcoal (MDAC): May be useful following specific ingestions, such as; salicylate, lithium, methanol, ethylene glycol, metformin-associated lactic acidosis, valproate, theophylline.
- Urinary alkalinization:
  - Intravenous (IV) bolus of 1 to 2 mEq/kg of 8.4% sodium bicarbonate followed by a continuous infusion made by diluting 150 mEq of sodium bicarbonate into one liter of 5% dextrose in water.
  - The goal is to achieve a urine pH >7.5 and serum pH no higher than 7.55 to 7.6.
- Isotonic fluid diuresis: This may enhance elimination of drugs that are predominantly eliminated unchanged by the kidney.
- Hemodialysis: This may be useful for patients with significant ingestion of alcohols, theophylline, lithium, salicylates.
- Hemoperfusion: This extracorporeal removal modality refers to the circulation of blood through an extracorporeal circuit containing an adsorbent such as activated charcoal or polystyrene resin.
- Hemofiltration: Continuous renal replacement therapy has lower clearance rates than conventional hemodialysis but may be used in the management of unstable patients.
- Exchange transfusion: This refers to the removal of a quantity of blood from a poisoned patient and its replacement with an identical quantity of whole blood.

7. Antidotes

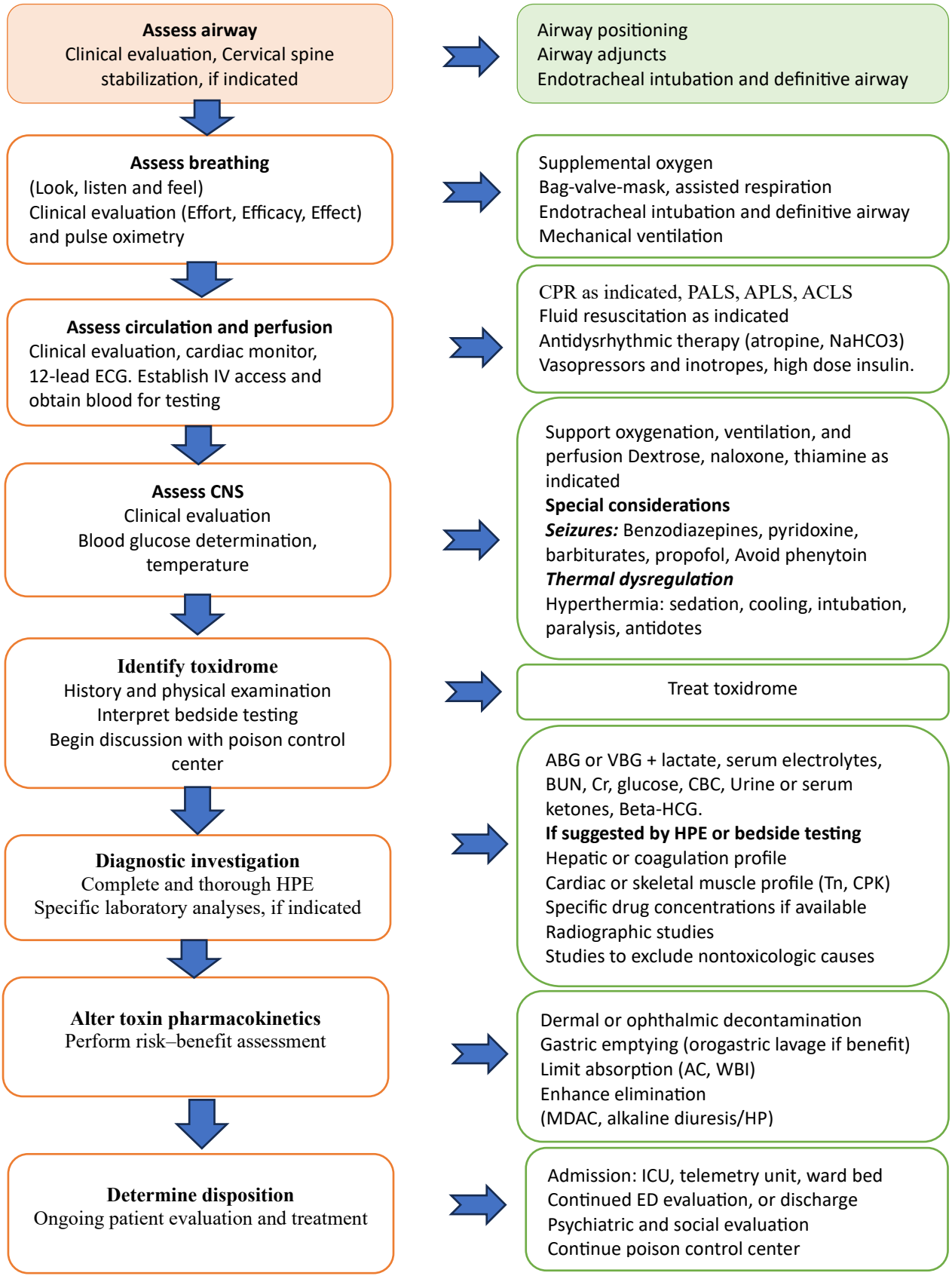
The risk assessment should determine if the potential benefit outweighs the possible adverse effects of the antidote.[15]

POISON	ANTIDOTE
Paracetamol	N-acetylcysteine
Opioids	Naloxone
Benzodiazepines	Flumazenil
Sodium channel blockers (Tricyclic Antidepressants…)	$NaHCO_3$
Iron	Desferroxamine
Glipizide	Octreotide
Digoxin	Digoxin fab-fragments (Digi-bind)
Organophosphates	Pralidoxime, atropine
Beta blockers, Ca^{2+} channel blockers	Insulin/dextrose euglycemic therapy

8. Disposition [7]

- The disposition will be determined by:
- The clinical risk assessment of the overdose
- The psychiatric safety of the patient (for deliberate overdoses)
- Other safety factors (parental neglect or drug use, domestic issues)
- Children should not be discharged home at night unless the risk assessment determines that the overdose is trivial and not requiring any form of observation.

Figure 1. *Principle of managing the acutely poisoned and overdosed patient* [18]



VI. Complications [11]

- Pulmonary aspiration
- Rhabdomyolysis
- Acute renal failure/ liver failure
- Compartment syndromes (snake, spider bite)
- Hypoxic brain injury.

VII. Specific poisoning

1. ACETAMINOPHENE [5,6,7,11]

a. *Major toxicity:* Hepatic damage and dysfunction.
Toxic dose: Acute ingestion more than 200mg/kg/dose in healthy children & 7-10g for healthy adult.

b. *Clinical Features:*

- Most patients who present within 24 hours of ingestion are asymptomatic.
- Occasionally they complain of nausea, vomiting, pallor and diaphoresis.
- Right upper quadrant tenderness may begin to develop subsequently.
- In untreated or undertreated cases, signs of hepatotoxicity and hepatic failure usually take 48–72 hours to develop and may include hypotension and encephalopathy.
- Signs of fulminant hepatic failure and coagulopathy can occur later than this.
- Most patients will initially present with no symptoms, or only mild gastrointestinal symptoms.
- Massive overdose is rare, but may cause coma and metabolic acidosis.

Four chronological phases are described in cases of significant acute overdose:

Under 24 hours	- Asymptomatic - Mild nausea and vomiting
Day 1 to 3 days	- Right upper quadrant tenderness - Hepatotoxicity
Day 3 to 4 days (severe cases)	- Fulminant hepatic failure and / or death - Acidosis - Renal failure
Day 4 to 2 weeks	- Recovery

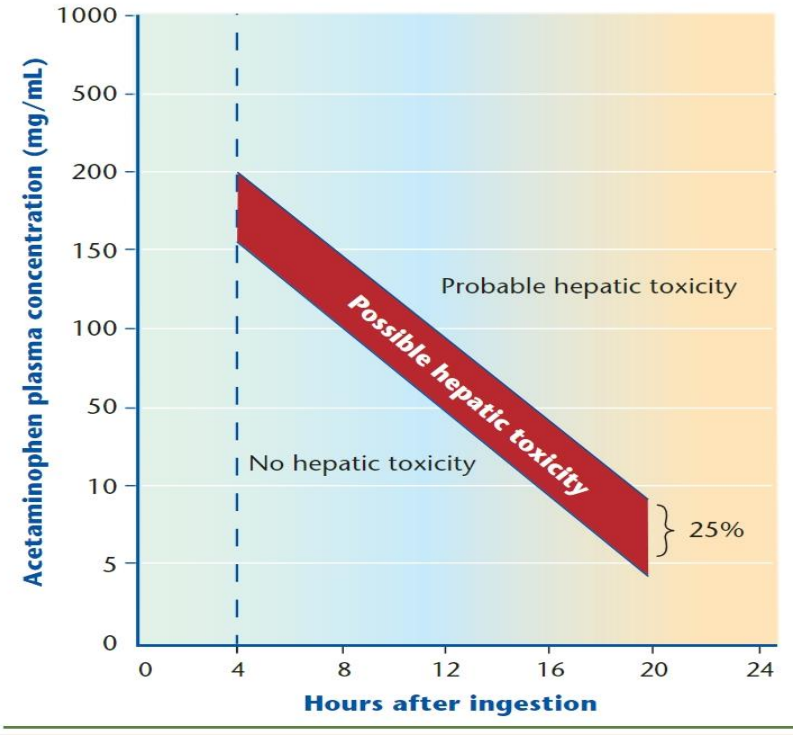
c. *Management* [6]

- *Treatment Criteria*
  - Serum acetaminophen concentration above the possible toxicity line on the Rumack-Matthew nomogram after single acute ingestion. Figure.2
  - History of ingesting more than 200 mg/kg or 10 g (whichever is less) and serum concentration not available or time of ingestion not known.
  - If time of ingestion is unknown or multiple/chronic ingestion, check acetaminophen level and AST. Treat if either is elevated.
- *Decontamination:* A single dose of Activated Charcoal 1g/kg (up to 50g) should be given to an awake, co-operative, older child if they present within 2 hours of ingestion.
- *Antidote: N-Acetylcysteine*
  - Per Oral (PO): 140 mg/kg loading dose followed by 70 mg/kg Q4 hours for 17 doses (18 total doses including loading dose).
  - Intravenous (IV): 150 mg/kg N-acetylcysteine IV loading dose over 60 minutes,

followed by 50 mg/kg over 4 hours, followed by 100 mg/kg over 16 hours for a total infusion time of 21 hours. Some patients may require more than 21 hours of N-acetylcysteine administration.

- Liver failure: Continue the 100 mg/kg over 16 hours infusion until resolution of encephalopathy, AST less than 1000 units/L, and INR less than 2.

Figure.2



2. **ASPIRINE** [11,16]
   a. *Acute toxic dose:* Ingestion 150-200mg/kg/dose mild intoxication and severe intoxication ingestion 300-500mg/kg/dose.
   Chronic intoxication: Ingestion more that 100mg/kg/day for 2days or more
   b. *Clinical signs*:[7]

Ingested Dose of Aspirin	Symptoms And Disposition
< 150mg/kg	**Minimal Toxicity** Patients do not require decontamination or referral to hospital except in cases of deliberate overdose
150 - 300mg/kg	**Mild to moderate intoxication** - **Nausea**, vomiting - Hearing disturbance, tinnitus - Increased respiratory rate - Primary respiratory alkalosis
> 300mg/kg	**Life-threatening effects** - Metabolic acidosis (late onset and pre-morbid) - Seizures - Altered mental state - Hypotension

   c. *Management:*

- Decontamination
  - Activated charcoal (oral) 1g/kg (maximum 50g) should be given to
  - Any patient with clinical signs of salicylate poisoning
  - Up to 8 hours after an acute ingestion of > 150mg/kg
  - A second dose of activated charcoal is indicated after four hours if serum salicylate levels continue to rise.
  - Ensure that the airway is secure prior to administration of charcoal.
- Urine Alkalinization
  - Give 1-2 mmol/kg of sodium bicarbonate (maximum 100 mmol) as an initial intravenous bolus over 5 minutes.
  - Child < 2 years: dilute to 0.5 mmol/mL with glucose 5% or water for injections
  - Child ≥ 2 years: administer undiluted
  - Start infusion of 150 mmol of sodium bicarbonate in 850 mL of glucose 5%, with initial rate of 2-4 mL/kg/hr.
  - Check the urine pH hourly and titrate the sodium bicarbonate infusion (up to a maximum of 1 mmol/kg/hour) to maintain a urinary pH greater than 7.5.
  - Check serum potassium and serum pH every 2-4 hours (along with salicylate level).
  - Hypokalemia is common with urinary alkalinization and intravenous potassium supplementation is often required.
- Hemodialysis
  - Hemodialysis is the definitive therapy for severe salicylate intoxication.
  - It rapidly removes aspirin from the serum and extracellular space, assists rapid movement of salicylate out of the brain, and assists correction of metabolic disorders.

3. ORGANOPHOSPHATE

a. *Organophosphates* are generally highly lipid soluble and are well absorbed from the skin, mucous membranes, conjunctiva, GI system, and respiratory system. [17]

b. *History and Clinical Feature*

- Children often ingest home pesticides they find in unmarked or poorly stored containers.
- Children can also be exposed when playing in areas recently treated with organophosphate compounds.
- Most symptoms appear within 12-24 hours of exposure.
- There are three categories of organophosphate poisoning:
  - Muscarinic
  - Nicotinic
  - Central nervous system (CNS).

	Signs and Symptoms	
Muscarinic "DUMBELS"	- **D**iaphoresis and **D**iarrhea, - **U**rination, - **M**iosis, - **B**radycardia, **B**ronchorrhea, **B**ronchospasm.	- **E**mesis, - **L**acrimation and - **S**alivation
Nicotinic	- Muscle fasciculations (twitching) - Fatigue - Paralysis - Respiratory muscle weakness	- Diminished respiratory effort - Tachycardia - Hypertension

	Signs and Symptoms	
Central nervous system	- Anxiety - Restlessness - Confusion - Headache - Central respiratory paralysis - Altered level of consciousness and/or hypotonia	- Coma - Slurred speech - Ataxia - Seizures

c. *Management* [11,18]

- Initial management:
  - ABCD follow as APLS and PALS
- Decontamination**:**
  - Activated Charcoal: Single dose 1g/kg/dose (50g in adult) with airway protection
  - Removing all of the patient's clothing and washing him or her with water and soap.
  - Make sure no further exposure to caregivers & health worker.
- Antidote**:**

- Atropine: 0.05-0.1 mg/kg/dose (2 to 5 mg IV for adults) IV every 5min
  - ⇨ Can repeat doses until no more cholinergic symptoms and clearing of bronchial secretions and pulmonary edema.
  - Pralidoxime: 25 to 50 mg/kg for children (30 mg/kg in adults) run slowly over 30 minutes, based upon the severity of symptoms, given as a continuous infusion of 10 to 20 mg/kg per hour (8 mg/kg per hour in adults).
- Benzodiazepine Therapy**:**
  - Prophylactic diazepam has been shown to decrease neurocognitive dysfunction after organophosphorus agent poisoning
  - Diazepam IV 0.1 - 0.2mg/kg/dose, repeat if seizures occur, do not give phenytoin.

4. IRON [11,14]

a. *Toxicity:*

- Directly damages GI mucosa
- Hemorrhagic necrosis of stomach and intestine
- Ingestion more than 40mg/kg/dosed is considered potentially serious.

b. *Clinical Features:* Iron dose-response relationship

- If symptomatic: can be life threatening
- If asymptomatic at 6 hours: unlikely to develop systemic illness
- <20 mg/kg: asymptomatic
  - 20-40 mg/kg: GI symptoms only. Symptoms usually last <6hrs
  - 40-60 mg/kg: GI symptoms, systemic toxicity not expected, last <8hrs
  - 60-120 mg/kg: potential for systemic toxicity
  - >120 mg/kg potentially lethal.

c. *Complications:* Pyloric stenosis, bowel obstruction.

d. *Management:*

- Fluid resuscitation
- Inotropes support
- Treat hypoglycemia (Dextrose solution: 10-25%)
- If severe signs of toxic: emesis, GI bleeding, shock, coma
- GI Decontamination (recommend lavage gastric only)
- Obtain abdominal X-ray

e. *Antidote:*

- Deferoxamine: 90mg/kg/dose IM (maximum 6g/24h) q8hs.

- If severe IV infusion 15mg/kg/h (6g/ 24 hours)
- The rate is reduced after four hours so that the total intravenous dose does not exceed 80 mg/kg/24 hours.

- Whole bowel irrigation: if iron visible on radiographic.
- Charcoal not effective.

5. ALCOHOLE/GLYCOLS [11,14]

A. Ethanol

a. Clinical features:

- Adolescents: coma, sensory or motor impairment, intoxication, vomiting, seizures, loss of protective airway reflexes.
- Infants and toddlers: respiratory depression, coma, hypothermia, hypoglycemia, seizures, metabolic acidosis

b. Management:

- Fast recognition and evaluation of blood glucose and electrolytes
  - Treat hypoglycemia
  - Treat electrolytes imbalance
- Glucose and Thiamine to treat coma, stupor and seizure
- Airway and breathing: may need intubation
- Warm the patient
- Charcoal not effective

B. Methanol:

a. *Toxicities:*

- Primary use is industrial solvent, also found in fuels for stoves, paint removers.
- Methanol not dangerous but its metabolites are.

b. *Clinical features:* CNS depression, vision changes, seizures, pancreatitis, metabolic acidosis, arrhythmias.

c. *Managements:*

- Sodium bicarbonate to correct acidosis.
- Folate and Thiamine to helps eliminate toxic metabolite
- Fomepizole or Ethanol to prevent toxic metabolite formation.
- Charcoal not effective.

6. HYDROCARBONS [11,14]

a. *Toxicity:*

- Inhalation injury may manifest up to 6 hours after exposure
- Chemical pneumonitis if aspirated (can be fatal)
- Mental status changes (drowsy, confusion, coma)
- Examples solvents: Lamp oils, Fuels, Household cleaners, Polishes, Baby oils, Lighter fluids, Camphor.

b. *Management:*

- Prevent vomiting, decrease risk of secondary aspiration
- CXR if symptomatic or after 6 hours if asymptomatic
- May develop to ARDS later
- Skin & eyes contamination: Remove the cloth and wash exposure skin with water and soap. Irrigate exposure eyes with water and saline
- Charcoal is contradicted.

7. ISONIAZID (INH)

a. *Toxicity:*

- Isoniazid >20 mg/kg/dose in children can be toxic
- Toxicity from reversal of Vit. B6 activity

- Decrease effects synthesis of catecholamine and neurotransmitter GABA (gamma-aminobutyric acid) pathway.

b. *Clinical Triad:* seizures, metabolic acidosis, and coma.

c. *Management:*

- Decontamination: Activated charcoal
- Lavage gastric: if massive ingestions
- NaHCO3 (treat acidosis)
- Anticonvulsants for seizures
- Pyridoxine (70 mg/kg/day up to 5g)
- The concomitant treat Diazepam and Pyridoxine may improve outcome.

8. INHALANTS

a. *Used as recreational drugs*

- World-wide problem, Cheap, easy to get
- Solvents: paint thinners, gasoline, glue, correction fluid, whiteout,
- Aerosol sprays: hair spray, cigarette lighter, other gases: ether, nitrous oxide, chloroform
- Sniffing: direct from the open container
- Bagging: concentrating vapor in a bag and inhaling
- Huffing: cloth soaked in liquid & held to mouth
- Spraying: spraying directly into the mouth

b. *Toxicity:*

- Inebriation, light-headedness, euphoria, hallucination, confuse and disorientation.
- Cardio toxicity, V-fib, respiratory arrest, suffocation from “bagging”
- Suddenly sniffing death syndrome
- Chronic use: Leuko-encephalomalacia with cerebral atrophy

c. *Management:*

- ABCD
- IV access, oxygen
- Cardiac monitoring for arrhythmias
- Electrolytes, blood glucose, LFTs, urea/creatinine
- Psychosocial evaluation and support
- No need for activated Charcoal.

VIII. Prevention and education

Children’s education program is very important as children under the age of 6 are the most frequent victims of poisonings.

- Teach young children the dangers of poisons
- Get poison prevention information to children home by distributing materials at school and day care center.
- Educate parents to keep the drugs or chemical substances out of children reach.
- Health professional provides poisoning education to the parents.

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CAUSTIC INGESTION IN CHILDREN

CHEA Siden, CHRUN Chhunny, EAR Vireak, KHUN Leangchhun, YAY Chantana, HENG Sothy

I. Key Facts

Ingestion of corrosive substances is most often accidental and occurs much more in children, especially in toddlers, than in adults.[1] It can cause severe acute injury and long-term complications, especially the development of esophageal strictures.[2]

account for over 200,000 exposures per year reported to US poison control centers, approximately 80% of caustic ingestions occur in children younger than 5 years. [3]

Developing countries have mean death rate of 4.1% (0%-11.9%) due to corrosive ingestion.[14]

In Cambodia, lye or lye solution "***Toeuk Kbong***" has been used traditionally in the purpose of making some Cambodian cakes and implicated in traditional treatment of silk product in Khmer culture. Accidental ingestion of corrosive substance is almost alkali-based solution, which caused esophageal stricture being the common motif of hospitalization in pediatrics. Incidence of hospitalized caustic-esophageal stricture was 34 cases (31%) compared with the total numbers of caustic ingestion with 110 cases during 2years period from January 2022 to December 2023 in Jayavarman VII children hospital Siem Reap-Angkor.

II. Overview

1. Definition

Corrosive (caustic) substances are acidic or alkaline substances that cause tissue damage upon direct contact.[1]

2. Etiology

a. Acids

- Sulfuric acids (batteries, batteries liquid)
- Oxalic acids (Rust-removal products)
- Hydrochloric acids (Toilet bowl–cleaning products, Hair relaxers/Bleaches hair) [1,3]

b. Alkaline

- Sodium carbonate (Lye water/powder)
- Potassium hydroxide (soaps, detergent, bleach)
- Sodium hydroxide (Automatic dishwasher detergent) [1,3]

3. Pathophysiology

- Substances strong bases and acids with extremes of pH (less than 2 or greater than 12) are very corrosive and can create severe injury and burns in the upper gastrointestinal tract. [1,4,6]
- The tissue injury following corrosive ingestion goes through three phases: [4]
    - The acute necrotic phase (phase 1): characterized by cell necrosis lasts for 24–72 hours
    - The second phase: the mucosal sloughing with ulceration and fibroblast colonization with granulation lasts for 3–12 days.
    - The stricture formation (phase 3) phase: begins approximately 3 weeks after the initial injury and can continue for 3–6 months or more.

c. Alkaline ingestions

- Ingestion of alkali called liquefactive necrosis.[5]
- Ingestion of even small quantities of an alkali with a pH above 12 may cause severe burns.
- The injury extends rapidly (within seconds) through the mucosa and wall of the esophagus
- Because liquid preparations do not stick, odorless, tasteless, larger quantities (200-300ml) are easily ingested, and damage may be widespread. Liquids may also be aspirated, leading to upper airway injury.
- Alkalis tend to affect the esophagus more than the stomach, but ingestion of large quantities severely affects both. [4,6]
- Extensive transmural damage may result in esophageal perforation, mediastinitis.

- Over the next 2-4 weeks, any scar tissue formed initially remodels and may thicken and contract enough to form strictures. [4,6]

d. Acid ingestion

- Acid ingestions typically produce superficial coagulation necrosis that thromboses the underlying mucosal blood vessels and consolidates the connective tissue.[5]
- Ingestion of even small quantities of an acid with a pH less than 2 may cause severe burns.
- Upper airway injuries are more common with ingestion of acid, perhaps related to their bad taste, which tends to stimulate gagging, choking, and attempts to spit out the ingested material.
- Unlike alkali ingestions, the stomach is the most commonly involved organ following an acid ingestion. This may due to some natural protection of the esophageal squamous epithelium.
- As the acid flows along the lesser curvature of the stomach toward the pylorus, pylorospasm impairs emptying into the duodenum, producing stagnation and injury that is particularly -prominent in the antrum. A gastric outlet obstruction may develop as the scar tissue contracts over a 2- to 4-week period.
- Acute complications include gastric and intestinal perforation and upper gastrointestinal hemorrhage. [4,6]

III. Signs and Symptoms

The physician should try to identify the specific agent ingested, as well as the concentration, pH, and amount of substance ingested. The time, nature of exposure, duration of contact, and any immediate on-scene treatment are important in determining management of toxicity.

1. Gastrointestinal tract injury

- Oropharyngeal lesion(burn)
- Drooling
- Dysphagia/ odynophagia
- Vomiting, hematemesis
- Abdominal pain, epigastric pain.[3]
- Gastric or esophageal perforation can occur between days 3 and days 12 following ingestion clinical course in the form of worsening abdominal pain and chest pain. [4]

2. Upper airway tract injury

- Nasal flaring, Cough,
- Stridor, Hoarseness,
- Dysphonia,
- Respiratory distress.[3]

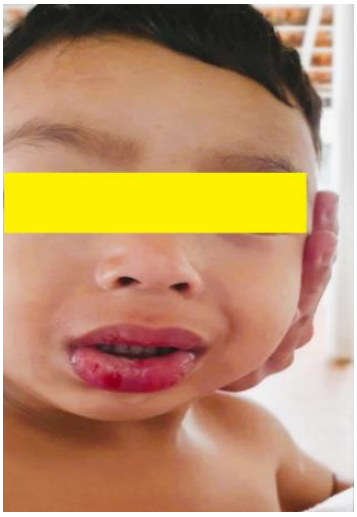


Figure 1. *3 years-old boy has swollen-lips and oral lesion post lye ingestion*

IV. Diagnosis

1. Lab test

- pH of product if <2 and >12 indicate for severe tissue damage.
- CBC, Electrolyte, BUN and Creatinine level indicate for systemic toxicity.
- If present metabolic acidosis with elevated lactate levels, leukocytosis, thrombocytopenia, high CRP level, and deranged liver function tests suggestive of transmural necrosis.
- it is important to understand that corrosives like phosphoric and hydrofluoric acid can cause systemic effects such as severe hypocalcemia, hypokalemia, and acidosis. [4]

2. Imaging Studies

- *Chest radiography*: may use in acute and second phase Obtain for Findings may include pneumomediastinum or other findings suggestive of mediastinitis, pleural effusions,

pneumoperitoneum, aspiration pneumonitis, or a button battery (metallic foreign body). [2,5]

- *Thoraco-abdominal CT scan*: is preferable to endoscopy as it avoids the risk of esophageal perforation and allows the evaluation of esophageal injuries as well as of the surrounding tissue and possible related thoracic complications caused by caustic ingestion. [2,9]
- *Upper- Endoscopy:* is important instrumental techniques in the acute phase (first 12h-48h), and is the mainstay of diagnostic evaluation and staging, as it allows you to check:

assessment of severity, treatment and surveillance in patients with caustic injury of the esophagus. [7,11]

❖ It is recommended to avoid Endoscopy at 3-15days after injury, suspicion of perforation, instable of hemodynamic and respiratory failure. [7,11]

Table 1: *Zargar classification of Caustic esophageal injury*

Grade	Injury Pattern	Risk of Esophageal stricture
Grade 0	Normal mucosa	-
Grade 1	Edema, erythema	None
Grade 2a	Hemorrhage, Erosions, Blisters superficial ulcers	Low
Grade 2b	Circumferential lesions	75%
Grade 3a	Focal deep ulcers	Near 100%
Grade 3b	Extensive deep ulcers	Near 100%
Grade 4	Perforation	Near 100% if patient survive

❖ *Transit Oeso-Gastro-duodenal (TOGD)* we use in the latest phase for finding the stricture.[9]

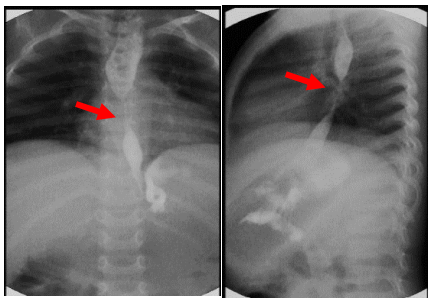


Figure 2: *Esophageal stricture post lye ingestion (Courtesy of Imagery Department of JV7)*

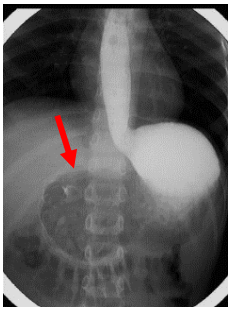


Figure 3*: Gastric outlet obstruction post Acid ingestion (Courtesy of Imagery Department of JV7)*

3. Differential diagnosis

- Gastrointestinal Bleeding (epigastric pain, hematemesis, melena without swollen lips or lesion).
- Perforated Peptic Ulcer (no swollen lips, abdominal pain, abdomen tenderness)
- Toxicity Iron (in first 6h sign: vomiting, diarrhea, abdominal pain, shock, without swollen lips)
- Plant Poison (fresh cashew nut, Urtica, angioedema signs: itchy, swollen lips, dyspnea).
- Croup (cold sign, barking cough, dyspnea).[5]

V. Complications

1. Short-term Complications

- Tracheoesophageal fistula formation
- Esophageal-aortic fistula formation
- Perforation of oesophagus or stomach
- Mediastinitis
- Pericarditis
- Pleuritis
- Peritonitis
- Pneumothorax
- Pneumomediastinum.[8]

2. Long term complications

- Esophageal strictures
- Gastric outlet obstruction.
- Esophageal carcinoma (both adenocarcinoma and squamous cell carcinoma). [8]

VI. Management

1. Initial management

Patients who are asymptomatic follow-up to ensure no long-term complications develop and to provide preventive teaching.

Symptomatic oral lesions should be admitted to the hospital and we need endoscope for this evaluation (first 12h-48h). [2,7,9]

a. Supportive care Maintenance of airway: the patients present respiratory distress should be evaluated for the need to do immediate intubation or tracheostomy. [2,9]

- Give IV: hemodynamic stabilization + NPO
- Nasogastric tube and gastric lavage are contraindicated because risk perforation or additional injury can occur while passing the tube but it should be placed under direct visualization during the endoscopic procedure. [9]

b. Proton Pump Inhibitor and H2 blocker:

allow faster mucosal healing and to prevent stress ulcers

- Esomeprazole :1mg/kg((IV) once day for three days [2] then
- Omeprazole: 1mg/kg/day (PO) for 4weeks
  Or Tagamet: 20mg/kg/day (PO) bid for 4weeks [12,13]

c. Steroid: have been proposed as a treatment to reduce stricture formation but in general are no longer recommended. for patients with documented grade 2B lesions (deep focal or circumferential ulcers) [9]

- High-dose corticosteroids, e.g. Methylprednisolone 1 g/1.73 m2 intravenously or Dexamethasone: 1mg/kg/d or prednisolone: 2mg/kg/d (intra veinous) for 3days. [2,9,11,13]
- For patients with grade 3 lesions, corticosteroids may soften the wound and increase the risk and/or mask the symptoms of perforation.

d. Antibiotics: infection reduce the bacterial count in the wound thus possibly decreasing inflammation and reducing scar.

Cephalosporin: Ceftriaxone 100mg/kg/d, once per day for 7-14 days. [2,13]

e. Analgesics:

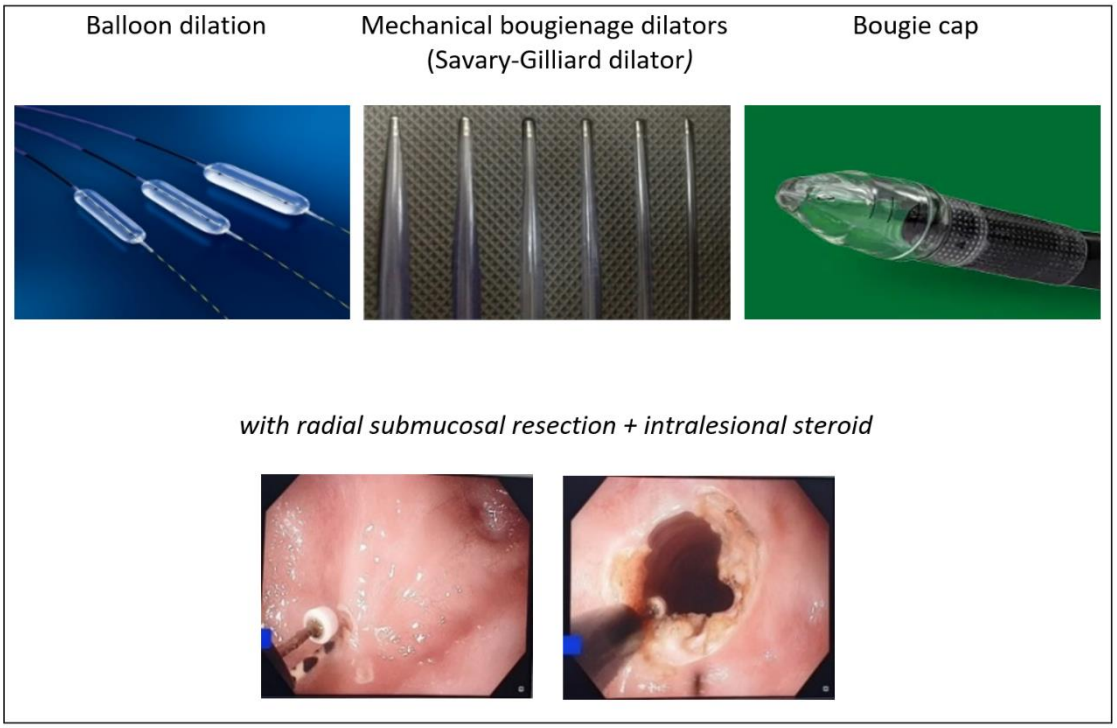
- Morphine: 0.1-0.2 mg/kg/dose, IV/IM/SC, 3 to 4 times per day or others Analgesic Narcotic
- Paracetamol (syrup): 15mg/dose orally, 3-4 times per day.
- Analgesics should be used to reduce the pain associated with these ingestions.[5]

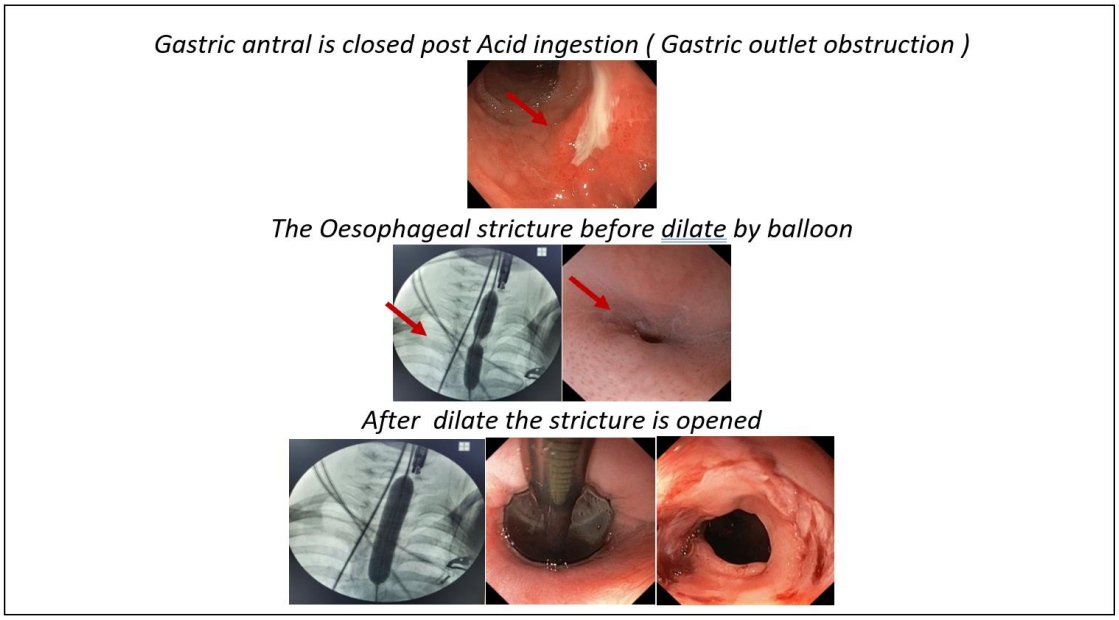
2. Late Complications management

a. The most common complications of caustic ingestion is stricture formation which can cause esophageal obstruction and severe gastric injury may develop pyloric stenosis.

The endoscopic therapy by the Balloon or mechanical dilators can both be used to dilate: [9,10,11]

b. Stricture management: start dilations after 21 days post ingestion and the interval between dilations varies from weekly to every 2 to 3 weeks. [9,10,11]





3. Surgery:

Corrective surgery for esophageal strictures from caustic injury is done only in severe cases where endoscopic therapy fails or is deemed harmful. [9,10,11]

- Discharged patients should be able to eat and drink
- Obtain a psychiatric evaluation for all patients with intentional ingestion.
- Arrange for a follow-up until 3-6months post ingestion.

VII. Prevention and Education

- Caustic substances should be kept in their original labeled containers to avoid accidental ingestion. They should be stored out of reach of toddler-aged children. [5]
- Induced vomiting is contraindicated after caustic ingestion to avoid re-exposing the esophagus and airway to the caustic material. [2]
- Do not give charcoal, weak acid or base to induce pH neutralization it is not recommended. [2]
- Early hospitalization in a good well-specialized hospital is the Key Factor determining the outcome of post–caustic ingestion because some of the conditions could be cured or prevented children from afterward esophageal stricture by proper medical treatment.[2]

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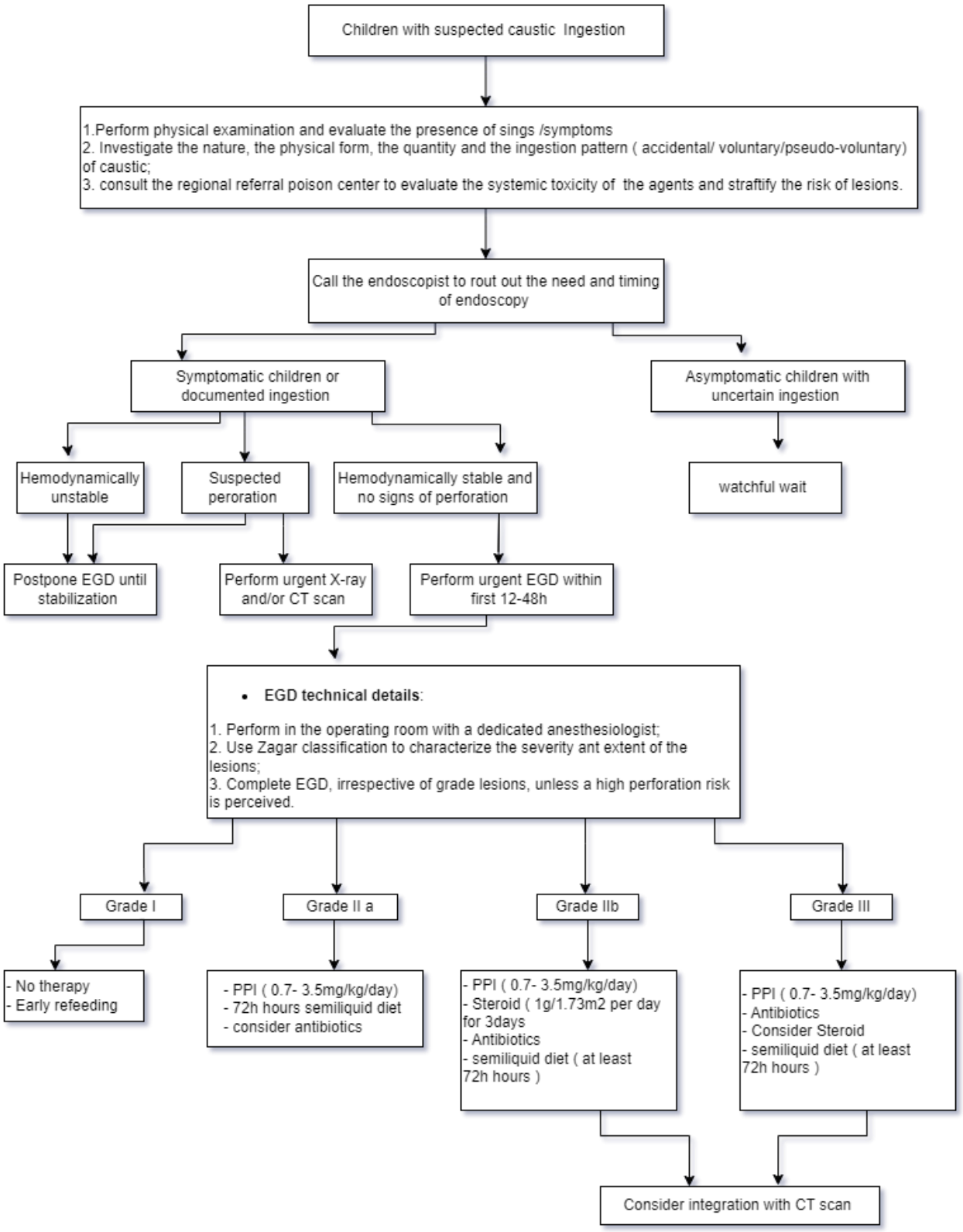
Management algorithm for caustic ingestion in children [11]



SNAKEBITE

CHHAM Sary, KHEAN Kimleng, HENG Sothy

I. Key Facts

- **Snakebite** is one of the most neglected public health issues in the poor rural communities living in Cambodia. The true burden of snakebite is not known because of large-scale misreporting.
- Cambodia is a heavily affected region due to widespread agriculture activities with home environmental exposure to hidden place of snakes, numerous venomous snake species and lack of functional snakebite control programs.
- In Cambodia, snakebites increase perceptibly during the rainy season particularly in provinces along the Mekong and Tonle Sap floodplains [1]. Despite this perception, snakebite incidence, disability, mortality are not currently reported due to lack of accurate data within health referral offices as well as the Ministry of Health. A majority of snakebites injuries are not treated in health facilities and naturally the victims seek traditional healers. [2]

II. Overview

1. Definition

According to the International Classification of Diseases code (E905 and E906) for bites and stings, a snakebite is definite if a snake bit or spat and was seen, probable if a snake was seen nearby with fang marks or clinical effects suggestive of snakebite without fang marks and possible if a snake was not seen but definite fang marks were found [3].

- **Dry bites** are bites not accompanied by any local effect because no venom is injected or the snake is non-venomous. [4]
- **Local envenoming** is defined as only local effects such as pain, swelling, blisters or tissue necrosis without systemic abnormalities because insufficient venom is injected [5, 6]
- **Systemic envenoming** is defined as both local effects and at least one of coagulopathy, neurotoxicity, myotoxicity and renal impairment or non-specific signs (nausea, vomiting, abdominal pain, dizziness and headache). [5, 6]

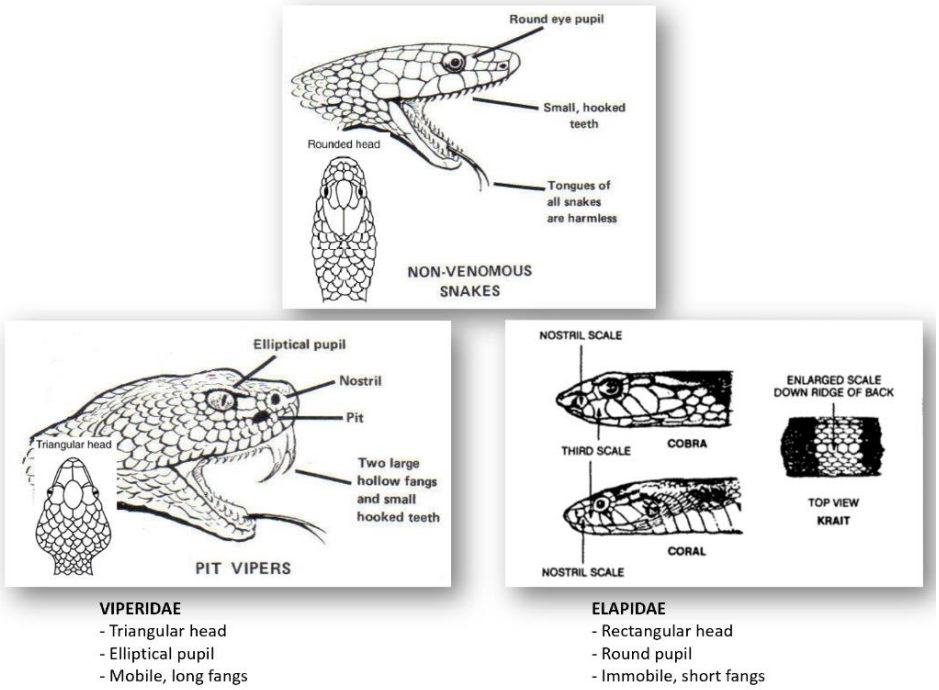
2. Venomous Snakes [10]

Cambodia's venomous snakes belong to 2 main groups such as Elapidae and Viperidae that are easily distinguished on the basis of external morphology (figure 1,2):

Figure 1. External morphology

Elapidae - Rectangular head - Round pupil - Immobile, short fangs 	Viperidae - Triangular head - Elliptical pupil - Mobile, long fangs 

Figure 2. External morphology



a. Hematotoxic Snakes - *Figure 3.*

Green Pit Viper

Malayan Pit Viper

Russell's Viper Bite

b. Neurotoxic Snakes - *Figure 4.*

Indo-Chinese spiting Cobra

Monocellate Cobra

King cobra

Banded Krait

Red-headed Krait

Malayan Krait

Sea Snake

3. **Physiopathology of venom** [8]

a. **Actions of snake venom**

Understanding the actions of venoms of each type of snake can sometimes help identification of the species responsible.

- Cytotoxins: destroy cell tissue by increasing membrane permeability and cell membrane hydrolysis & proteolysis
- Haemorrhagins: damage blood vessel walls
- Haemolysins: damage blood cell membranes
- Procoagulant toxins:
  - disruption of normal hemostasis by causing abnormal activation of blood clotting factors
  - factor depletion (consumptive coagulopathy)
- Platelet toxins: destroy platelets, may either initiate aggregation or inhibit aggregation.
- Neurotoxins:
  - α-neurotoxins (postsynaptic- reversible) block acetylcholine binding to receptors in neuromuscular synaptic
  - β-Neurotoxins (pre-synaptic irreversible) target nerve terminals and destroy them from inside after being internalized by endocytosis
- Myotoxins: Rhabdomyolysis can lead to indirect nephrotoxicity due to accumulation of cellular debris in kidney nephrosis
- Nephrotoxins: induce direct nephrotoxicity by causing renal tubular necrosis
- Cardiotoxins: poisoning general myocardial cell membranes causing irreversible cellular depolarization.

b. **Commonly** bites **by the Viperidae result in hemotoxicity while bites by the Elapidae cause neurotoxicity**.

4. **Risk factors**

- People working, farming, forestry, construction
- Snake species: krait, Russel's viper, king cobra
- Preexisting coagulopathy
- Malnutrition.

III. Signs and Symptoms [3,9]

1. **Symptoms and signs of Viper bite (Hematotoxic snake)** - *Figure 5.*

- Dry bite: no local effects
- Local envenoming: starts progressively in hours after bite: pain-edema-blisters-necrosis
- Systemic envenoming:
  - Coagulopathy: Local bleeding, systemic bleeding (skin ecchymosis – gum bleeding, GI bleeding).
  - Nephrotoxicity: Russel's viper can cause nephrotoxicity and neurotoxicity. Severe rhabdomyolysis often causes renal failure

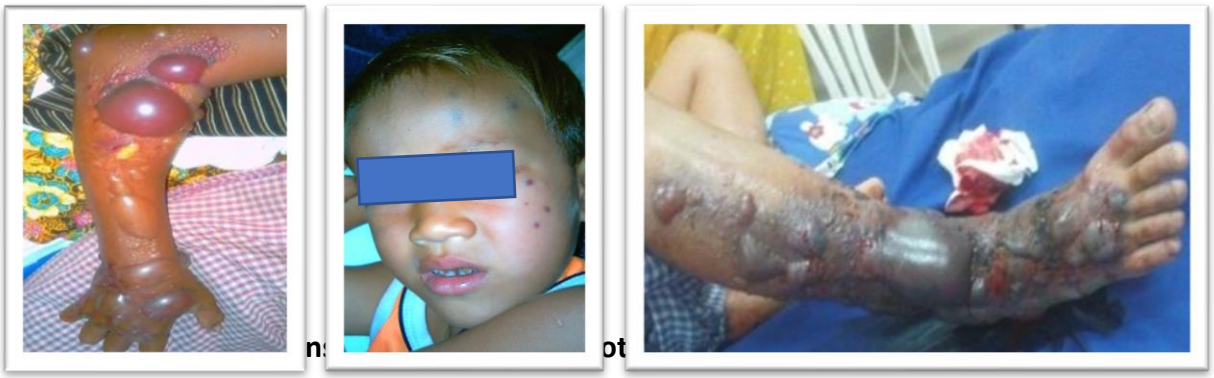
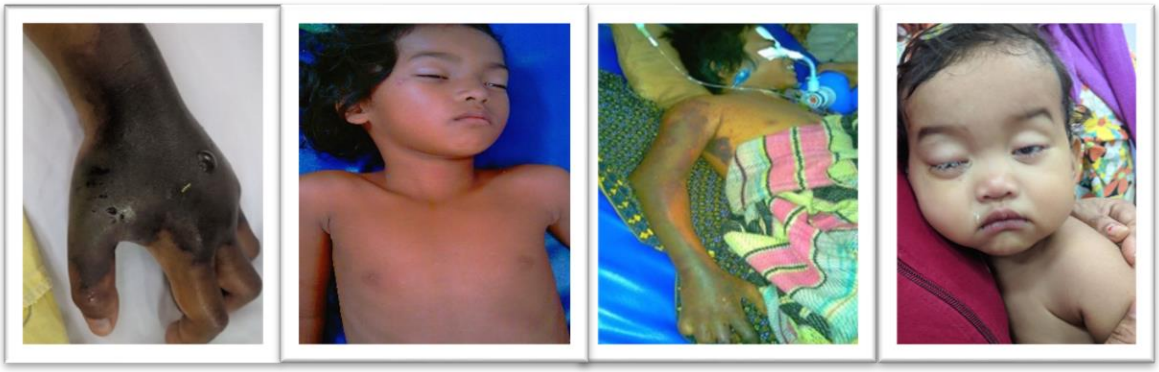


Figure 5.

- Dry bite: no local effects or local envenoming: starts progressively in hours after bite: pain-edema-blisters-necrosis (for cobras), numbness (for kraits)
- Systemic envenoming:
  - Neurotoxicity: starting from drowsiness to descending paralysis: face-respiratory –trunk & limb Blurring of vision, pupillary abnormalities (some patients may have long-term pupil dilation after krait envenoming), abnormalities of taste & smell (may persist for many months after bite), urinary retention
  - Cardiotoxicity: arrhythmias

Figure 6.



IV. Diagnosis [9]

1. Snakebite identification

- Identify the likely snake responsible for bite: the victim or entourages describe or point the snake species (on pictures of snakes) that he or they have seen on spot.
- Usually, two fang marks are found.
- All patients will be kept the patient under 24 h observations
- Determine the exact time of the bite
- Timing of onset of toxidromes after bite
  - Coagulopathy: 1-2h.
  - Neurotoxicity: 3-4h
  - Cytotoxicity- Myotoxicity: hours
  - Nephrotoxicity: 12-24h.
  - Cardiotoxicity: 2-6h.

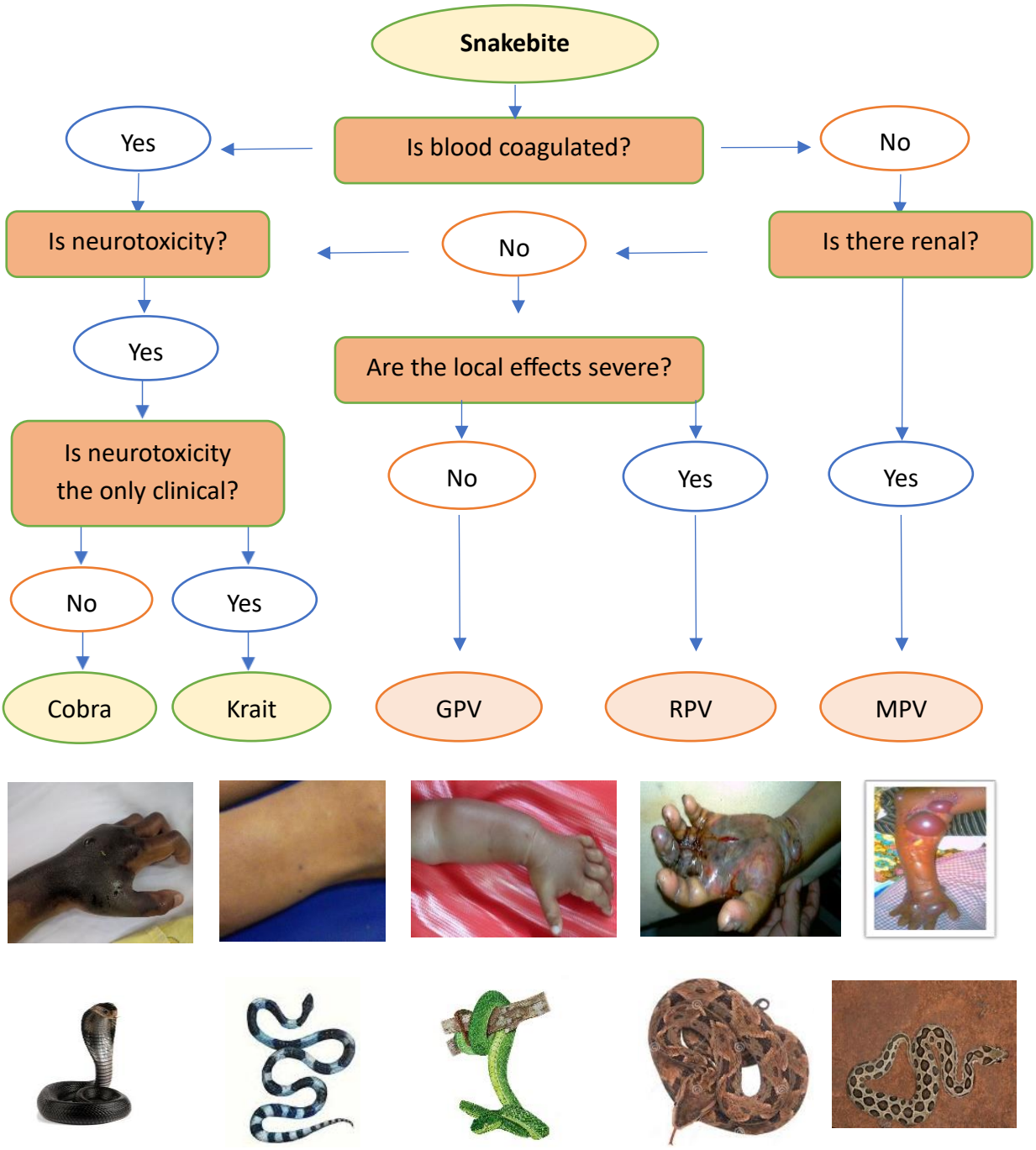
2. Laboratory investigations - *Figure 7.*

Figure 7.

- 20-minute whole blood clotting test (20' WBCT)
- If the 2 ml of freshly sampled venous blood in a small, dry,
- glass vessel left undisturbed for 20 minutes is still unclotted
- and runs out, the patient has hypofibrinogenemia as
- a result of venom-induced consumption coagulopathy.
- In Cambodia, incoagulable blood is diagnostic of a viper bite
- and rules out an elapid bite.
- Prothrombin Time (PT): Normal range is 12-16 seconds.
- Partial Thromboplastin Time (PTT): Normal range is 25-47 seconds.
- Fibrinogen level: Normal range is 1.5-4.5 g/L. In DIC involving
- defibrination, the fibrinogen level will be critically below these ranges, and is often undetectable.
- Fibrin-degradation products (FDP): defibrination, the FDP levels may be extremely high.

- Whole blood cell count
- CK, Kaliemia, Urea-Creatinemia.

3. **Imaging**
   - ECG, X ray, Ultrasound, CT scan are performed once distant bleeding is suspected.
4. **Presumptive identification of snakebite**



Algorithm 1. ***Presumptive identification of snakebite***

❖ **Differential diagnosis**

If a killed snake was not brought, based on wound characteristics (see signs & symptoms) and labs finding the diagnosis was differentiated with:

- Insect sting like millipedes, centipedes, scorpions…

- Rodent species like mice, squirrel…
- Between snake species.

V. Management

1. First Aid treatment Protocol

a. Recommended Method for Cambodia: "Do it R.I.G.H.T"

- Reassure the patient: 80% of all Cambodian snakes are non- venomous.
- Only 60% of bites by venomous species actually envenomate the patient.
- Immobilize in the same way as a fractured limb, use bandages
- Get to Hospital immediately
- Tell the doctor of symptoms

b. Discarded Method

- Tourniquets
- Cutting and Suction
- Electrical Therapy and Cryotherapy

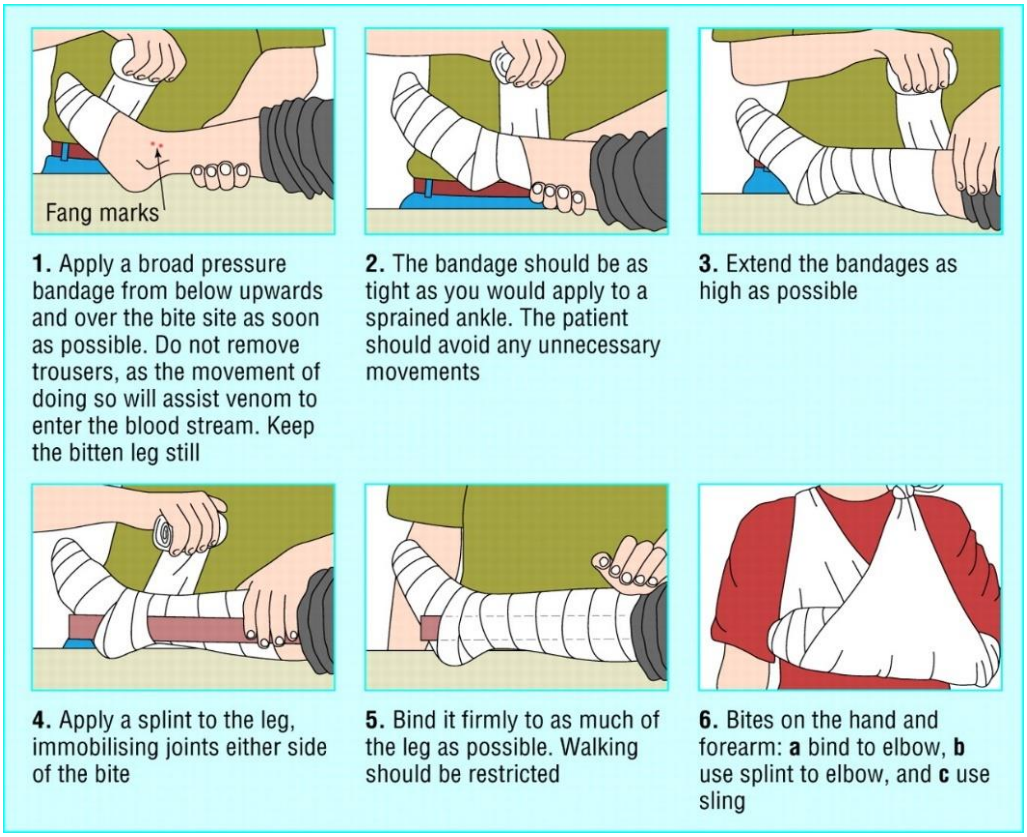
c. Newer Method

- Immobilization for viper bites or unidentified snakebite
- Pressure Immobilization bandages (PIB) for Elapid bites

d. Eye Irrigation

- After venom spitting onto eyes: water or Saline or milk irrigation
- Treatment: Topical steroid and antibiotic eyes drop (Tetracycline) or Topical anesthetic eyes drops.

❖ *See the diagram below for a walkthrough on how to apply a pressure-immobilization bandage to a patient with a neurotoxic snakebite:*



2. Snakebite Treatment Protocol at the hospital

a. Patient assessment on arrival

- Resuscitation of ABC (Airway, Breathing, Circulation)
- Tetanus vaccination (after ASV if clotting disorder)
- Antibiotics: Antibiotic is considered if large wounds
- Eyes irrigation: topical antibiotic prophylaxis and copious lubricants.
- Pain killer: Tylenol (20mg/kg/dose)
- Handling Tourniquets: sudden removal of the tourniquet can lead to hypotension/respiratory distress due to massive surge of venom, but it is safe to remove it slowly or after ASV (anti-snake venom).

b. Antivenom treatment

- Choice *of anti-snake venom (ASV) – Figure 8.* [11]

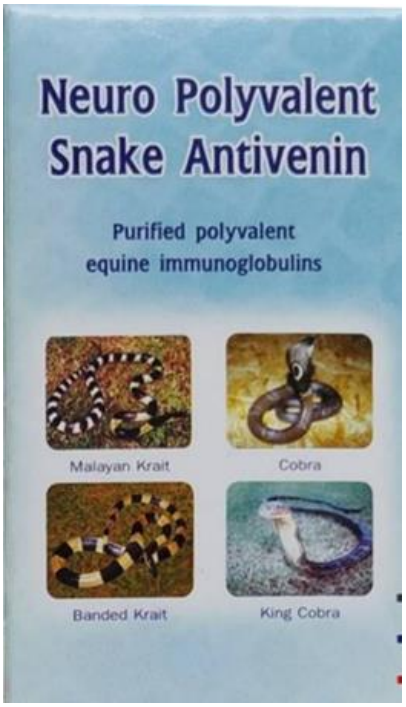
For Viper bites	For Elapid bites
	

Table 1. *ASV dosage by snake species*

Snake species	Antivenom	Starting dose: IV in 30-1h
Malayan pit viper	TRC Hemato Polyvalent	10 vials
Russell's viper	TRC Hemato Polyvalent	10 vials
Green pit viper	TRC Hemato Polyvalent	2-5 vials
Monocellate cobra	TRC Neuro Polyvalent	10 vials
Spitting cobra	TRC Neuro Polyvalent	10 vials
King cobra	TRC Neuro Polyvalent	20 vials
All species of kraits	TRC Neuro Polyvalent	5 vials

- *ASV* indication*:* Best results when given early! Never delay! If either:
  - Severe current local envenoming (swelling>50% of the limb) or
  - Systemic envenoming: coagulopathy, neurotoxicity, cardiotoxicity nephrotoxicity, rhabdomyolysis
- *ASV dosage- no ASV test doses (see table 1)*

  Children should receive the same initial dose of ASV as adults, as snakes inject the same amount of venom into children as adults.
- *Treatment of ASV reactions*

  ASV reactions: fever, chills, urticaria, itching or itchy throat. Monitor closely vital signs during infusion of ASV: watch for stridor, wheezing, dyspnea, syncope or arrythmias.
  - Discontinue ASV
  - H1 Antihistamine: Promethazine/ Chlorpheniramine maleate (0.2mg/kg IV) + Paracetamol PO (20mg/kg/dose)
  - Hydrocortisone IV: 10mg/kg
  - Restart ASV after recovery.
  - Adrenaline IM 0,01mg/kg is reserved for moderate to severe anaphylaxis.
- *Recovery phase*

  Reassessment, if an adequate dose of appropriate ASV:
  - Systemic bleeding stops within 15-30 mn.
  - 20'WBCT (-) in 6 h.
  - Paralysis by Cobra improves in 30' or hours.
  - Paralysis by Krait improves in considerable time
  - Active hemolysis & rhabdomyolysis cease within a few hours
  - Shock disappears after 30 mn.
  - Rising platelet rate is not significantly accelerated and blood CK was not decreased after ASV.
- *Repeat* ASV *doses*

  Persistent bleeding:
  - Same dose every 6h until coagulation has been restored (max dose: 30 vials)
  - Vitamin K1 (10mg IV)/ others hemostatic agents
  - Use Fresh Frozen Plasma if available.
  - Blood products: only use if severe uncontrollable bleeding or adequate ASV has been given

  Persistent neurotoxicity:
  - Same dose after 1-2h (maximum dose: 20 vials)
  - Neostigmine IM (0,04mg/ kg) + Atropine IV (0,05mg/kg) half hourly x 8h

  Neostigmine is an anti-cholesterase that prolongs the life of acetylcholine and can therefore reverse the respiratory failure and neurotoxic symptoms
- *Others* treatments
  - Rhabdomyolysis*:*
    - Mild (no complication): Rehydration
    - Severe: Alkalinize urines by IV fluids (30ml of 8, 4%NaHCO3/l of serum) or hemodialysis
  - Hyperkaliemia*:*
    - Mild (no ECG changes): Diet, stop medications responsible
    - Severe: Diuretic (Lasix: 1mg/kg/dose) or (Glucose and Insulin, Ca, NaHCO3)

- Hypotension*:* Beside a number of causes, Russell's viper is known to cause acute pituitary adrenal insufficiency. So, Dopamine and Hydrocortisone are helpful.
- Renal failure: Diuretic, Dialysis. ASV has no efficacy
- Serum sickness: Antihistaminic/ Prednisolone(1mg/kg/day) x 5days.

3. **Wound care:**
   - *Prevent rupture of bullae; aspirate aseptically if large*
   - *Clean skin daily gently with Antiseptic or soap & water*
   - *Elevate limbs to reduce bleeding & swelling*

   Surgical intervention: When stable after ASV:
   - *Debridement: tissue necrosis*
   - *Fasciotomy: compartment syndrome*
   - *Skin Grafting: loss of tissues*
   - *Amputation: gangrene.*
4. **Rehabilitation**
   - *Kinesis especially for patient is bite by Elapidae*
   - *Some patients develop delayed serum sickness (fever, rash, joint pain and flu like illness) between 5-10 days after ASV therapy*
   - *Prescribe Prednisolone 1mg/kg x 5days after ASV administration.*

VI. Complications

1. **Local complications**
   - *Dangers of venipuncture*
   - *Superinfection*
   - *Compartment Syndrome-Gangrene*.
2. **Systemic complications**
   - *Septic/Hemorrhagic shock*
   - *Kidney failure*
   - *Prolonged bilateral mydriasis*.

VII. Prevention and Education

1. **How can we avoid snakebites?** [10]

   Most snakebites occur between April and October, when outdoor activities are popular. You can avoid snakebites by taking the following steps:
   - *Avoid places where snakes may live. These places include tall grass or brush, rocky areas, fallen logs, bluffs, swamps, marshes, and deep holes in the ground.*
   - *When moving through tall grass or weeds, poke at the ground in front of you with a long stick to scare away snakes and walk with a heavy step.*
   - *Watch where you step, where you sit when outdoors and pay close attention to the leaves and sticks collecting.*
   - *Wear loose, long pants and high, thick leather or rubber boots.*
   - *Shine a flashlight on your path when walking outside at night.*
   - *Never handle a snake, even if you think it is dead. Recently killed snakes may still bite by reflex.*
   - *Avoid sleeping on the ground.*
2. **Refer** to a hospital where labs and antivenoms are available when person is snakebitten.

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ACUTE FEVER

KDAN Yuvathana, TE Haypheng, EANG Kim-Ean

I. Key Facts

- Most acute fever is caused by viral infections.
- Causes and evaluation of acute fever differ depending on the age of the child; in young infants, fever may indicate a serious, life-threatening disease and requires careful evaluation.
- Number of children < 36 months of age with fever without localizing signs (primarily those who are incompletely immunized) can have pathogenic bacteria in their bloodstream (occult bacteremia) and be early in the course of a potentially life-threatening infection.
- Teething does not cause significant fever.
- Antipyretics do not alter the outcome but may make children feel better. [1]

II. Overview

1. Definition

- A fever is defined by the body temperature of 100.4°F (38°C) and higher when taken rectally.
- The classification of fever base on duration is acute (≤ 14 days), acute recurrent or periodic (episodic fever separated by afebrile periods) and chronic (> 14 days), which is more commonly referred to as fever of unknown origin (FUO). [2]

2. Background

- In infants <3 months of age, hypothermia or temperature instability can be signs of serious bacterial infection (or other serious illness).
- The severity of illness cannot be predicted by the degree of fever, its rapidity of onset, its response to antipyretics or the presence of febrile seizures, the appearance of the child is the most useful indicator.
- The most common causes of fever in children are viral infections; however serious bacterial infection (SBIs) need to be considered.
- The most common SBIs found in children without a focus are urinary tract infections and other need to consider include pneumonia, meningitis, bone and joint infection, skin and soft tissue infections, mastoiditis, bacteriaemia, sepsis.
- Since the introduction of the pneumococcal vaccine, the rate of occult bacteremia has fallen to <1% in healthy, immunized children.
- Children with fever for > 5 days should be assessed for Kawasaki diseases or PIMS-TS if there is a history of COVID-19 infection.
- Other uncommon causes of prolonged fever in children include inflammatory, immune-mediated and neoplastic conditions, specialist input may be required. [3]

3. Etiology

A. Acute Fever

a. Infectious

- Viral infection:
  - < 1 month: TORCH infections (toxoplasmosis, other pathogens [varicella-zoster, parvovirus B19], rubella, cytomegalovirus [CMV], herpes simplex

virus [HSV]), coxackievirus, enterovirus, COVID-19 or other coronavirus, human immunodeficiency virus (HIV)

- ≥ 1 month: Enterovirus and respiratory virus (e.g., respiratory syncytial virus , parainfluenza, adenovirus, influenza, influenza, rhinovirus, metapneumovirus, COVID-19 or other rhinovirus), CMV, Epstein-Barr virus (EBV), HSV, human herpesvirus 6

- Bacterial infections (most common pathogens vary by age)
  - < 1 month: Group B streptococci, Escherichia coli and other enteric pathogens, Listeria monocytogenes (these organisms can cause bacteremia, pneumonia, pyelonephritis, meningitis, and/or sepsis; also, Salmonella species and Staphylococcus aureus [e.g., in nursery outbreaks], which in addition to bacteremia and sepsis, can cause soft-tissue, bone, and joint infections), syphilis.
  - 1–3 months: Streptococcus pneumoniae, group B streptococci, Neisseria meningitidis, L. monocytogenes (these organisms can cause bacteremia, pneumonia, meningitis, and/or sepsis; other common infections include otitis media [S. pneumoniae, Hemophilus influenzae, Moraxella catarrhalis], urinary tract infection [E. coli and other enteric pathogens], enteritis [Salmonella species, Shigella and others], skin and soft-tissue infections [S. aureus, group A and B streptococci], bone and joint infections [S. aureus, Salmonella species]).
  - 3–24 months: S. pneumoniae, N. meningitidis (these organisms can cause bacteremia, meningitis, and/or sepsis; other common infections include otitis media and pneumonia [S. pneumoniae, H. influenzae, M. catarrhalis], urinary tract infection [E. coli and other enteric pathogens], enteritis [Salmonella species, Shigella and others], skin and soft-tissue infections [S. aureus, group A streptococci], bone and joint infections [S. aureus, Salmonella species, Kingella kingae]).
  - > 24 months: S. pneumoniae, N. meningitidis (these organisms can cause bacteremia, meningitis, and/or sepsis; other common infections include otitis media, sinusitis, and pneumonia [S. pneumoniae, H. influenzae, M. catarrhalis, mycoplasma], pharyngitis or scarlet fever [group A streptococci], urinary tract infection [E. coli and other enteric pathogens], enteritis [Salmonella species, Shigella and others], skin and soft-tissue infections [S. aureus, group A streptococci], bone and joint infections [S. aureus, Salmonella species, K. kingae])
  - Other Bacterial infections: mycobacterium tuberculosis in exposed or at-risk populations. Rickettsial infections in appropriate geographic locations and vector-transmitted infection (e.g., Lyme disease)
- Fungal infections on *neonates or immunocompromised hosts:* Candida species most common (urinary tract infection, meningitis, and/or sepsis).

b. Non-infectious

- Kawasaki disease
- Acute rheumatic fever
- Heatstroke
- Thermoregulatory disorders (e.g., dysautonomia, diabetes insipidus, anhidrosis)
- Toxic ingestions (e.g., anticholinergics)
- Drugs, Vaccines.

B. Acute recurrent fever/periodic Fever

a. Viral infection**,** frequent or back-to-back minor viral illnesses in a young child

b. Periodic fever syndromes

- Cyclic neutropenia
- Periodic fever with aphthous stomatitis, pharyngitis, adenitis (PFAPA) syndrome
- Familial Mediterranean fever (FMF)
- TNF receptor-associated periodic syndrome (TRAPS)
- Hyper-immunoglobulinemia D syndrome (HIDS).

C. Chronic Fever (fever of unknown origin)

a. Infectious

- Viral infections (e.g., EBV, CMV, hepatitis viruses, arboviruses)
- Sinusitis
- Pneumonia
- Enteric infections (e.g., Salmonella)
- Abscesses (intra-abdominal, hepatic, nephric)
- Bone and joint infections (e.g., osteomyelitis, septic arthritis)
- Endocarditis
- HIV infection (uncommon)Tuberculosis (uncommon)
- Parasitic infections (e.g., malaria—uncommon)
- Cat-scratch disease
- Lyme disease (rarely causes chronic fever).

b. Noninfectious

- Inflammatory bowel disease
- Connective tissue disorders (e.g., juvenile idiopathic arthritis, systematic lupus erythematosus (SLE), acute rheumatic fever)
- Cancer (most commonly lymphoreticular malignancies such as lymphoma or leukemia but also neuroblastoma or sarcomas)
- Drugs
- Thermoregulatory disorders (e.g., dysautonomia, diabetes insipidus, anhidrosis)
- Pseudo FUO
- Factitious fever (e.g., factitious disorder imposed on another) [1].

4. Physiopathology

- Fever occurs in response to the release of endogenous pyrogenic mediators called cytokines (in particular interleukin-1 [IL-1]). Cytokines stimulate the production of prostaglandins by the hypothalamus; prostaglandins readjust and elevate the temperature set point.
- Fever plays an integral role in fighting infection and, although it may be uncomfortable, does not necessitate treatment in an otherwise healthy child. Some studies even indicate that lowering the temperature can prolong some illnesses. However, fever increases the metabolic rate and the demands on the cardiopulmonary system. Therefore, fever can be detrimental to children with pulmonary or cardiac compromise or neurologic impairment. It can also be the catalyst for febrile seizures, which although typically benign, are very

concerning to parents and must also be distinguished from more serious disorders (e.g. meningitis). [1]

III. Signs and symptoms

- In addition to an elevated temperature, you may experience the following symptoms:
  - Chills, feeling cold, shivering and shaking
  - Body aches and headaches
  - Fatigue (tiredness)
  - Sweating
  - Flushed complexion or hot skin
  - Tachypnea.
- Additional fever symptoms in babies and children may include:
  - Lack of appetite – not eating and drinking well
  - Earache or pulling at their ears
  - High-pitched crying
  - Fussiness
  - Paleness of flushness
  - Excessive thirst
  - Decreased urination.

IV. Diagnosis

1. History

- History of present illness:
  - Degree and duration of fever, method of measurement and drug-induced fever
  - Associated symptoms that suggest serious illness include poor appetite, irritability, lethargy, crying, vomiting, diarrhea, cough, difficulty breathing …
- Past medical history:
  - Previous fevers or infections and known conditions predisposing to infection (e.g., congenital heart disease, sickle cell anemia, cancer, immunodeficiency).
  - A family history of an autoimmune disorder or other hereditary conditions.
  - Vaccination history is reviewed to identify patients at risk of infections that can be prevented by a vaccine.
- Physical examination
  - Vital signs are reviewed
  - Temperature should be measured rectally in infants for accuracy. Any child with cough, tachypnea, or labored breathing requires pulse oximetry.
    - In ill-appearing children, blood pressure should also be measured. [1]
- Laboratory test
  - CRP are markers of inflammation.
    - A moderate elevation (20 to 50 mg/L) compatible with a viral condition or bacterial focus (bronchitis, rhinopharyngitis)
    - A clear elevation (>50 mg/L) should lead to a search for a bacterial focus or parenchymatous.
  - CBC provides several pieces of information.

- Hyperleukocytosis with polynuclear neutrophils mainly evokes a bacterial infection.
- The presence of non-segmented polymorphonuclear cells indicates an acute bacterial infection.
- A majority of lymphocytes are compatible with viral infection and a lymphocytosis comprising activated lymphocytes defines the syndrome mononucleosis.
- Sometimes, the presence of abnormal cells allows the diagnosis of hemopathy malign.

- Blood cultures make it possible to look for occult bacteremia, to establish the diagnosis of certain systemic infections (brucellosis, typhoid) and document bacteriologically, certain focal infections (osteomyelitis, pneumonia).
- ECBU and urine test strip look for the presence of nitrites or leukocyturia which leads to the search for a urinary infection.
- Lumbar puncture will be carried out well before the age of 6 months, in whom a Meningitis can have crude signs and the progression can then be rapid.
- Dipstick and Blood smear (searched for Plasmodium) if suspecting malaria.,
- Imaging examinations:
- Abdominal ultrasound should be done when there is a fever of bacterial origin is suspected and which has not been proven, which may in particular lead to the discovery nephritis or signs of pyelitis.
- Chest x-ray looks for focused alveolar opacity, opacities bronchial or interstitial, an abscess.
- X-ray of the sinuses is only indicated after the age of 3 to look for a maxillary sinusitis (Blondeau) or ethmoid sinusitis (Frontal). [4]

V. Management

- Surveillance:
- In the absence of signs of seriousness and identified infection, you must know how to wait and repeat the examination clinic (once or twice a day) and establish a thermal curve.
- Treatment
  - Physical Methods:
    - Undressing the child,
    - Fresh wraps
    - Lukewarm bath (body temperature - 1°C) are especially useful in an emergency if the temperature is very high and there is a significant risk of convulsion hyperthermic.
  - Antipyretic:
    - Paracetamol 40-60mg/kg/day, in 4 doses if necessary (orally, rectally, muscle or intravenous injection)
    - Ibuprofen 20-30mg/kg/day, in 2-3 doses if necessary (orally)

- ***Aspirin*** 50 mg/kg/day, in 4 doses if necessary (orally). It can make complications of Reye syndrome and is not recommended to use in case of dengue hemorrhagic fever.
- Diazepam 0.5 mg/kg/dose in case of convulsions (rectally).

- Etiological treatment:
  - Etiological treatment is based on anti-infectious agents that are chosen according to the type infection.
  - Finally, we will remind you that there is no indication for antibiotic therapy in the absence of infection identified. [4]

VI. Education

- Reduce fever by using:
  - Paracetamol (15mg/kg/dose) orally or rectally. "Avoid overdose"
  - Undress clothes
  - Cold bath
  - Encourage the child drink fluids to prevent dehydration
  - Monitor the child for serious signs (such as cold extremities, convulsion…)
- If the serious signs above are present, the child must be taken to the hospital to have the conformation for appropriate diagnosis and treatment. [4]

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HEAD INJURY

KROUCH Dila, NUON Neathvibol, CHAN Mardi

I. Key Facts

The priorities when assessing a child with head injury are to identify those with:

- Moderate to severe head injury who need immediate management, urgent investigation, and transfer.
- Mild head injury who can be immediately discharged home.
- Head injury who needs observation and/or neuroimaging.

II. Overview

1. Definition

A head injury is a broad term that describes of injuries that occur to the scalp, skull, brain, and underlying tissue and blood vessels in the head.

Head injuries are also commonly referred to as brain injury, or traumatic brain injury (TBI), depending on the extent of the head trauma.

2. Epidemiology

Traumatic brain injury (TBI) is one of the most important cerebral pathologies encountered nowadays, therefore, estimating the global incidence of TBI is importance. It is often referred to as the "silent epidemic" due to its contribution to global death and trauma-related disability. Each year there are about 500-800 new cases of TBI per 100,000 people, according to multiple studies from the United States and New Zealand.

Age-related traumatic brain injury differences demonstrate three main age groups with the highest prevalence:

- Early childhood (falls being the main cause)
- Late adolescence / early adulthood (road traffic accidents (RTAs) being the main cause)
- Elderly (falls being the main cause).

III. Assessment of severity of head injury

A. Primary survey and resuscitation [3], *see more Algorithm 1*

a. *Severity* [6]: Mild, moderate, and severe brain injuries all have symptoms that indicate their severity. The following table shows the symptoms of each categorization.

Table1.

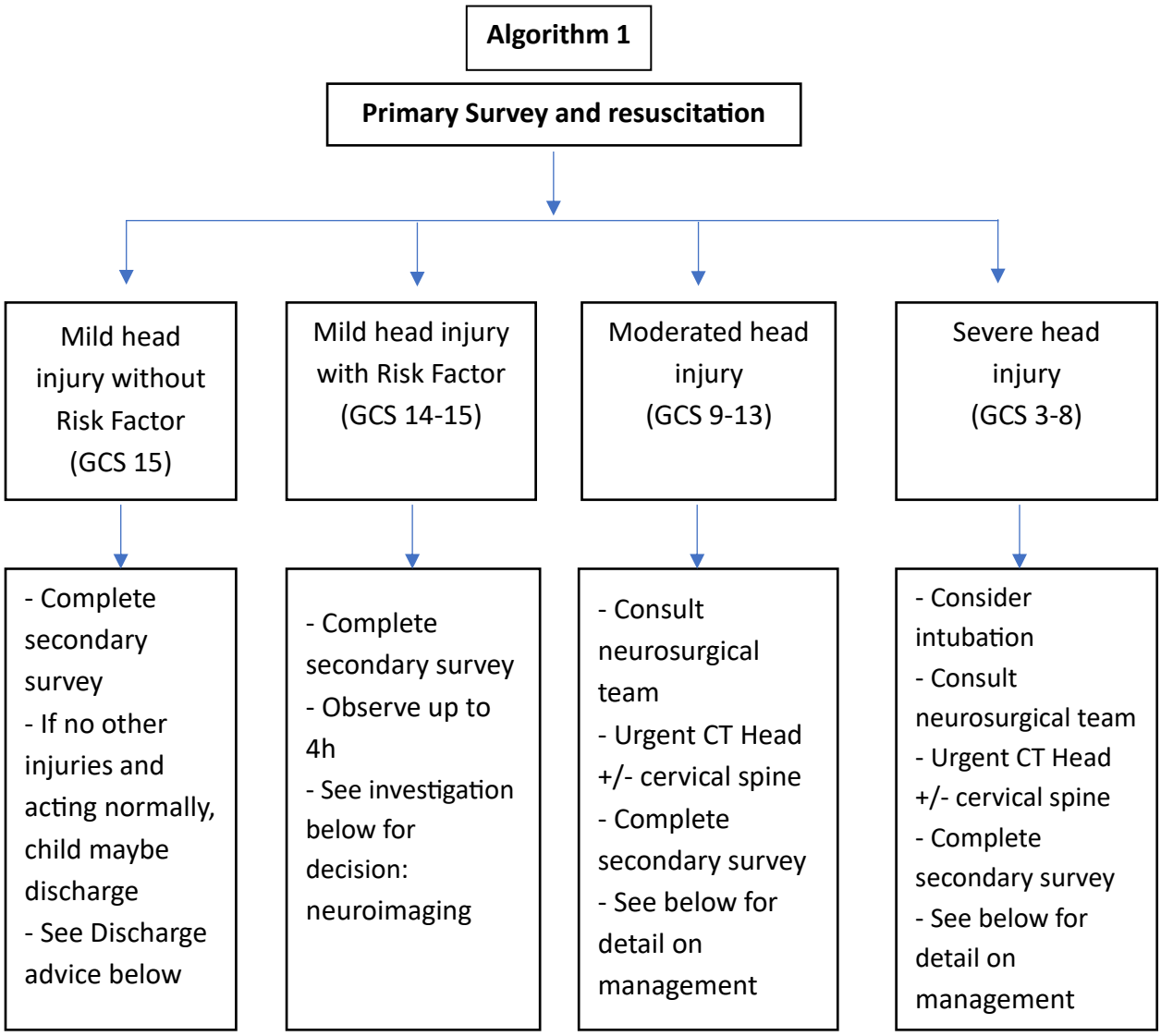
Mild brain injury	Moderate brain injury	Severe brain injury
1. Brief, if any, loss of consciousness **2.** Vomiting and Dizziness **3.** Lethargy **4.** Memory Loss	**1.** Unconsciousness up to 24 hours **2.** Signs of brain trauma **3.** Contusions or bleeding **4.** Signs of injury on neuroimaging	**1.** Unconsciousness exceeding 24 hours (coma) **2.** No sleep/wake cycle during loss of consciousness (LOC) **3.** Signs of injury appear on neuroimaging tests

b. *Risk factors* [7]

- Age: young and elderly, children, especially newborns to 4-year-olds, young adults, especially those between ages 15 to 24
- Alcohol use
- Playing certain sports: football, basketball, ice hockey

c. Severe mechanism

- motor vehicle accident with patient rollover
- pedestrian or cyclist struck by motor vehicle
- falls of ≥1 m (<2 yr)
- fall >1.5 m (>2 yr)
- head struck by high impact object.


Algorithm 1
Primary Survey and resuscitation
Mild head injury without Risk Factor (GCS 15)
Mild head injury with Risk Factor (GCS 14-15)
Moderated head injury (GCS 9-13)
Severe head injury (GCS 3-8)
- Complete secondary survey
- If no other injuries and acting normally, child maybe discharge
- See Discharge advice below
- Complete secondary survey
- Observe up to 4h
- See investigation below for decision: neuroimaging
- Consult neurosurgical team
- Urgent CT Head +/- cervical spine
- Complete secondary survey
- See below for detail on management
- Consider intubation
- Consult neurosurgical team
- Urgent CT Head +/- cervical spine
- Complete secondary survey
- See below for detail on management

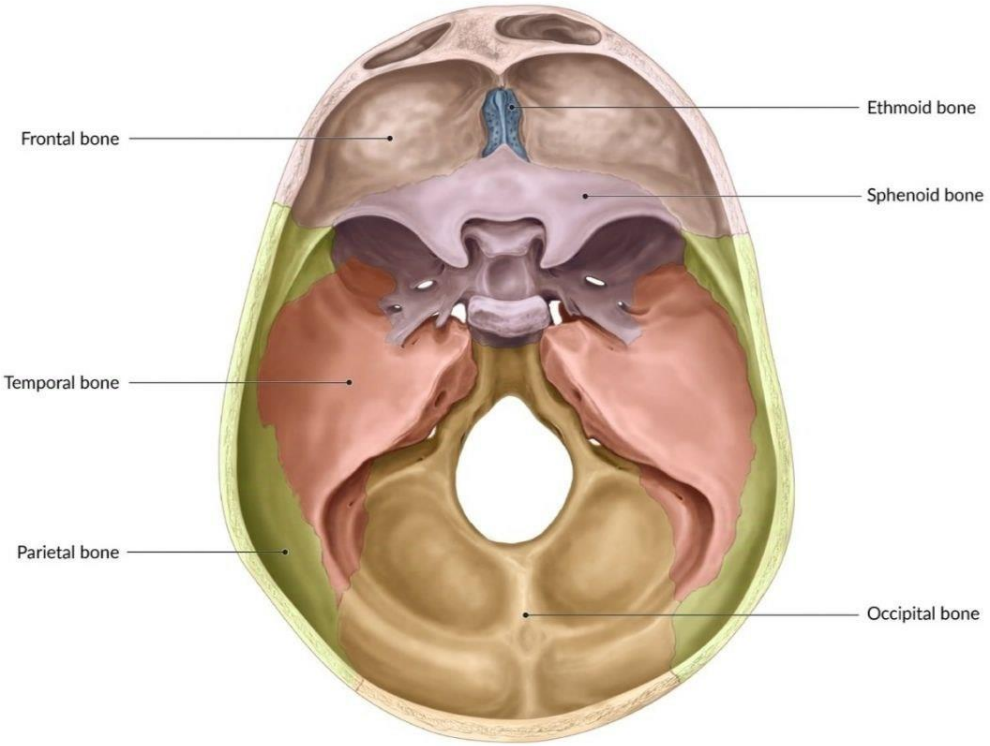
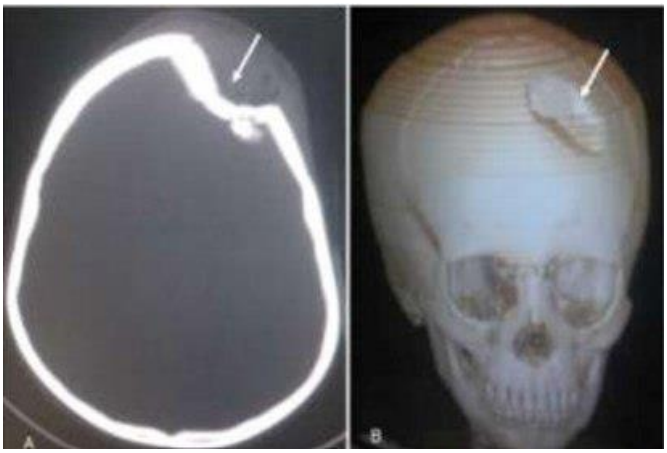
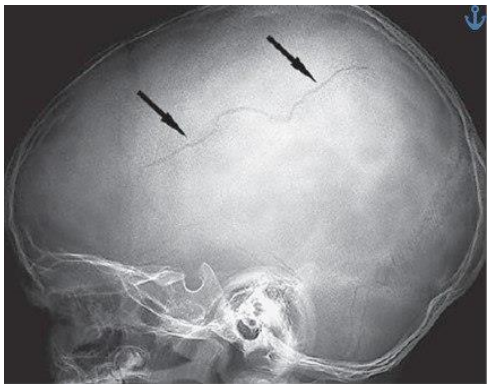


Figure 1: *Head Skull bone Anatomy*





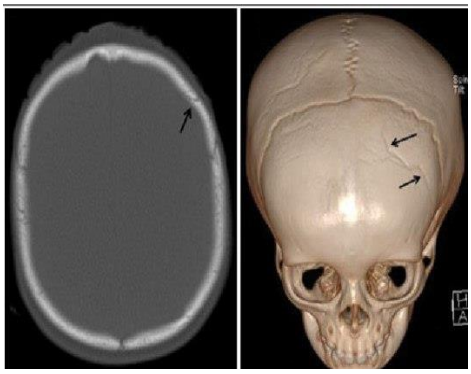
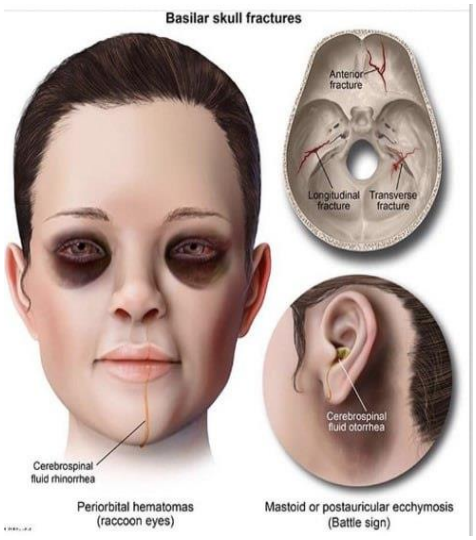


Figure 2: *skull fractures*



Raccoon eyes

Figure 3: *Signs of fractured base of skull*

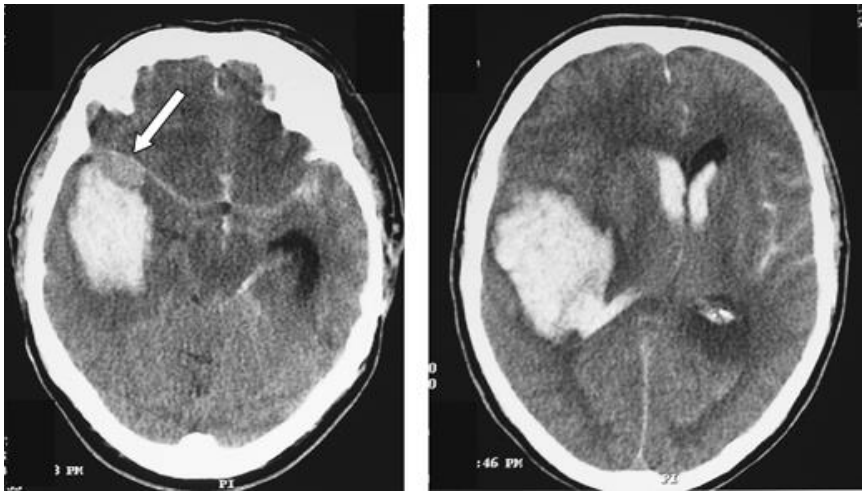


Figure 4: *Subarachnoid hematoma*

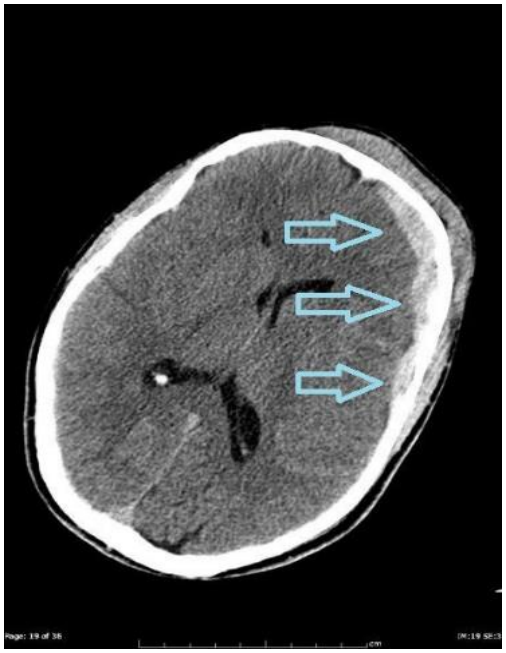


Figure 5: *Subdural hematoma*

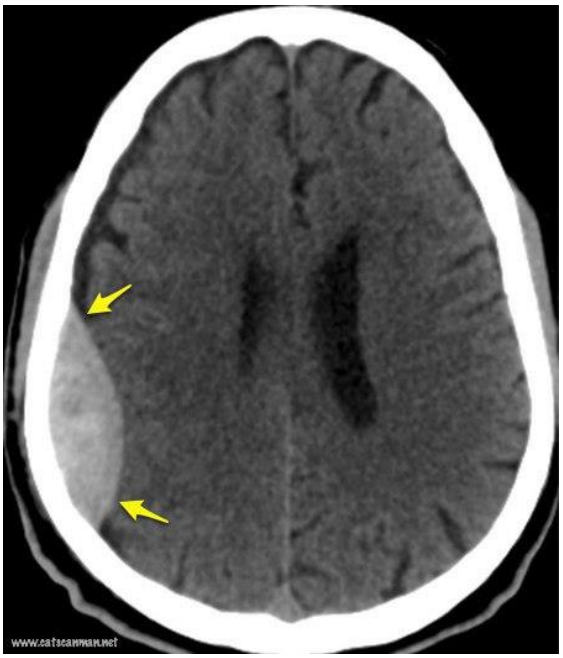


Figure 6: *Epidural hematoma*

Table 2*: Glasgow coma scale (GCS)* [4]

<4 years		≥4 years	
Response	**Score**	**Response**	**Score**
Eye opening		**Eye opening**	
Spontaneously	4	Spontaneously	4
To verbal stimuli	3	To verbal stimuli	3
To pain	2	To painful stimuli	2
No response to pain	1	No response to pain	1
Verbal response		**Verbal response**	
Alert	5	Orientated and converses	5
Less than usual words, spontaneous irritable cry	4	Confused and converses	4
Cries only to pain	3	Inappropriate words	3
Moans to pain	2	Incomprehensible sounds	2
No response to pain	1	No response to pain	1
Motor response		**Motor response**	
Spontaneous or obeys verbal commands	6	Obeys verbal commands	6
Localizes to pain or withdraws to touch	5	Localizes to stimuli	5
Withdraws from pain	4	Withdraws to stimuli	4
Abnormal flexion to pain (decorticate)	3	Abnormal flexion to pain (decorticate)	3
Abnormal extension to pain (decerebrate)	2	Abnormal extension to pain (decerebrate)	2
No response to pain	1	No response to pain	1
Total scores: 3-15			
- Mild head injury from 14-15 - Moderated head injury 9-13 - Severe head injury 3-8			

B. Secondary survey [4]

Table 3. *Secondary survey*	
Head and face	- Face, scalp and skull: bleeding, lacerations (to suggest skull fracture), ("Racoon eyes"): may indicate base of skull fracture - Eyes: Palpate bony margins of orbit for fracture - Ears: bleeding, blood behind tympanic membrane (suggestive of base of skull fracture) - Nose: bleeding, septal hematoma, CSF leak, palpate for bony crepitus or deformity - Mouth: wounds to the lips, gums, tongue, or palate - Teeth: subluxed, or fractured teeth - Jaw: identify pain, or malocclusion
Neck	Inspect neck whilst maintaining manual in-line stabilization of spine. Examine anterior neck for blunt or penetrating trauma by looking/feeling for the following (TWELVE-C): - Tracheal deviation - Wounds - Emphysema (subcutaneous) - Laryngeal tenderness/crepitus - Venous distension - Esophageal injury - Carotid hematoma/bruits/swelling
Chest	- Observe of asymmetrical or paradoxical chest wall movement - Inspect for signs of injury such as bruising, wounds - Palpate for bony tenderness over ribs, subcutaneous emphysema
Abdomen	- Inspect for bruising, abdominal distension - Palpate for signs of peritonism - Palpate for tenderness over the liver, spleen, kidneys and bladder
Limbs	- Inspect for wounds, bruising, open fractures, burns, abrasions - Feel for soft tissue and bony tenderness or swelling, joint movement and stability - Examine pulses - Examine sensory and motor function of any nerve roots or peripheral nerves that may have been injured
Back and spine	- Inspect entire length of back and buttocks - Inspect anus when indicated - Palpate then percuss spine for tenderness - Palpate scapula and sacroiliac joints for tenderness

IV. Paraclinical examination

1. Neuro-imaging:

- For children with mild head injury, a decision about whether to image should be based on the presence or absence of risk factors

- Indications for neuroimaging may be present on initial assessment, or may developed during the period of observation.

Table 4.

Definite indications	Relative indications (if more than one, observe child and consider neuroimaging)
- Any moderate or severe head injury (GCS ≤13) - Focal neurological deficit - Signs of base of skull fracture - Palpable skull fracture - Suspected non-accidental injury - Post-traumatic seizure - Persistent signs of altered mental status (agitation, drowsiness, repetitive questioning, slow response to verbal communication)	- GCS persistently 14 - Severe mechanism of injury - History of loss of consciousness - Headache - Vomiting - Non-frontal scalp hematoma (<2 years)

2. Neuro-imaging for children with special conditions

Children with any of the following conditions, although not at increased risk of intracranial injury, require greater consideration of neuroimaging:

- Age <6 months
- Bleeding disorder, or taking either anticoagulation or anti-platelet therapy
- Immune thrombocytopenia
- Ventriculoperitoneal shunt
- Neurodevelopmental disorders
- Drug or alcohol intoxication

3. Type of neuroimaging

- Plain skull X-ray or head ultrasound should not be performed instead of a CT
- CT scan or MRI may be equivalent in terms of clinical utility, but should only be considered in settings where it can be performed quickly and safely.

V. Management

1. Mild head injury without other risk factors

GCS 15 and meets the following criteria: no concern about abusive head trauma, age over 6 months, no special conditions (bleeding tendency, neurodevelopmental disorder, VP shunt), non-severe mechanism.

- If based on history and examination there are no other clinical concerns, the child has
- returned to normal conscious state, and is acting normally, they may be discharged to the care of their parents

- Treat pain with simple analgesia
- Ensure discharge and advice given to parents

2. Mild head injury with other risk factors

- Child should be observed for up to 4 hours post injury, with:
  - Neurological observations (conscious state, PR, RR, BP, pupils, and limb power) for the first 2 hours
  - One-hourly neurological observations there-after
- Treat pain with simple analgesia
- Consider anti-emetics
- A persistent headache, ongoing vomiting, GCS of 14 or persistent altered mental status requires further observation and likely investigation.
- The child may be discharged home if there is return to normal conscious state for at least one hour, is acting normally, and they can tolerate oral fluids

3. Moderate head injury

- Consult a neurosurgeon for advice
- Urgent CT of head (and consideration of imaging of c-spine if relevant)
- Ensure early specialist consultation

4. Severe head injury

- Look for signs of severe head injury which may include presence of focal neurological deficit, signs of increased intracranial pressure or signs of basal skull fracture
- The initial aim of management of a child with a severe head injury is prevention of secondary brain damage
- The key aims are to maintain oxygenation, ventilation, and circulation, and to avoid rises in intracranial pressure (ICP)
- Urgent CT of head (and consideration of c-spine imaging if relevant)
- Ensure early neurosurgical consultation
- Cervical spine movement should be minimized until formal assessment occurs.
- Do not give steroid to the victim of head injury.

a. Consider intubation if:

- Child unresponsive or not responding purposefully to pain
- GCS persistently <8
- Loss of protective laryngeal reflexes
- Respiratory irregular or suspected hypoventilation
  - Avoid hypotension, hypoventilation and hypoxia during intubation and minimize cervical spine movement
  - If possible, a neurological examination should be performed before intubation and any motor deficits or cranial nerve signs documented
  - Intubation should be performed by the most skilled clinician available. For children requiring mechanical ventilation:
- Analgesia and sedation with morphine and midazolam should be administered by careful titration. Children with head injury are often more sensitive to opioids
- Consider muscle paralysis (e.g. pancuronium or vecuronium)

- Maintain circulation and cerebral perfusion
- Ensure adequate blood pressure with isotonic fluids (e.g., 0.9% sodium chloride) or inotropes if necessary

b. Treat signs of raised intracranial pressure

In consultation with neurosurgical team, consider measures to decrease intracranial pressure:

- Maintain head position: 30 degrees head up (after correction of shock) with head in midline position to help venous drainage
- Ventilate to PaCO2 35-40 mmHg or PaO2 100mmHg (saturation >95%)

- Consider hypertonic saline (sodium chloride 3% 3 mL/kg IV over 10-20 min) or 20% mannitol (0.25-0.5 g/kg IV over 20-30 min) duration 24-48h
  - Parameter surveillance for mannitol:
  - urine output 1-2ml/kg/h, if less than 1ml/kg/h can combine with furosemide dose 0,1mg/kg/dose
  - kaliemia (hypokaliemia) cause by osmotic diuresis
- Associated with Thiopental IVSE (**intravenous via infusion pump)**: duration 48h
  - With pulmonary contusion: dose 0.5mg/kg/h
  - Without pulmonary contusion: dose 1-2mg/kg/h
  - Morphine IVSE, dose 20-40mcg/kg/h.

c. Control seizures

- Treat with benzodiazepines to immediately control seizures
- Give midazolam use in IVSE with a maintenance loading dose (1 to 5 mcg/kg/mn)
- Seek neurosurgical advice early
- Observe closely for subsequent hypotension or hypoventilation and manage appropriately.

d. Other measures:

- Maintain normal sodium by keeping Na+ between (145-155mmol/L) and glucose levels
- Maintain normothermia, give antipyretic agent in systematic
- Check for coagulopathy.

VI. Follow up

1. Consider consultation with local pediatric or pediatric neurosurgical team when:

- Failure to return to normal within 4 hours
- Suspected child abuse
- Any child with a ventricular shunt
- Any child with a bleeding disorder, or who is taking anticoagulant or anti-platelet therapy (discuss with pediatric haematologist).

2. Consider transfer to a tertiary centre when

- All severe head injuries
- Deteriorating conscious level (especially motor response changes)
- Focal neurological signs
- Seizure without full recovery
- Definite or suspected penetrating injury
- Cerebrospinal fluid leak
- Child requiring care beyond the comfort level of the hospital.

3. Consider discharge when

- The child is acting normally for at least one-hour, normal neurological examination and can tolerate fluids
- There are no other factors warranting admission or longer observation (eg other injuries or underlying medical concerns, drug and alcohol intoxication, social factors, possible abusive head injury).

4. Parent advice and follow-up

- Ensure the parents have clear instructions regarding the management of their child at home, and when to seek medical attention
- Children discharged following a mild to moderate head injury should consider follow-up within 1 to 2 weeks to assess post-concussive symptoms
- Advise parents that children with anything other than a trivial head injury may take up to 4 weeks to recover, and graded return to activity is recommended.

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CARDIAC BERIBERI OR SHOSHIN BERIBERI

HINH Sally, Miliya Thyl, LONGTRI Patric, EANG Habsreng

I. Key Facts

- Infantile beriberi, a potentially fatal disorder caused by thiamine deficiency, is often viewed as a disease confined to history in regions of the world with predominant white rice consumption. [1]
- Recent case reports have highlighted the persistence of thiamine deficiency as a cause of infant mortality in South and Southeast Asia. [1]
- Poor dietary diversity, food preparation and cooking practices and traditional post-partum food restrictions likely play a role in these high-risk regions.[1]
- A study in Cambodia reported that 27% of reproductive-age women and 15% of children 6 months to 5 years old had thiamin deficiency; the highest prevalence of deficiency (38%) was among infant age 6-12 months.[3]

II. Overview

1. Definition

- Infant Beriberi, a disease caused by the mother's thiamine deficiency. The heart of infant is primarily affected and these infants have classical heart failure and sudden death. [5]
- Shoshin syndrome is a rare fulminating heart failure caused by thiamine deficiency. In Japanese “sho” means acute damage and “shin” means heart. [6]

2. Cause [5]

- Beriberi can occur in breast-fed infants when the mother’s body is lacking in thiamine.
- The condition can also affect infants who are fed unusual formulas that don’t have enough thiamine.
- Beriberi may be found in mother, whose diet consists mainly of polished white rice, which is very low in thiamine because the thiamin-bearing husk has been removed.
- It can also be seen in mother chronic alcoholics, arsenic poisoning.
- A rare condition known as genetic beriberi is passed down through families. People with genetic beriberi lose the ability to absorb thiamine from foods.
- The peak prevalence of this form occurs in fat breastfed babies of 2-12 months with predominant pick of 3 months of age.

3. Physiopathology [2]

- Thiamine is present in the body as free thiamine, as well as in several phosphorylated forms:
- Thiamine monophosphate (ThMP), Thiamine diphosphate (ThDP), and Thiamine triphosphate (ThTP).
- ThDP, also called thiamine pyrophosphate, is the metabolically active form, constituting some 80% of total body thiamine.
- ThDP is an essential cofactor in multiple enzyme complexes involved in the metabolism of carbohydrates and amino acids.
- These enzyme complexes include the pyruvate dehydrogenase complex (which converts pyruvate to acetyl-CoA), the alpha-ketoglutarate dehydrogenase complex (which converts alpha-ketoglutarate to succinyl-CoA), and the branched chain alpha-keto acid dehydrogenase complex (which converts branched chain alpha-keto acids to the corresponding acyl-CoAs).
- It seems that the alpha-ketoglutarate dehydrogenase is most sensitive to thiamine deficiency, and reduced activity of this enzyme complex can quickly lead to reduced ATP synthesis, oxidative damage, and, ultimately, cell death. (Figure 1)

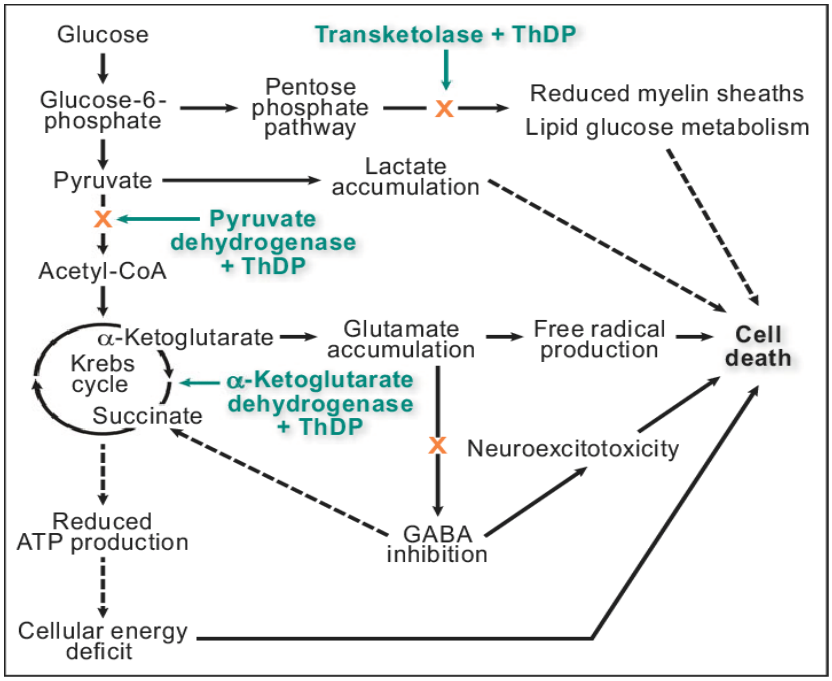

Figure 1. *The three thiamine-dependent enzymes and their role in the pathogenesis of cell death in thiamine deficiency*.[2]

- **Wet beriberi** affects the cardiovascular system and is divided into acute and chronic form:
  - Acute beriberi or Shoshin beriberi, the predominant injury to the heart, and rapid deterioration occurs because of the heart inability to maintain function.
  - Chronic wet beriberi with high-output cardiac failure has 3 stages:
    - Initially, peripheral vasodilatation occurs, yielding high-output cardiac failure.
    - Then, the progression of vasodilation is perceived by the kidney as a relative loss of volume. The ensuing activation of the renin angiotensin system produces greater salt and water retention.
    - Consequently, further fluid overload results in peripheral edema, and pulmonary effusion. [3]

4. Risk factors:

a. High risk mother:

- Low socio-economic status
- Peripheral edema and tender sole
- Intermittent parenthesis in the hands and feet during and after pregnancy without
- Subjective or clinical evidence of neurological deficit.
- Excessive alcohol intake

b. Infant present history

- Breast feeding from high-risk mother.
- Sibling died with the same symptoms.

III. Signs and symptoms [5]

Urgent clinical sign and symptoms:

- Acute respiratory distress and characteristic hoarse voice (Aphonic beriberi)
- Lethargy or drowsiness
- Shortness of breath (clear lung) with or without shock
- Central and peripheral cyanosis
- Liver enlarged and low urine output
- Convulsion
- Poor feeding.

IV. Diagnosis [3]

1. Laboratory test:

- The best rapid, best diagnosis test for beriberi in urgent situation, is observing a clinical response to administration of IV Thiamine (a few hours duration).
- Elevated measurement of following substance because thiamine work as coenzyme:
  - Pyruvate
  - Alpha ketoglutarate
  - Lactate
  - Glycosylate

2. Additional investigation:

- Urinary thiamine
- Thiamine metabolites (thiazole or pyrimidine)
- Methylglyoxal value

The most reliable test in-vitro: whole blood or Erythrocyte transketolase activity (increase activity after add thiamine). However, it is not point of care test.

3. Imagery services [5]

- Chest radiography: Cardiomegaly (mean cardiothoracic ratio 56,1%)
- Heart ultrasound:
  - Cardiomegaly (right ventricular hypertrophy and dilatation)
  - Pulmonary arterial hypertension
  - Tricuspid valve regurgitation.

4. Differential diagnosis [3]

- Congenital heart disease:
  - Cyanotic or non-cyanotic,
  - Murmur heart sound,
  - Desaturate oxygen despite supply oxygen.
  - Clubbing nail
- Anemia:
  - Pale or jaundice conjunctiva,
  - RBC or Hemoglobin decreased
- Infantile kwashiorkor:
  - History of porridge feeding,
  - Generalize edema,
  - Normal heart exam
- Pediatric Diabetic ketoacidosis (DKA):
  - Polydipsia, polyphagia,
  - Polyuria, lost body weight,
  - Hyperglycemia
  - ketone in urine.

V. Complications [3]

Unrecognize child with thiamine deficiency, may develop to heart failure state then sudden death.

VI. Treatment [5]

- If patient is emergency condition, follow the resuscitation in these clinical guidelines for pediatrics.
- In suspected of thiamine deficiency, prompt administration of parenteral thiamine is indicated.
- Recommended dose vitamin B1: 50 mg IV/IM q24hr for at least 3 to 7 days.
- Possible switch to PO treatment when condition is available
  - If enfant is breast feed: Treat mother with Thiamine 100mg PO QD for 1month.

- If the child has been weaned: Treat the child with Thiamine 10mg PO QD for 1 month.

VII. Prevention and Education [5]

Population at risk must be educated regarding:

- The diversification of diet.
- The incorporation of foods rich in thiamine (liver, brown rice, green leaves, and Potatoes).
- Proper food preparation (shorter cooking time for vegetables, reduction in amount of rice washing prior to cooking).
- The value of whole grains.
- Avoidance of alcohol.
- Thiamine supplementation.

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Chapter II: Respiratory diseases

ACUTE PHARYNGITIS IN CHILDREN

MILIYA Thyl, LOV Ke, LANG Bunlay, NGETH Pises, NGOUN Chanpheatra

I. Key Facts

- Pharyngitis is common diagnoses in pediatric practice. pharyngitis is reported to account for 2% to 5% of primary care office visits. [1]
- Pharyngitis (sore throat) is a very common condition and one of the main causes of antibiotic overuse in primary health.
- Most pharyngitis is caused by viruses and does not require antimicrobial treatment
- Streptococcus pyogenes (Group A streptococcus) is the most common bacterial cause of pharyngitis and tonsillitis
- Clinically guided testing for GAS is important to avoid unnecessary antimicrobial use.

II. Overview

1. Definition

Pharyngitis is commonly defined as an inflammation of the pharynx characterized by sore throat and painful swallowing.

2. Causes

- More than 80% cause by respiratory virus such as rhinovirus, adenovirus, SARS-CoV2, and Epstein Bar Virus (EBV) etc.;
- Group A Streptococcus (GAS) account about 5% of the bacteria case. Diphtheria and acute toxoplasmosis should consider in individual present
- Other cause of non-infectious also mimic the same clinical such as allergy, toxins, traumatism, and malignancy.

3. Risk Factor

There is no specific no risk factor identify because the likelihood of getting those viruses is depend on their contact. While the below factors are some degrees to make the individual an increase risk such as

- Exposure to inhaled toxins (exhaust, cleaning fluids)
- Environmental allergies
- Smoke
- Immunocompromised
- Increased stress
- Age (5-15 years).

4. Pathophysiology

Viruses and bacteria responsible for pharyngitis gain access to the mucosal cells of the pharynx through different mechanisms and start replicating in these cells. Damage is caused to the cells where pathogens are replicating. Streptococcal protein/toxins facilitate local invasion and may lead to complications later on.

III. Signs and symptoms

- Pharyngitis is characterized by sore throat and painful swallowing. Typical accompanying signs and symptoms can vary depending on the aetiology.
- If the cause is viral, symptoms match those of a viral upper respiratory tract infection, and cough, headache and myalgia are likely to be present.
- If the cause is bacterial, a more severe presentation is usually seen, with fever (≥ 38.0 °C), tender cervical lymph nodes and pharyngeal exudates. Several clinical scoring systems have been developed to identify patients with higher likelihood of pharyngitis being caused by Streptococcus pyogenes (see the next section)
- Score systems, like the Cantor Clinical scoring system, help differentiate between viral and bacterial infections to guide antibiotic treatment (Table1). However, those systems have low specificity and can lead to unnecessary antibiotic use as well.

However, even with the highest score of 4, the probability of an infection cause by Streptococcus pyogenes is only 50%. [2]

Table 1. *Cantor score for the clinical assessment of pharyngitis*

Relevant sign and symptoms	**Points**
Fever >38.0°C	1
No cough	1
Tender anterior cervical lymphadenitis	1
Tonsillar exudates	1
Total score	Likelihood of Streptococcus pyogenes infection (%)
0	
1	
2	
3	
4	
Interpretation Cantor score	
Cantor score 0-1-2	- Streptococcus pyogenes pharyngitis unlikely - Give symptomatic treatment only
Cantor score 3-4	- Score suggest of Streptococcus pyogenes pharyngitis

IV. Diagnosis

1. Laboratory

When pharyngitis is suspected, blood tests are not usually needed unless a complication is thought to be present. The choice of whether microbiological tests are helpful and which to consider is base of the likelihood of *Streptococcus pyogenes* infection. In general, most guidelines prefer rapid test over the culture because they give result more quickly. However, in many setting in Cambodia no tests are available.

2. Imaging

When pharyngitis is thought to be the cause of clinical symptoms, imaging is usually no required unless a complication is suspected.

3. Differential diagnosis:

- Diphtheria
- Epiglottitis
- Hand foot and mouth disease
- Peritonsillar Abscess
- Herpes Simplex Virus (HSV)
- Retropharyngeal Abscess

V. Complications

- Suppurative complication
  - Tonsillo-pharyngeal cellulitis or abscess.
  - Otitis media.
  - Sinusitis.
- Non-suppurative complications
  - Acute Rheumatic fever
  - Post-streptococcal reactive arthritis

- Scarlet fever
- Streptococcal toxic shock syndrome
- Acute glomerulonephritis Suppurative Complication.

VI. Treatment and management

1. Initial treatment:

Most cases of pharyngitis are of viral origin and do not benefit from antibiotics. In most cases, including those of bacterial origin, symptoms resolve within a week. Symptomatic treatment with oral analgesics and/or antipyretics, such as paracetamol and/or ibuprofen may be helpful.

Table2. *Medicines to consider for fever and pain control in pharyngitis*

Medicine name	Dose and frequency	Purpose
Paracetamol (acetaminophen)	10 – 15 mg/kg given every 6 hours	- Pain control/antipyretic treatment - Use careful in patients with hepatic impairments
Ibuprofen	5 – 10 mg/kg given every 6 to 8 hours	- Pain control/antipyretic treatment - Not for children less than 3 months

2. **Empirical antibiotic treatment** usually given if the likelihood of Streptococcus pyogenes is high (e.g., Cantor score 3 -4). The rational is to prevent rheumatic fever or its recurrence. [3]

Table 3. *Empiric antibiotic treatment in patient with a high likelihood of Streptococcus pyogenes pharyngitis*

Antibiotic of choice	**Dose/ frequency**	**duration**
First line		
Phenoxymethylpenicillin (as potassium):	10-15 mg/kg/dose (16 000-24 000 IU/kg/dose) q6-8h ORAL	**5 – 10 days**
Amoxicillin	80-90 mg/kg/day ORAL	**5 – 10 days**
Second line		
Cefalexin	25 mg/kg/dose q12h ORAL	**5 days**
Clarithromycin	7.5mg/kg/dose q12h ORAL	**5 days**

VII. Education

- rest and enough hydration at home
- Hand washing is an essential and highly effective way
- Alcohol-based hand rubs are a good alternative for disinfecting
- Vaccination is the best way to prevent influenza.

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Acute Sinusitis in children

MILIYA Thyl, LOV Ke, LANG Bunlay NGETH Pises, NGOUN Chanpheaktra

I. Key Facts

- Sinusitis, or infection of the paranasal sinuses, is common in children, affecting 5–13% of viral upper respiratory tract infections (URTIs)
- Children typically develop 5–10 URTIs per year, and sinusitis can occur at any age. It's most common in children 4–7 years old, and rare in children under (1)
- Sinusitis is a common problem in pediatric primary care. Symptom can last for long time (up to 4 weeks)
- Antibiotic are not needed in the great majority of cases.

II. Overview

1. Definition

- Acute sinusitis is a symptomatic inflammation of the paranasal sinuses and nasal cavity. Most cases occur as a complication of a viral upper respiratory tract infection (e.g., a common cold caused by respiratory viruses such as rhinovirus) and symptoms can last up to 4 weeks. Acute sinusitis can also be associated with asthma, allergic rhinitis, smoking or exposure to smoke. This guidance applies mainly to maxillary sinusitis as this is the most common clinical condition.
- In children a symptomatic inflammation of the paranasal sinuses and nasal cavity. Much less common than in adults because sinuses are not fully developed (figure 1) [2]

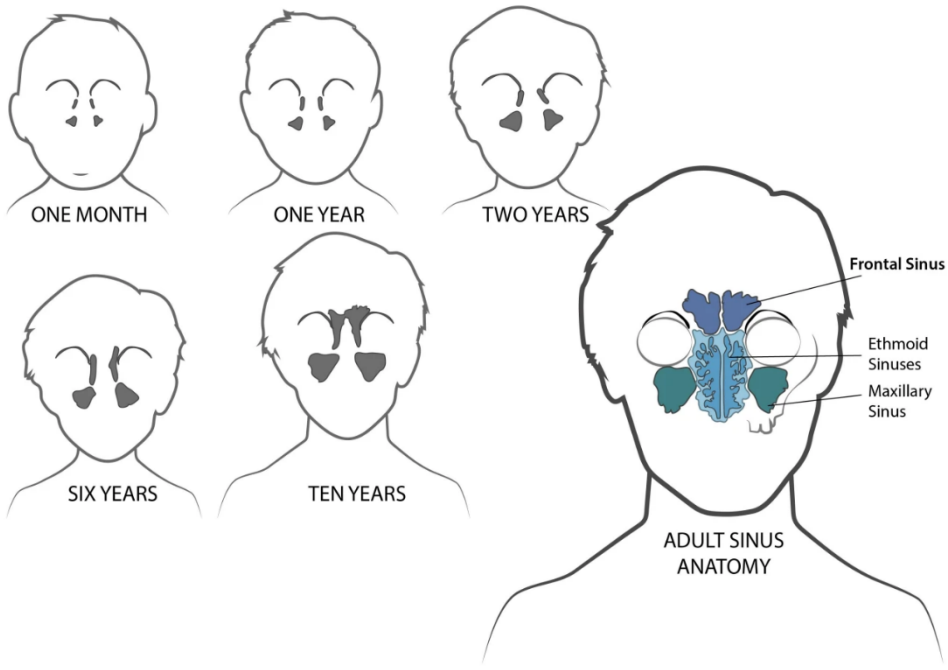

Image 1. *Normal Sinus development: illustrate showing development of the sinuses from one month to adulthood.* *Copyright ©2015 EBSCO Information Services.*

2. Etiology

- Acute sinusitis is usually caused by respiratory viruses; only a small percentage (usually less than 2%) of cases are complicated by bacterial infection (Table 1). [3]

Table1.

Respiratory virus (most cases)	Bacteria (Rarely)
- Influenza virus (A and B) - Respiratory syncytial virus (RSV) - Parainfluenza virus - Rhinovirus - Coronavirus including (SARS-CoV-2) * - Other respiratory viruses	- Streptococcus pneumoniae - Haemophilus influenzae - Very rarely - Moraxella catarrhalis - Streptococcus pyogenes (group A streptococcus) - Staphylococcus aureus

**SARS-CoV-2: severe acute respiratory syndrome coronavirus 2. About 98% of case are caused by respiratory viruses.*

- Rhino-orbital mucormycosis is a severe fungal infection that is primary affected immunocompromised individual. This topic will be explicitly in another section and will not be included here.

3. Physiopathology

Nasal congestion, usually triggered by an infection of the upper respiratory tract, can lead to obstruction of the sinus ostia with consequent hypoxia of the sinuses and mucus retention. Mostly the maxillary and the anterior ethmoid sinuses are involved. The inflammatory response that develops produces the signs and symptoms of acute sinusitis.

III. Signs and symptoms

- Clinical presentation acute sinusitis in children is similar to those of virus upper respiratory infection. Children six years old or younger should be based on criterial (history taking and physical examination) to presumptive sinusitis. In older patient, imaging studies maybe necessarily to confirm diagnosis.
- The major symptom presentation including (severity score)
  - Nasal congested or obstruction
  - Purulent OR discolored nasal OR post - nasal discharge
  - Headache or facial pain
  - facial pain on pressure
  - Persistent fever or temperature ≥ 39 Cº
  - Sign and symptom are lasting more than 10 days without clinical improvement

IV. Diagnosis

1. Sinusitis in children usually a clinical diagnosis not needed microbiology test and other laboratory tests
2. Imaging is usually not needed unless a complication OR an alternative diagnosis is suspected
3. Differential diagnosis
   - Viral Upper Respiratory infection (URTI)
   - Allergic rhinitis
   - Migraine
   - Nasal foreign body
   - Dental disease

V. Complications

Child with untreated bacterial Sinusitis is at risk for serious complications. Complications may result from **orbital** or **intracranial extension**; orbital complications are most common (Table2). The exact rate of complications of acute bacterial sinusitis is unknown, but they are estimated to occur in approximately 5 percent of patients hospitalized for sinusitis. [4,5]

Table 2.

Orbital complication	Intracranial complication
- Preseptal cellulitis - Orbital cellulitis - Orbital abscess	- Meningitis - Brain abscess - Subdural abscess - Osteomyelitis of the frontal bone with subperiosteal abscess (Pott puffy tumour)

VI. Treatment

Treatment is to improve symptoms, but antibiotics have minimal impact on symptom duration in most cases

- Symptomatic treatment includes antipyretic and analgesic medications, nasal irrigation with a saline solution and topical intranasal glucocorticoids or decongestants
- Most guidelines recommend using disease severity (age, duration and intensity of symptoms) to direct treatment. [6]

Table 3: Empirical antibiotic treatment of choice

Antibiotic	Dose/frequency/route	duration
Amoxicillin	80 – 90 mg/kg/day divide 2 time per day orally	7 to 10 days
Co-amoxiclav (4:1 ratio) [b]	80 – 90 mg/kg/day divide 2 time per day orally	
Ceftriaxone	80 mg/kg/ one per 24 hours IV	If the first choice for severe complicated sinusitis which present of protrusion or cannot tolerance to PO.

Maximum dose 2000 mg/dose for amoxicillin and co-amoxiclav

[b] Co-amoxiclav at a ratio of 4:1 should be used to ensure there is sufficient clavulanic acid: 20mg amoxicillin/5mg clavulanic acid per kg.

VII. Prevention and education

Prevention of sinusitis is based on the prevention of upper respiratory tract infections. All strategies (e.g. hand and respiratory hygiene, influenza, pneumococcal and COVID-19 vaccines) that help prevent upper respiratory tract infections could be useful in preventing sinusitis, including vaccination against Streptococcus pneumoniae and Hemophiles influenzae type b for all children worldwide (35,36). For countries considering vaccination programs for influenza, vaccination of high-risk groups could be considered, for example, children aged 6 months to 5 years. [7]

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CROUP (LARYNGO-TRACHEO-BROCHITIS)

SENG Soputhirith, KITH Daronic, LEK Yat, KIM Ang

I. Key Facts

Croup is inflammation of the upper airway, larynx and trachea caused by viral infection. It is most commonly seen in children <6 years old with the peak incident between the age of 6 months to 3 years old. In the United State, there are approximately 350,000 to 400,000 young children visits Emergency Department each year, accounting for 1.3 percent of all ED visits. Boy is more affected than girl with reported male: female ratios ranging from 1.4:1 to 2:1. [1]
Although croup is usually a mild and self-limited illness, significant upper airway obstruction and respiratory distress can occur.

II. Overview

1. Definition

The term Croup (laryngotracheobronchitis) refers to viral infection of the larynx, glottic and subglottic regions that are characterized by barking cough, inspiratory stridor, hoarseness and respiratory distress. [2]
Spasmodic croup occurs most commonly in the evening or nighttime. The child awakens at night to cough with a characteristic barking, noisy inspiration, and respiratory distress and get better in the next morning. Spasmodic croup might represent more of an allergic reaction to viral antigens rather direct infection. However, the exact pathogen is still unknown. [2]

2. Etiology

Parainfluenza viruses (type 1,2,3) are the most common cause of viral croup. Type 1 and 2 are responsible of hospitalization cases. Whereas Parainfluenza type 3 is less more common, but may cause more severe disease than others.[3]
Other viruses including RSV, Adenoviruses, Influenza, Rhinoviruses, enteroviruses (especially coxsackie types A9, B4, and B5 and echovirus types 4, 11, and 21), herpes simplex virus and SARS-CoV-2 are also found to be the causative agents. [1]

3. Pathogenesis

Viruses are spread through either direct inhalation from cough or sneeze, or by contaminated hands. The primary ports of viral entry are the nose and nasopharynx. The infection spreads to involves the larynx and trachea. The viral infection triggers an immune response, leading to inflammation and swelling of the mucous membranes lining the upper airways.
Inflammation and edema are mostly pronounced in the subglottic region, the narrowest part of the airway just below the larynx. The vocal cords of the larynx become grossly swollen, causing obstruction to the inflow of air, which is manifested by inspiratory stridor. [4]

III. Signs and Symptoms

Croup can present with a wide range of symptoms ranging from mild inspiratory stridor to severe respiratory distress.
Viral Croup is usually presented with viral symptoms as the following:

- Fever
- Cough
- Runny nose and stuffy nose
- Barking cough
- Inspiratory Stridor

The typical features of a barking cough, harsh inspiratory stridor and hoarseness are often preceded by fever and coryza for 1–3 days. The symptoms often start, and are worse, at night.

Table 1. *Severity*

Score	Severity
≤ 2	Mild
3-7	Moderate
8 to 11	Severe
≥ 12	Impending Respiratory failure

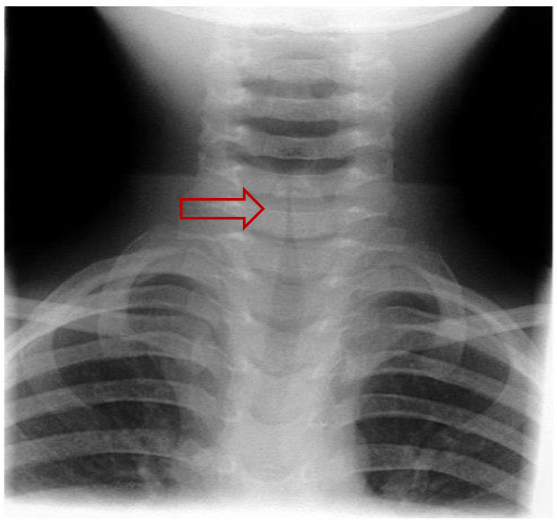
Table 2. *Clinical features*

Clinical Features	Assigned score
Level of Consciousness	Normal, including sleep: 0 Disoriented: 5
Cyanosis	None: 0 With Agitation: 1 At Rest: 2
Stridor	None: 0 With Agitation: 1 At Rest: 2
Air Entry	Normal: 0 Decrease: 1 Markedly Decrease: 2
Retraction	None: 0 Mild: 1 Moderate: 2 Severe: 3

Children with croup should have gentle handling so as not to aggravate the symptoms further. Throat examination is rarely required. [5,10]

Spasmodic croup usually presents similar symptoms to viral croup; however, it begins with a sudden onset that may be preceded by mild to moderate coryza and hoarseness. The patient is usually afebrile. The severity of the symptoms generally diminishes within several hours, and the following day, the patient often appears well except for slight hoarseness and cough. Such episodes often recur several times. [2]

There are numbers of validated croup severity scoring system. However, Westley score has been used by most countries including Australia and United Sates. [1]



The arrow shows tapering of the upper trachea, known as the "steeple sign" of croup.
(Source: UpToDate.com)

IV. Diagnosis

Croup is a clinical diagnosis. Laboratory and Radiograph are not routine requested. (Evidence rating C). [9,11,12]

It is classically presenting with Barking cough, inspiratory stridor and precipitate by viral symptoms such as cough, colds and fever.

Neck Radiograph can show subglottic narrowing or "**Steeple sign**" on posterior-anterior view.

However, neck x-ray is not routinely requested unless the diagnosis is in doubt such as in the exclusion of Epiglottitis or Foreign Body ingestion. X-ray doesn't correlate well with disease severity. [1]

❖ **Differential diagnosis**

- Laryngomalacia: congenital abnormality, it presents in early age. Stridor may disappear when changing position.
- Epiglottitis: It is caused by bacterial infection mostly Haemophilus Influenzae type B. It presents with rapid onset of high fever, dysphagia, drooling. Child has ill-looking appearance, and prefers to sit forward 'Tripod position'. Lateral neck x-ray demonstrates swelling of epiglottis known as "Thumb Sign".
- Bacterial Tracheitis: less common, causes by bacterial infection. S. aureus is most commonly found. Child usually developed sudden high fever, toxic looking, but the child can lie flat and no drooling. Lateral neck x-ray shows ragged trachea air column, pseudo membrane detachment in the trachea.
- Foreign body ingestion: Symptoms can vary depending on the location of the foreign body. It may present with sudden choking, coughing, wheezing, stridor, difficulty breathing and absence sign of infection.

V. Treatment

Most children can be managed safely at home. The mainstay treatment of croup is airway management and hypoxia. Treatment of respiratory distress is the priority.

1. **Corticosteroid**

   Evidence rating A [9,14,15] decreases the edema in the laryngeal mucosa through anti-inflammatory effect. It is measured by reduced and shorter duration of hospitalization, and reduced need the use of epinephrine nebulization. Dexamethasone is the preferred medication. It is given as single dose at 0.15-0.6mg/kg. Given as IV/IM/PO have been proven equal efficacy. [2,4,5,6,7] A single dose of nebulized Budesonide 2 mg is an alternative option, particularly for children who are vomiting and who lack IV access. Single dose of oral prednisolone 1-2mg/kg is less effective. [2,4] Studies showed the rate of return hospital visit is higher among Prednisolone group compared to Dexamethasone group. [2,5,6]

2. **Nebulized Adrenaline**

   Evidence rating A [9,16,17] is indicated in moderate to severe croup. It produces arteriole vasoconstriction in the upper airway mucosa, which eventually leads to decreased edema. Adrenaline is typically used in conjunction with corticosteroids because it has a quick onset of action but a short half-life, whereas corticosteroids have a slower onset of action but a longer half-life. Recommended dosing is 0.5mL/kg/dose of epinephrine 1:1000 (1mg/ml) with maximum dose of 5ml. It can be repeat if needed. [2,6,7,8]

3. **Antibiotic**

   No roles of antibiotic in treatment of croup due to it viral in nature unless bacterial infection is strongly suspected.

4. **Humidified Air**

   Evidence rating B [9,13] may be helpful to comfort the child by loosen the thicken secretion. In addition, moist air may reduce irritation of air way causes by inflamed mucosa. However,

studies showed no change in severity score compared to children without treatment. Mist air can be provided using saline nebulization. [5,6]

5. **Other Therapies:**
    a. Antipyretic is given to child with Fever
    b. IV Fluid is given to child with vomiting or unable to take oral feeding
    c. Respiratory support such as Oxygen therapy is indicated in severe croup or percutaneous SaO2 < 93%. [3]

Medication	Dose	Route	Note
Dexamethasone	0.15-0.6mg/kg (Max:16mg)	PO/IM/IV	Single Dose
Prednisolone	1-2mg/kg (Max:60mg)	PO	If oral Dexamethasone is not available
Budesonide	2mg	Nebulize	Single Dose
Adrenaline/Epinephrine (1:1000)	0.5mg/kg/dose (Max:5mg or 5ml)	Nebulize	• Dose of 5ml can be given undiluted Dose <5 ml: Dilute with sodium chloride 0.9% to make 5ml • It may be repeated after 15mins if necessary.

VI. Prognosis and Complications

Croup mostly resolves within 3 days, but may persist until 7days. Prognosis of children with croup is generally good and mortality is rare.

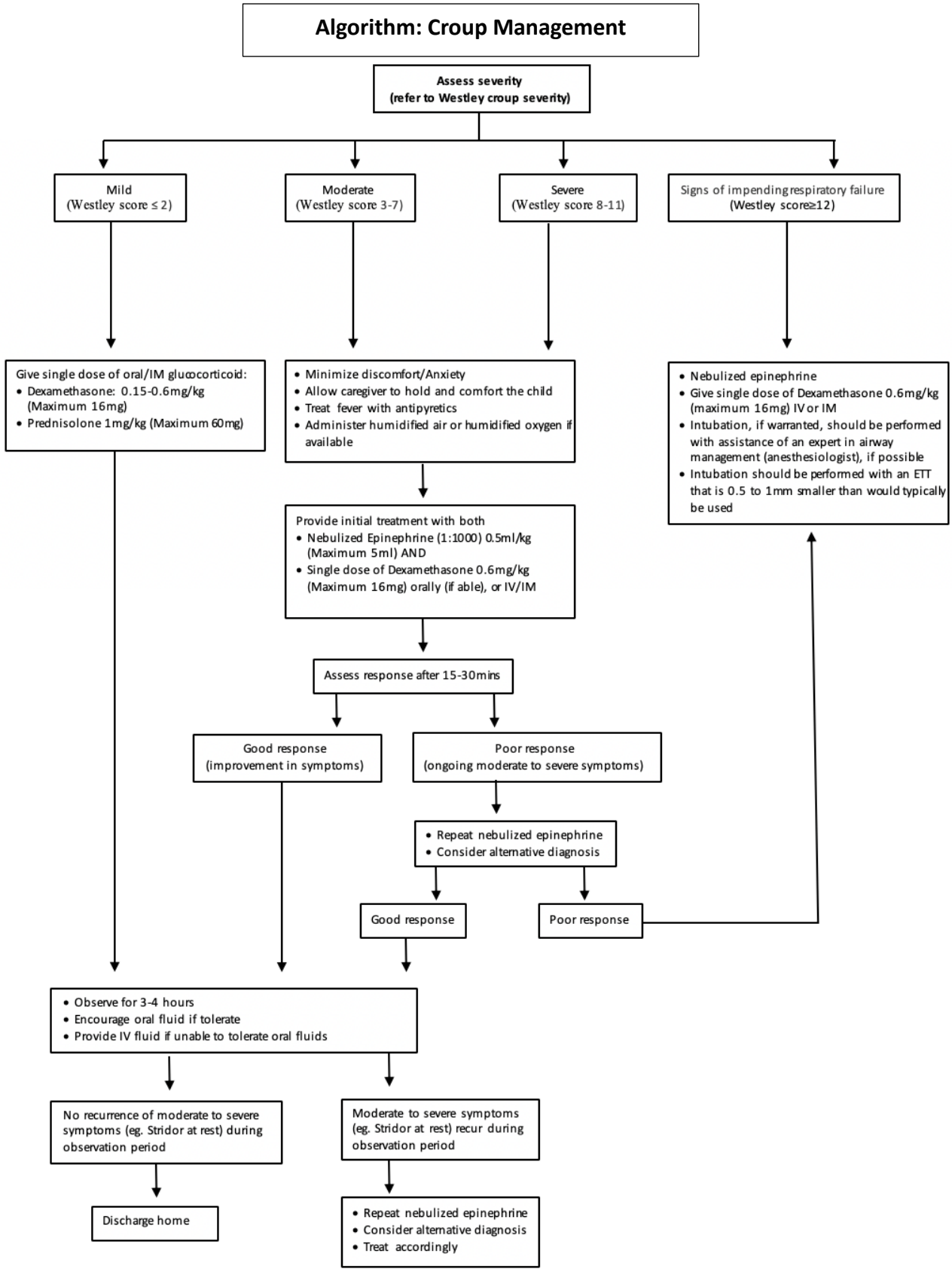
Children with moderate and severe croup are at risk of respiratory failure. Other complication including pulmonary edema, pneumothorax and pneumomediastinum. Secondary bacterial infection such as bacterial tracheitis and pneumonia may lead to life-threatening conditions. [6,7]

In mild croup, patient can be treated at home. Caregivers should be clearly instructed regarding **when to seek medical attention as the following:**

- Stridor at rest
- Difficulty breathing
- Pallor or cyanosis
- Severe coughing spells
- Drooling or difficulty swallowing
- Fatigue
- Persistent or high fever and prolonged symptoms (longer than seven days)
- Suprasternal retractions.

VII. Prevention [6]

- Wash your hands and the child's hands often with soap and water, or use alcohol hand rubs.
- Stay away from other adults and children who are sick.
- Make sure that the child gets all of the recommended vaccines, including the flu shot.



Summary of Pharmacotherapy

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Evidence Rating [9]

Strength of recommendation	Interpretation
A	Consistent, good-quality patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usually practice, expert opinion, or case series

ACUTE OTITIS MEDIA (AOM) IN CHILDREN

MILIYA Thyl, SUY Keang PAUL Turner

I. Key Facts

- The estimated global incidence of acute otitis media (AOM) in 2017 was 317 million cases, for all ages and both sexes combined [(1)].
- The incidence declines with age and adults are rarely affected. In countries where vaccination programmes against pneumococcal infection have been implemented, the incidence of AOM among children has declined substantially (2).
- AOM is very common in children under 5 years of age with most experiencing at least one episode before the age of 3 years. AOM can complicate upper respiratory tract infections in up to a third of cases especially in the first year of life (3)(4).
- Most non-severe cases can be managed symptomatically with no antibiotic treatment, especially in children >2 years of age
- Antibiotic should be considered if severe symptoms, immunocompromised children or bilateral acute otitis media in children less than 2 years.

II. Overview

1. **Acute otitis media** is defined as an infection of the middle ear following an upper respiratory infection (viral or bacterial). This guideline is not covering the acute exacerbated of chronic suppurative otitis media, because this a different pathogen and condition.

2. **Causes**

Several bacterial and viral respiratory pathogens are associated with AOM. Most case of AOM are triggered by respiratory viruses (table1) [(10)], which can be complicated by a bacterial super infection.

Table1. *Represent the common aetiology of AOM*

Respiratory virus (most cases)	Bacteria (rarely)
Respiratory syncytial virus (RSV) Rhinovirus Coronavirus including (SARS-CoV-2) Influenza virus (A and B) Other respiratory viruses	*Streptococcus pneumoniae* *Haemophilus influenzae* *Moraxella catarrhalis* *Streptococcus pyogenes* (group A *streptococcus)*

3. **Risk factors**

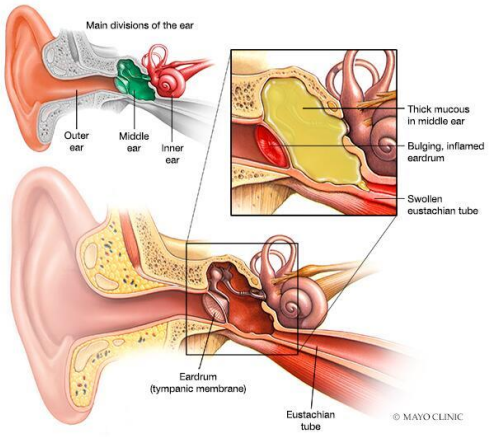
There are many risk factors for otitis media. The below is not an exhaustive list [(11)]

- Family history of otitis media
- Upper respiratory tract infections
- Low socioeconomic status
- Exposure to tobacco smoke
- Day care attendance
- Short duration of breastfeeding
- Low birth weight
- Immunodeficiency
- Craniofacial anomaly such as cleft palate.

4. **Physiopathology**

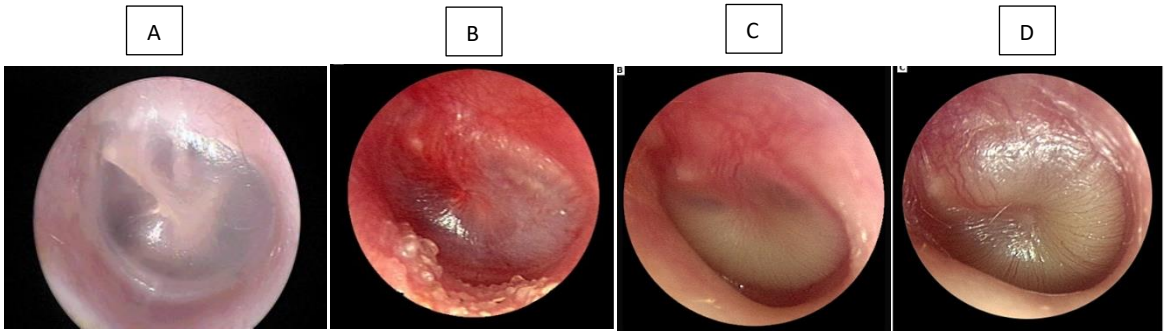
Pathogens reach the middle ear from the nasopharynx through the Eustachian tube usually following a viral infection of the upper respiratory tract. Inflammation and oedema cause narrowing of the tube and accumulation of mucosal secretions which

favours growth of pathogens in the middle ear. This sequence of events triggers the typical signs and symptoms of AOM.



III. Signs and symptoms

- The onset of signs and symptoms of ear infection is us www.mayoclinic.org
- Fever 38.0ºC
- Otalgia (ear pain)
- Tugging or pulling at the ear
- Crying more than usual
- Ear discharge
- Examination: otoscopy is required for a definitive diagnosis of AOM. Health care personnel required skill and available otoscopy at the time of examination. Classic findings include (Photo)



(A)Normal left tympanic membrane with pearly grey colour. (B) Early acute otitis media with inflammation; subsequently progressed to effusion. (C) Purulent effusion with air-fluid level. (D) Bulging purulent effusion filling the middle ear. [12]

IV. Diagnosis

1. Laboratory test: Not indicated unless the patient requires hospitalization to exclude more serious causes.
2. Microbiology: Ear swab for microbiology culture if develop ear discharge and no improvement despite adequate treatment.
3. Imagery: Not indicated for non-complicated AOM. Head CT-scan may be indicated if available and clinical suspicion of AOM complication, such as mastoiditis.
4. Differential diagnosis: The main consideration in the differential diagnosis of AOM is otitis media with effusion (OME).

V. Complications

1. Tympanic membrane perforation is common and results in otorrhea and frequently pain. Otorrhea from tympanic membrane perforation should be distinguished from

otitis externa.

2. Acute mastoiditis although rare, is the most common suppurative complication of AOM and may be associated with intracranial complications such as mastoiditis, meningitis, and brain abscess ect.
3. Facial nerve palsy secondary to AOM should be discussed with ENT specialist.

VI. Treatment

1. Most non-severe cases of AOM can be managed symptomatically and do not require antibiotic treatment, especially in children older than 2 years.

2. Non-severe cases usually have mild symptoms, often pain in one ear, and mild fever (< 39.0 °C), which improves with antipyretics. Pain management and assessments consideration

- Paracetamol (acetaminophen) 10 to 15 mg/kg given every 6 hours
- Ibuprofen 5 to 10 mg/kg given every 6 to 8 hours

3. A watchful waiting approach with symptomatic management (i.e., analgesics and antipyretics) is appropriate. Watchful waiting involves careful monitoring of the child by caregivers, with instructions to seek care in case of worsening of fever, pain or persistence of the symptoms. Reassessment (follow up) could be considered if symptoms do not improve over 3 days.

4. The great majority of cases usually resolve spontaneously over a few days with no need for antibiotic treatment and the risk of complications (e.g., acute mastoiditis) is very low.

5. Antibiotic treatment should be considered in specific cases [10]

a. Severe symptoms (e.g. systemically very unwell, ear pain despite analgesics, fever ≥39.0 °C)

b. Immunocompromised children

c. Bilateral acute otitis media in children < 2 years

d. Antibiotic selected

- First line: Amoxicillin (oral) 80 – 90 mg/kg/day duration 5 days
- Second line: Amoxicillin + clavulanic acid (oral) 80 – 90 mg/kg/day (of amoxicillin base) – duration 5 days
- Alternative Antibiotic: Ceftriaxone 50 mg/kg IV once daily for up to 3 days who cannot tolerance oral (PO) medication.

VII. Prevention and education

All strategies (e.g., hand hygiene) that prevent upper respiratory tract infections can be useful in preventing AOM, including vaccination against *Streptococcus pneumoniae* and *Haemophilus influenzae* type b for all children [7,8].

For countries considering vaccination programs for influenza, vaccination of high-risk groups could also be considered (e.g. young children less than 2 years) [9].

Caregivers should receive indications to provide adequate supportive care at home.

- Avoid swimming or getting the ear wet.
- If pus discharge, wick the ear three times a day until there is no more pus.
- DO NOT apply heat or cold.
- DO NOT instil any substances like oils or herbal extracts.

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ACUTE BRONCHIOLITIS

LEK Yat, KITH Daronic, SENG Soputhirith, KIM Ang

I. Key Facts

Bronchiolitis typically affects infants younger than two years and children less than one year are more likely to have more severe disease requiring hospital admission.

The most common infectious agent causing acute bronchiolitis in children is the Respiratory Syncytial Virus (RSV), detected in up to 80% of patients.

Acute bronchiolitis is a clinical diagnosis, based on typical history and physical examination findings.

In most infants presenting to hospital and/or hospitalized with bronchiolitis no investigations are required. Neither laboratory tests nor radiological exams are usually indicated for the routine work-up of infants with bronchiolitis.

Infants with moderate to severe bronchiolitis or any risk factors for severe disease usually require hospitalization. The main management of bronchiolitis is largely supportive, involves ensuring appropriate oxygenation and hydration/fluid intake.

II. Overview

1. Definition

Bronchiolitis is an illness in children <2 years of age characterized by wheezing and airway obstruction due to primary infection or reinfection commonly by virus, resulting in inflammation of the small airways/bronchioles. [1,2,3]

It is commonly caused by Respiratory Syncytial Virus (RSV), secondary bacterial infection may occur but is rare. [2,3]

2. Physiopathology

The pathogenesis of bronchiolitis involves a combination of airway edema, increased mucus production, and necrosis of airway epithelial cells due to cytotoxic injury. **RSV** transmission occurs from person to person either by direct inoculation of nasal mucosa with contaminated secretions or by inhalation of large infectious droplets.

In approximately one-third of infected patients, infection then spreads to the lower respiratory tract by resultant immune response in the lower tract leads to edema, further sloughing of epithelial cells, and mucus secretion. This leads to airway narrowing and obstruction, further worsened by impaired ciliary function. [4]

3. Etiology

Bronchiolitis is typically caused by a viral infection [1], secondary bacterial infection may occur but is rare [3], and most commonly occur in the winter season and in tropical regions in the rainy season but can be seen all year round. [4,6]

The most common infectious agent causing acute bronchiolitis in children is the Respiratory Syncytial Virus (**RSV**) [1,2,3,4,5] detected in up to 80% of patients. [4]

Followed by other causal agents: Rhinovirus (**RV**), Parainfluenza virus, Metapneumovirus (MPV), Influenza virus, Adenovirus, Coronavirus, Mycoplasma pneumoniae less common cause.

III. Diagnosis

1. Clinical assessments:

Acute bronchiolitis is a clinical diagnosis, based on typical history and physical examination findings. [4,5,6,7] [B]

The peak severity of the disease occurs around 3-5 days from the disease onset and improvement occurs in 7-14 days, with 90% of infants having a resolution of cough within 2-3 weeks. [2,4,6,7]

Acute Bronchiolitis typically begins a few days of initial with an acute upper respiratory tract infection and progressing into lower respiratory tract symptoms followed by: [1,4,5,6]

- Low grade fever (in around 30% of cases, usually less than 39°C)
- Nasal discharge/Nasal congestion
- Difficulty in feeding, breastfeeding or drinking (typically after 3-5 days of illness)
- Wheezy cough
- Fine inspiratory crackles and/or high-pitched expiratory wheeze
- Signs of increased work of breathing (intercostal, subcostal, supraclavicular retractions, nasal flaring or grunting)
- Apnea can be the presenting feature of bronchiolitis, especially in the very young (<2 month) and in premature or low birth weight infants
- Historical risk factors for severe illness: [2,4,6,8]
- Preterm infants
- Low birth weight
- Chronological age at presentation less than 12 weeks
- Chronic lung disease
- Congenital heart disease
- Chronic neurological conditions
- Immunodeficiency
- Environmental factors: exposure to tobacco smoke and or air pollution

❖ **Assessment Severity of Acute Bronchiolitis**

This table is meant to provide guidance in order to stratify severity. The more symptoms the infant has in the mod-severe categories, the more likely they are to develop severe disease. [2,4]

Severity of Acute Bronchiolitis			
	Mild	**Moderate**	**Severe**
Behavior	Normal	Some/intermittent irritability	Irritability and/or lethargy Fatigue
Respiratory rate	Mild tachypnea	Increasing respiratory rate	Marked increase or decrease in respiratory rate
Use of accessory muscles	Nil to mild chest wall retraction	Moderate chest wall retractions Suprasternal retraction Nasal flaring	Marked chest wall retractions Marked suprasternal retraction Marked nasal flaring
Oxygen saturation/oxygen requirement	O_2 saturations greater than 92% (room air)	O_2 saturations 90-92% (room air)	O_2 saturations less than 90% (room air). Hypoxemia may not be corrected by O_2
Apneic episodes	None	May have brief apnea	May have increasingly frequent or prolonged apnea
Feeding	Normal	May have difficulty with feeding or reduced feeding	Reluctant or unable to feed

❖ **Indication for hospitalization**: Infants with moderate to severe bronchiolitis and any of the following risk factors for developing severe bronchiolitis must be considered for hospital admission: [B]

- Historical risk factors for severe disease
- Clinical risk factors for severe disease:
  - Oxygen saturation < 92% on pulse oximetry or central cyanosis
  - Severe respiratory distress: gasping, grunting, very severe chest indrawing
  - Apnea or history of apnea
  - Inability to drink, breastfeed or vomiting everything
  - Lethargy, convulsions or altered consciousness

❖ **Indication for Intensive Care Unit**: Infants with acute bronchiolitis must be referred to the ICU when the following occur: [7][B]

- Respiratory failure requiring ventilator support
- Oxygen saturation reduced despite O2 therapy and/or Continuous Positive Airway Pressure (CPAP)
- Apnea with desaturation
- Severe impairment of general conditions

2. Investigations

In most infants presenting to hospital and/or hospitalized with bronchiolitis no investigations are required. [2,6] Neither laboratory tests nor radiological exams are usually indicated for the routine work-up of infants with bronchiolitis. [7][B]

- Oxygen saturation: Pulse oximetry should be performed in every child who attends hospital with respiratory difficulties.
- Full blood cell count (FBC): There is no role for blood tests in managing infants presenting to hospital and hospitalized with typical acute bronchiolitis. [D]. However, where other causes of respiratory illness are suspected, a FBC may help with the differential diagnosis.
- Other tests (if needed and/or available):
  - Blood gas: Blood gas analysis is not usually indicated in acute bronchiolitis. It may have a role in the assessment of infants with severe respiratory distress or in those who are tiring and may be entering respiratory failure.
  - Blood culture if pneumonia is suspected
  - RSV serology (acute and convalescent serum samples)
  - Rapid viral identification: best samples for testing (nasopharyngeal aspirate, nasopharyngeal wash)
- Chest X-ray: Not routine recommended as it does not improve management in infants presenting with simple bronchiolitis and may lead to treatments of no benefit. [D] Should be considered in those infants where there is diagnostic uncertainty or course suggests alternate diagnosis. [1]

3. Differential Diagnosis

- Pneumonia (viral or bacterial)
- Congestive heart failure
- Aspiration pneumonia due to gastroesophageal reflux disease (GERD)
- Foreign body aspiration
- Vascular rings.

IV. Management

Infants and children with mild bronchiolitis usually can be managed in the outpatient setting unless there are concerns about the caregivers' ability to care for them at home. Supportive care is the mainstay of management of mild bronchiolitis. Supportive care includes maintenance of adequate hydration, relief of nasal congestion/obstruction and monitoring for disease progression. [8]

1. Outpatient Management [1,3,8]

- Clear secretions from the child's nose before feeds with normal saline when nasal blockage causes respiratory distress
- Give Paracetamol or Ibuprofen if your child has fever
- Make sure your child drinks enough and give extra fluids or breast milk if there is fever. Small frequent drinks are more likely to be tolerated and less likely to be vomited
- Return to doctor/hospital if your child
    - Increase in respiratory effort
    - Becomes toxic
    - Develops high fever
    - Unable to drink or breastfeed

2. Inpatient Management

Clinicians should assess risk factors for severe disease when making decisions about evaluation and management of children with bronchiolitis. [2,4,6] [B]

Infants with moderate to severe bronchiolitis or any risk factors for severe disease usually require hospitalization. The main management of bronchiolitis is largely supportive, involves ensuring appropriate oxygenation and hydration/fluid intake.

- Oxygen therapy: supplemental O2 should be administered if O2 saturation levels are persistently below 92% in room air. [7][A] CPAP should be considered in all patients with worsening severe respiratory distress despite oxygen therapy.
- Nasal suction: superficial nasal aspiration especially in younger children is recommended to improve airway patency, O2 saturation measured by pulse oximetry and feeding. [7][A]
- Feeding and hydration: adequate feeding and hydration are recommended in treating bronchiolitis since respiratory distress in infants with bronchiolitis can negatively affect the hydration status. [7][A] Guidelines recommend nasogastric feeding or intravenous fluids for patients who cannot tolerate oral feeding.
- Chest physiotherapy: as standard clinical practice for hospitalized infants with bronchiolitis cannot be recommended, [7][A] but only recommended for those admitted to intensive care. [1]
- Medication management:
    - Inhaled bronchodilators: Infants and children with bronchiolitis and moderate to severe respiratory distress should receive a trial of nebulized Salbutamol 2.5mg/dose, repeated twice at an interval of 30 minutes. If effective, continue 2.5mg/dose every 2-4 hours in the acute phase and then reduction as recovery takes place. If ineffective, discontinue the treatment. [1]
    - Nebulized adrenaline: should not administer epinephrine to infants and children with a diagnosis of bronchiolitis due to the lack of studies, short duration of action, and potential adverse effects, nebulized adrenaline is not recommended. [4,7] [B]

- Nebulized and systemic steroids: using nebulized and systemic corticosteroids alone or in combination with other therapies (epinephrine or bronchodilators) in treating acute bronchiolitis is not recommended. [1,2,4,7] [A]
- Nebulized hypertonic saline solution: may administer nebulized to infants and children hospitalized for bronchiolitis, but should not be administered to infants with a diagnosis of bronchiolitis in the emergency department [4][B].
- Antibiotics: using antibiotics in bronchiolitis is not recommended except in cases with a strong suspicion or clear evidence of a secondary bacterial infection. [4,5,7] [B]
- Mucolytic: no indication in acute bronchiolitis.

- Discharge criteria: when deciding on the timing of discharge for babies and children admitted to hospital, make sure that they: [7][B]
  - Protracted autonomy from any respiratory support and O2 saturation levels greater than 92% in room air
  - Patient clinically stable
  - Adequate oral intake of fluids and feeds (>75% of usual volume)
  - Family unit able in coping, clinical risk factors for severe disease, monitoring and administering therapy at home.

V. Prognosis

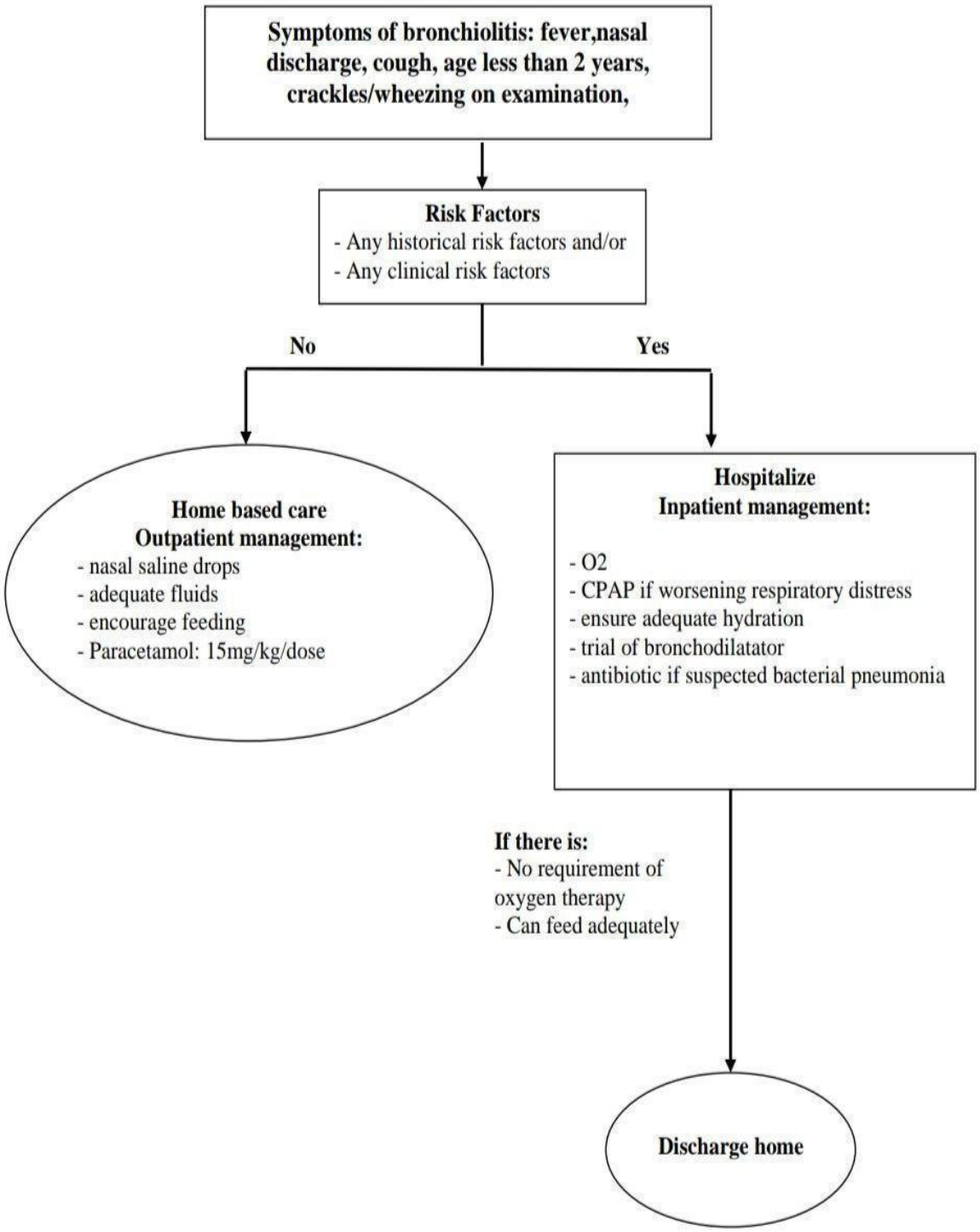
Overall prognosis for infants and children with bronchiolitis is good because it is a self-limited illness. The most common sequela attributed to bronchiolitis is the development of reactive airway disease or asthma later in childhood.

VI. Prevention and Education

Environmental prophylaxis

- Exclusive breastfeeding for at least six months should be encouraged to decrease the morbidity of respiratory infections. [B]
- Before and after direct contact with the patient, after contact with potentially contaminated objects, all people should disinfect hands
- Exposure to tobacco smoke must be discouraged
- Stethoscope cleaning practices should be followed to prevent the transmission of hospital-acquired infections
- Pharmacological prophylaxis:
- Palivizumab prophylaxis during RSV season for infants of gestational age < 29 weeks and age <12 months at the beginning of the epidemic season and for infants of 29-35 weeks gestational age and age < 6 months in the presence of risk factors. Palivizumab is also recommended for infants diagnosed with Bronchopulmonary Dysplasia (during their first year of life and during the second year of life in children who require medical therapy) and infants with hemodynamically significant congenital heart disease who are < 12 months of age at the beginning of the epidemic season. [7][B]
- It is administered via intramuscular injection once each month during the RSV season for five doses (15 mg/kg).

ALGORITHM



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❖ Strength of Recommendation Definition

A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendations but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

COMMUNITY ACQUIRED PNEUMONIA

KITH Daronic, SENG Soputhirith, LEK Yat, KIM Ang

I. Key Facts

- Community acquired pneumonia (CAP) accounts for nearly one-fifth of death in children worldwide
- CAP can be diagnosed clinically and is due to viruses or bacteria.
- Chest x-ray, blood tests and microbiological investigations are not recommended for routine use in the diagnosis and management of CAP [3,4,5]
- Oral antibiotic is as effective as IV antibiotic prescribing in CAP in children. [3,4,5] [A+]

II. Overview

1. Definition

Pneumonia is defined as an inflammatory disorder of the lung characterized by consolidation due to the presence of exudate in the alveolar spaces and, as a result, associated inflammation in the surrounding interstitial tissues, and is acquired outside of a hospital setting.

2. Causes

It is caused by viruses or bacteria. It is usually not possible to determine the specific cause of pneumonia by clinical features or chest x-ray appearance.

- Common bacteria in pneumonia in children are: [3,5] *Streptococcus pneumoniae* (pneumococcus): the most common [A-], *Haemophilus influenzae type b* (HiB) and non-typable species, *Group A streptococci* (mainly *Streptococcus pyogens*), *Staphylococcus aureus*, *Burkholdoria pseudomallei* (Melioidosis) should not be forgotten as one of the causes of very severe pneumonia with risk of septic shock in our population [2], *Mycoplasma pneumoniaeMycoplasma tuberculosis:* our country is still considered as a high incidence of tuberculosis .
- Common virus in pneumonia in children is [3,5] *Respiratory syncytial virus (RSV) Influenza virus (A+B), Human metapneumovirus, Parainfluenza virus, Corona virus (including SARS-CoV-2), Adenovirus, Rhinovirus.*

  Patient with history contact of dead poultry, Influenza A H5N1 should be considered as one of the causes of pneumonia. [2]

  Overall, viruses account for 30-67% of CAP cases in childhood and are more frequently identified in children aged < 1 year than in those aged > 2 years. [A-]

  One-third of cases of CAP (8-40%) represent a mixed infection. [5] [B+]

3. Risk factors [6]

- Prematurely born children
- Age < 12month
- Unvaccinated / not fully vaccinated child
- Congenital heart disease
- Chronic lung disease: Bronchopulmonary dysplasia, bronchiectasis or history of recurrent respiratory illness in the past 12months
- Malnutrition
- Immunocompromised
- Low socio-economic level**.**

III. Signs and symptoms

1. Patients may present the following signs and symptoms: [3, 4]

- Cough
- Fever
- Difficulty in breathing

- Tachypnea with
  - > 60 breaths/minute in infants aged <2months
  - > 50 breaths/minute in infants aged between 2 and 12 months
  - > 40 breaths/minute in toddlers aged 12 months to 5 years
  - > 20 breaths/minute in children aged > 5 years
- Intercostal, subcostal or supra-costal retractions
- Nasal flaring
- Grunting
- Chest pain or abdominal pain
- Presence of crackles
- Decreased vesicular breath sounds
- General dangers signs: inability to breastfeed or drink, lethargy or unconscious, convulsion, central cyanosis or oxygen saturation <90% on pulse oximetry.

2. Atypical pneumonia: [10]

- Children at school age
- Cough that is persistent and may last three to four weeks
- Mild, prolonged symptoms with gradual resolution
- Unusual extra-pulmonary symptoms: rash, arthralgia, GI symptoms etc.
- Unusual radiographic manifestation
- Failure to isolate pathogen with use of routine bacteriologic testing methods
- Not respond to beta-lactam
- The most common cause: Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumonia.

IV. Diagnosis

1. Classification of the severity of pneumonia (WHO classification)

Sign or symptoms	Classification
Cough or difficult breathing plus at least one of the following: - Central cyanosis or oxygen saturation < 90% on pulse oximetry - Unable to breastfeed or drink or vomiting everything - Convulsion, lethargy or unconsciousness - Severe respiratory distress (e.g. head nodding, grunting, very severe chest indrawing)	Severe pneumonia

Cough or difficult breathing plus at least of the following:
- Definite crackle on auscultation
- Lower chest wall indrawing
- Fast breathing:
  o > 60 breaths/minute in infants aged <2months
  o > 50 breaths/minute in infants aged between 2 and 12 months
  o > 40 breaths/minute in toddlers aged 12 months to 5 years
  o > 20 breaths/minute in children aged > 5 years
	Pneumonia

No sign of very severe pneumonia or severe pneumonia or pneumonia	No pneumonia

2. Investigations

- Septic screening: should not routinely be tested, especially in milder case, and are not able to distinguish viral from bacterial infection. [5] [A-]

- Complete blood count
- CRP: the range from 150-350mg/l evocates in invasive bacterial infection. It is not useful in the management of uncomplicated pneumonia. [5] [A+]
- Procalcitonin (elevation >2ng/ml indicate bacterial infection, but case with normal value and short duration should be monitored). [9]

- Blood culture: less than 10% of blood culture are positive in patient with pneumonia. [5] [A-] It should be performed in severe pneumonia or when there is poor response to the first line antibiotics [5][C]
- Chest x-ray: is not routinely requested. It is useful to identify pleural effusion, empyema, pneumothorax, pneumatocele, interstitial pneumonia, or pericardial effusion [3,4,5] [A-]
- Indication for repeating or follow up chest x-ray
- Patient became deteriorated at any time or fails to clinically improve after 48-72 hours of appropriate antibiotics therapy. [D]
- Follow up x-ray: recommended after 6 weeks for complicated pneumonia or recurrent pneumonia involving the same lobe or if initial suspicion of a chest mass, anatomical abnormality or foreign body. [B+]
- Chest ultrasound: in case associated with pleural effusion. Pleural fluid should be sent for microscopy, culture, pneumococcal antigen detection and/or PCR. [5][C]
- Chest CT scan: in case with complication or difficulty in differentiate pneumonia from other pathology
- Nasopharyngeal swab for detection of virus detection by PCR and/or immunofluorescence. [C] In case suspected of TB (severe pneumonia, HIV, immune-compromised, history of contact with TB patient), it is recommended to do nasopharyngeal aspiration or sputum collection for detection of tuberculosis with TB Gene-xpert Ultra
- Throat swab: in case severe pneumonia, suspicion of Melioidosis, earlier detection with sensibility higher than blood culture

3. Differential diagnosis [3]

Diagnosis	In favor
Croup	- Inspiration stridor - Barking cough - Hoarse voice
Bronchiolitis	- Accompanied with upper respiratory tract symptoms - Wheeze and crackles - Age usually <1 year - Hyperinflation of the chest
Asthma	- Recurrent episodes of shortness of breath or wheeze - Night cough or cough and wheeze with exercise - Response to bronchodilators - Known or family history of atopy disease
Congenital heart disease	- Cyanosis - Finger clubbing - Heart murmur - Signs of cardiac failure - Failure to thrive
Foreign body	- History of sudden choking - Sudden onset of stridor or respiratory distress - Focal areas of wheeze or reduced breath sounds

V. Complications

- Parapneumonic pleural effusion and empyema: a persistent fever despite adequate antibiotic treatment should always lead the clinician to be suspicious of the development of empyema. Around 0.7% of children hospitalized with CAP will develop empyema, which 68% of the cases are from Streptococcus Pneumoniae (primarily serotype 1, 19a, 3) [5,6]
- Necrotizing pneumonia and lung abscess: some serotypes of pneumococcal (serotype 1, 3, 9V and 14) and Staphylococcus aureus (PVL strain) are more likely to lead to necrotizing pneumonia and abscess formation than others [5,6]
- Septicemia and metastatic infection: Metastatic infection such as osteomyelitis or septic arthritis should be considered particularly with Staphylococcus aureus infections [5]
- Pneumothorax: Air-filled cavities (pneumatoceles) are common in necrotizing pneumonia, where if necrosis occurs adjacent to the pleura, a bronchopleural fistula may form, resulting in pneumothorax or pyo-pneumothorax. [5]

VI. Treatment

1. **Oxygen therapy:** provide supplemental oxygen if
   - If saturation is <90% or in agitation child
   - If saturation is < 94% in a child with severe respiratory distress, lethargy, convulsions, or altered consciousness, to maintain oxygen saturation >94%. [B]
2. **Antibiotic therapy**
   - Patient with a clear clinical diagnosis of pneumonia should receive antibiotics since we cannot reliably distinguish between viral and bacterial pneumonia. [5][C]
   - **Empirical antibiotics:** [1,2,3,4,5,11]

	Antibiotics
Pneumonia Antibiotic duration recommendation is 3-5days	- First line: Oral **amoxicillin** 90mg/kg/day, BID or TID [B] - Alternative: Oral **Amoxicillin clavulanate** [B] - If suspect atypical pneumonia: Azithromycin 10-20mg/kg once a day for 3-5days or Clarithromycin 15mg/kg/day BID - If suspect Influenza: Oseltamivir PO for 5days
Severe pneumonia Antibiotic duration recommendation is 7 to 10days	- First line: Ampicillin 50mg/kg/dose, q8H IV + Gentamicin 7.5mg/kg/dose, q24H IV - Second line: Ceftriaxone 80-100mg/kg/dose, q24H, IV - If suspect Staphylococcus pneumonia: Cloxacillin 50mg/kg/dose, q6H, IV - If suspect atypical pneumonia: Azithromycin 10-20mg/kg once a day, PO, for 3-5days or Clarithromycin 15mg/kg/day BID, PO [D] - If suspect Melioidosis: Ceftazidime 50mg/kg/dose, q8H, IV - If suspect Influenza: **Oseltamivir or Zanamivir** PO for 5days

   - **Selection of antimicrobial therapy for specific pathogens** [1,3,4,5,11]

Pathogens	**Parental therapy**	**Oral therapy** (step-down therapy or mild infection)
Streptococcus pneumoniae	-Preferred: Ampicillin (150–200 mg/kg/day every 6 hours) -Alternatives: Ceftriaxone (50–100 mg/kg/day every 12–24 hours)	-Preferred: Amoxicillin (90 mg/kg/day in 2 or 3 doses); -Alternatives: second- or third-generation cephalosporin (cefpodoxime: 5mk/kg/day in 2 dses, cefuroxime: 30mg/kg/day in 2 doses; oral levofloxacin:10–20 mg/kg/day in 2 doses

Pathogens	Parental therapy	Oral therapy (step-down therapy or mild infection)
Group A Streptococcus	-Preferred: Ampicillin (200 mg/kg/day every 6 hours); -Alternatives: Ceftriaxone (50–100 mg/kg/day every 12–24 hours)	-Preferred: Penicillin V (45 mg/kg/day in 3 doses), -Alternative: Azithromycin (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5), or Clarithromycin 15mg/kg/day BID (in case of Penicillin allergy)
***Staphylococcus aureus*,**	-Preferred: Cloxacillin (150–200 mg/kg/day every 6–8 hours) -Alternatives: Clindamycin (40 mg/kg/day every 6–8 hours) or Vancomycin (40–60 mg/kg/day every 6–8 hours)	-Preferred: oral Cloxacillin (75–100 mg/kg/day in 3 or 4 doses); -Alternative: oral Clindamycin (30–40 mg/kg/day in 3 or 4 doses)
***Haemophilus influenza*, typeable (A-F) or non-typeable**	-Preferred: Ceftriaxone (50–100 mg/kg/day every 12–24 hours) -Alternatives: intravenous Ciprofloxacin (30 mg/kg/day every 12 hours) or intravenous Levofloxacin (10-20 mg/kg/day every 12 hours ; maximum daily dose, 750 mg)	-Preferred: Amoxicillin (75-100 mg/kg/day in 3 doses) or Amoxicillin clavulanate (amoxicillin component, 45 mg/kg/day in 3 doses or 90 mg/kg/day in 2 doses) -Alternatives: Cefdinir 14mg/kg/day in 2 doses, Cefixime 4-8mg/kg/day in 1-2doses.
Mycoplasma pneumonia Chlamydia trachomatis* or *Chlamydophila pneumoniae	- Preferred: intravenous Azithromycin (10 mg/kg on days 1 and 2 of therapy; transition to oral therapy if possible); - Alternatives: Levofloxacin (10-20 mg/kg/day in 2 doses maximum daily dose, 750 mg)	-Preferred: Azithromycin (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5); -Alternatives: Levofloxacin (10–20 mg/kg/day in 2 doses.

- **Influenza antiviral therapy:**
  Oseltamivir dose recommendation with duration 5days
  - < 12months: 3mg/kg/dose, 2 times daily
  - <15 kg: 30 mg 2 times daily
  - 15–23 kg: 45 mg 2 times daily
  - 24–40 kg: 60 mg 2 times daily
  - >41 kg: 75 mg 2 times daily.

3. Supportive therapy

- Adequate hydration and nutrition: adequate enteral feeding (Nasogastric tube feeding if oral feeding is impossible or failed), IV fluid
- Antipyretic: Acetaminophen, Ibuprofen.
- Bronchodilators: in presence of wheeze, give Salbutamol nebulizer. The dose for children < 5 years old is 2.5mg/dose and ≥ 5 years old is 5mg/dose [3,4,11]
- Steroid is not routinely use or recommended: may be beneficial in co-existing asthma [11]
- Antitussive and mucolytic agents are not recommended [3,4,5,11]
- Chest physiotherapy: no beneficial and should not be performed in children with pneumonia [3,4,5,11] [A-]

VII. Prevention and education [5,11]

- Breastfeeding [A-]
- Hand hygiene

- Promote immunization for Streptococcus pneumoniae, Haemophilus Influenzae B, Pertussis, measles and Influenza vaccine in children. [A+]
- Smoke-free home [A-]
- Good nutrition, enriching vitamin D, Zinc and vitamin A.

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Generic levels of evidence and guideline statement grades used

Evidence level	Definition	Guideline statement grade
Ia	A good recent systematic review of studies designed to answer the question of interest	A+
Ib	One or more rigorous studies designed to answer the question, but not formally combined	A-
II	One or more prospective clinical studies which illuminate, but do not rigorously answer the question	B+
III	One or more retrospective clinical studies which illuminate, but do not rigorously answer the question	B-
IVa	Formal combination of expert views	C
IVb	Other information	D

EMPYEMA

LEK Yat, KITH Daronic, SENG Soputhirith, KIM Ang

I. Key Facts

Empyema is an uncommon complication of pneumonia developed in 2-12 % of children and represents an accumulation of infected fluid in the pleural space [1,2,3]

Parapneumonic effusion and empyema have an incidence with rate: 3.7, 3.9 and 1.3 cases per 100 000 population among children <2 years, 2-4 years, and 5-17 years respectively. Males and females are equally affected and mortality rate is low but may be higher in infants. [2]

Empyema should be suspected in any child with pneumonia with persistent fevers despite 48 hours of intravenous (IV) antibiotics. [1,3,6]

Appropriate antibiotics should be used to cover at least *Streptococcus pneumoniae* and *Staphylococcus aureus.* [3,6,7] [D]

Moderate to large effusions require drainage. Chest drainage alone is not recommended and the intervention of choice is either percutaneous small-bore drainage with Urokinase or video-assisted thoracoscopic surgery. [3]

II. Overview

1. Definition

Parapneumonic effusion (PPE) is defined as an exudative pleural effusion associated with lung infection (pneumonia). [2]

Empyema is the presence of pus in the pleural cavity. [1,4]

Complicated parapneumonic effusion is often used to refer to either loculated effusion or empyema with changes in the pleural fluid due to bacterial invasion into the pleural space, significant increase in pleural fluid white cell counts and deposition of fibrin. [2]

2. Physiopathology

The pleural space normally contains 0.3 ml/kg body weight of pleural fluid. There is a continuous circulation of this fluid and the lymphatic vessels can cope with several hundred milliliters of extra fluid per 24 hours. However, an imbalance between pleural fluid formation and drainage will result in a pleural effusion.

The progression of pleural fluid collection evolves from 3 stages: [4]

- Exudative stage (first 1-3 days of PPE): the pleural inflammation from a contiguous infection's result in increased permeability and a small fluid collection. At this stage, the effusion is thin and has normal pH and glucose levels and is often sterile.
- Fibrinopurulent stage (day 4-14 of PPE): is characterized by invasion of the organism into the pleural space, progressive inflammation and significant polymorphonuclear (PMN) leukocyte invasion. Inflammation is characterized by progressive decreases in the pleural fluid glucose and pH levels and increased protein and lactate dehydrogenase (LDH) levels.
- Organization stage (after 14 days): a pleural peel is created by the resorption of fluid and associated with fibroblast proliferation that can result in parenchymal entrapment.

3. Etiology

Parapneumonic effusion/empyema in children occurs primarily in association with an underlying bacterial pneumonia.

Common bacterial pathogens in parapneumonic effusion/empyema are: [1,7]

- Streptococcus pneumoniae (pneumococcus), Streptococcus pyogenes and Staphylococcus aureus include methicillin-resistant S aureus (MRSA).
- Other organisms to consider include Hemophilus influenzae, Pseudomonas aeruginosa, and anaerobes. Mycoplasma pneumoniae is a rare cause.

- Mycobacterium tuberculosis has been reported to account for up to 6% of all empyema cases worldwide.

III. Signs and symptoms

Some children present with symptoms directly related to the parapneumonic effusion/empyema, whereas others are seen earlier in the course and are treated for pneumonia but fail to respond [2].
The most common presenting signs and symptoms in children with empyema are: [1,2,4]

- Fever, malaise, decreased appetite, cough, abdominal pain, chest pain, vomiting and dyspnea possible cyanosis.
- On physical examination: crackles, reduced chest movement and expansion, dull on percussion, reduced or absent breath sounds. Children may lie on the affected side to splint hemithorax for temporary analgesia.

IV. Diagnosis

Diagnostic depends on clinical signs, symptoms and investigations:

1. Laboratory test

Most children with empyema have:

- CBC: leukocytosis, secondary thrombocytosis
- Inflammatory markers: CRP and ESR usually are elevated
- Serum lactate dehydrogenase (LDH) level: elevated
- Albumin: low serum albumin is common
- Electrolytes
- Renal function
- Blood cultures should be performed in all patients with parapneumonic effusion or empyema. [7][D]
- Sputum examination and culture: in case tuberculosis suspected.
- Pleural fluid must be sent for microbiological analysis including Gram stain and bacterial culture[C] and should be sent for differential cell count. [7][D]

<table>
<tr><th colspan="3">Pleural fluid</th></tr>
<tr><th>Macroscopic</th><th colspan="2">Basic Pleural fluid analysis</th></tr>
<tr><td>Pus</td><td colspan="2">It is an empyema:
- WBC > 10 000/ml
- LDH > 1 000 UI/l
- PH < 7,2
- Glucose < 2,2 micromol/l
Do gram stain (bacteria seen in <20% cases)</td></tr>
<tr><td rowspan="2">Yellow fluid
Sero-fibrinous</td><td>- Protein >30g/l Or Rivalta (+)
- WBC > 1000/ml</td><td>Exudate Inflammatory fluid:
- Early stage of empyema
- Tuberculosis
- Simple reactive pleural effusion (not infected)</td></tr>
<tr><td>- Protein < 30g/l Or Rivalta (-)
- WBC < 1000/ml</td><td>- Transudate non inflammatory fluid:
- Cardiac
- Renal
- Hypoproteinemia: liver diseases, severe malnutrition</td></tr>
</table>

2. Imaging

Children admitted to hospital with pneumonia who remain unwell or pyrexial at 48H of admission should have parapneumonic effusion or empyema excluded. [2,7] [D]

The aim of imaging is to determine the presence of fluid, differentiate a simple parapneumonic effusion from an empyema. [3]

- Chest X-ray: should be performed in all children with suspected empyema, areas of consolidation may be difficult to differentiate from a pleural effusion.
- Chest Ultrasound: able to differentiate pleural fluid from lung consolidation, estimates of volume of fluid, shows optimal site for thoracentesis and demonstrates a complicated effusion.
- Chest CT scan: should not be performed routinely, indicate if surgical intervention is required to guide surgical approach.
- Bronchoscopy: no indication for flexible bronchoscopy and it is not routinely recommended unless there is concern of an inhaled foreign body.

V. Complications

Complications are uncommon in children but may include bronchopleural fistula, lung abscess, pyopneumothorax, septicemia and rarely perforation through the chest wall (empyema necessitates).

VI. Treatment

All children with parapneumonic effusion/empyema should be admitted to hospital [D]:

1. Supportive therapy

- Oxygen to maintain saturations ≥95%
- Fluid management
- Antipyretics should be given
- Analgesia is important to keep the child comfortable, particularly in the presence of a chest drain [D]
- Chest physiotherapy is not beneficial and should not be performed in children with empyema [D]
- Early mobilization and rehabilitation of respiratory function.

2. Antibiotherapy

Children with moderate to large effusions or empyema require hospitalization and treatment with intravenous (IV) antibiotics should be high dose to ensure pleural penetration. [3,4]

Empiric antibiotics should cover common organisms (*Streptococcus pneumoniae* and *Staphylococcus aureus*). [1,3,5,6,7] [D]

Total duration of antibiotics should be 4-6 weeks (Parenteral: 2-3 weeks, Oral: 2-3 weeks) [4]

The choice of oral antibiotic is dependent on the organism identified or the class of antibiotic used successfully in intravenous. [3]

- 1st line: Ceftriaxone (IV) + Cloxacillin (IV) [6]
- 2nd line: switch Cloxacillin to Vancomycin [6] or Linezolid (IV) in case MRSA [1] or Clindamycin (IV) if associated soft tissue involvement [1,6]
- If anaerobic infection is suspected in those children at risk of aspiration Metronidazole should be consider.

Antibiotics	
Ceftriaxone: 100 mg/kg/day IV q24H or q12H	Cloxacillin:200 mg/kg/day IM or IV q6H
Clindamycin: 15 mg/kg/dose IV q8H	Vancomycin:40-60 mg/kg/day IV q8H
Metronidazole:30mg/kg/day IV q12H or q8H	Linezolid: 10 mg/kg/dose IV q8H

3. Indication for evacuation of pleural fluid

The indication for pleural fluid evacuation is: [2]

- Moderate to large pleural fluid
- Compromised pulmonary function
- Loculated effusion
- Lack of clinical improvement

Recommended treatment options for evacuation. [1]

- Chest drain inserted by interventional radiology or pediatric surgery using ultrasound guidance under general anesthetic
- A chest X-ray should be performed after chest drain insertion. [D]
- The chest drain should be clamped for one hour after the first 10 mL/kg is drained to reduce the risk of re-expansion pulmonary edema.
- All children receiving a chest drain for drainage of suspected or confirmed empyema should receive intrapleural Urokinase/Streptokinase.
- Intrapleural fibrinolytics shorten hospital stay and are recommended for any complicated parapneumonic effusion or empyema. [7][B]

Urokinase	Streptokinase
- <1 year: 10,000 U in 10 mL NS - >1 year: 40,000 U in 40 mL NS - 4H dwell time (instillation) - Twice daily (12 H apart) - Six instillations in 3 days	- <1 year: 10,000 units/kg - >1 year: 20,000 units/kg - Dissolved in 50 mL NS - 4H dwell time (infusion over 1H) - Three consecutive days - Four to six doses (superior to 3 doses)

4. Surgical intervention

Surgical intervention considers when sepsis and infected fluid are not effectively controlled with antibiotics and chest drain or presence of significant respiratory compromise. [1,7]

- Video-assisted thoracic surgery (VATS) [4]
  - Alternative to more invasive procedures (e.g., open thoracotomy/decortication)
  - Debridement through pleural visualization and lysis of adhesions/loculations
- Open thoracotomy with rib resection: Encapsulated empyema [4]
- Decortication [4]
  - Symptomatic chronic empyema
  - Relief of thick fibrous peal

5. Follow up and Monitoring

Criteria for improvement response to therapy include: [2]

- Resolution of fever
- Decreasing white blood cell count and C-reactive protein (CRP)
- Decreasing respiratory and heart rates
- Improvement in appetite
- Sense of well-being
- Auscultation (better air entry on auscultation)

Chest tube should remove when: [6]

- Clinical resolution
- Chest X-ray or pleural ultrasound improve
- Fluid drained < 1-2 mL/kg/day (or <10-20 mL/day)

Daily monitoring: [4]

- Monitor chest tube output: how many ml per day and color of fluid.
- Check and ensure permeability of chest tube from patient to collect bag (no torsion)
- Change dressing and disinfect around the drain
- If you suspect that the drain is obstructed:
    - NEVER push drain deeper into the thoracic cavity
    - Do not inject anything into the drain
    - You can try to remove drain a few centimeter
    - And/or, using aseptic technique, perform gentle suction through the drain

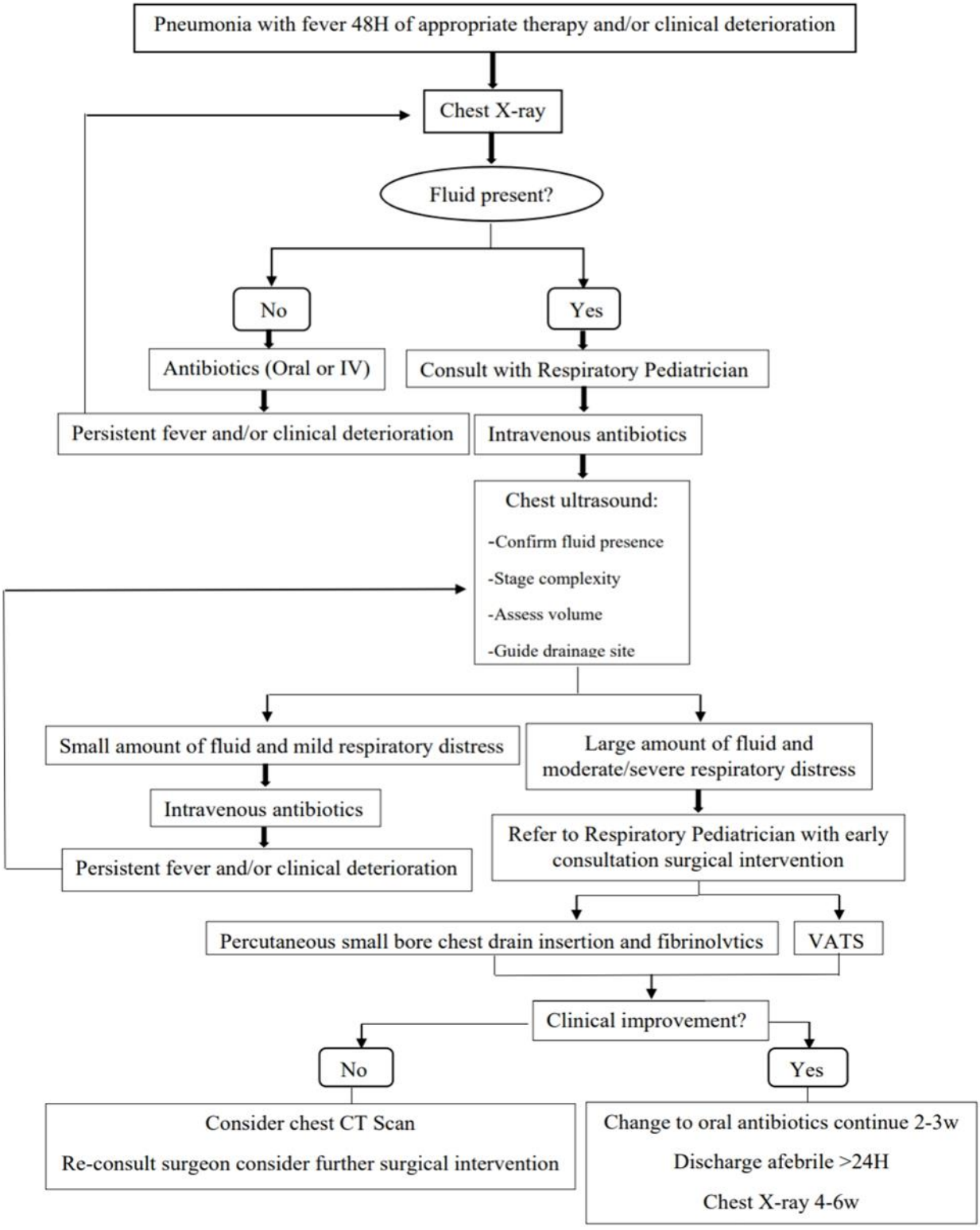
Follow up [5]:

- Children can be discharged if SaO2 > 95% in room air and afebrile for 24H on oral antibiotics
- A repeat chest X-ray should be done at 4 to 6 weeks post discharge to confirm changes are resolving. Most chest X-ray are not completely normal at this time point.
- Encouragement of deep breathing and airway clearance techniques to aid resolution or prevention of atelectasis.

VII. Prevention and Education

Vaccines are available that prevent certain types of pneumonia. Yet there are many bacteria that cause pneumonia, children are not guaranteed to avoid it even with a complete immunization. If a child is suspected of having pneumonia based on the signs or symptoms, bring him to see a physician as soon as possible [4].

Algorithm for management of Empyema in children



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Grades of recommendation
A At least one meta-analysis, systematic review, or randomized controlled trial (RCT) rated as I++ and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as I+ directly applicable to the target population and demonstrating overall consistency of results
B A body of evidence including studies rated as II++ directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as I++ or I+
C A body of evidence including studies rated as II+ directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as II++
D Evidence level III or IV; or extrapolated evidence from studies rated as II+

PNEUMOTHORAX

SENG Soputhirith, KIT Daronic, LEK Yat, KIM Ang

I. Key Facts

Pneumothorax is uncommon in children however it can cause life threatening condition. The incidence of spontaneous pneumothorax has been estimated to be 4 per 100,000 in male and 1.1 per 100,000 in female among American children. This condition may be idiopathic or linked to underlying lung diseases. The prognosis is generally good if appropriate treatments are given. [1]

II. Overview

1. Definition

- Pneumothorax is the accumulation of extrapulmonary air within the chest, most commonly from leakage of air from within the lung. [2]
- Tension pneumothorax is a life-threatening emergency wherein a large air collection in the pleural space compromises respiration and cardiac function. [3]

2. Etiology [2]

a. Spontaneous Pneumothorax

- Primary Idiopathic (no underlying lung disease): Occur in otherwise tall thin adolescent boys, smoking is the risk factor.
- Secondary (underlying lung disease):
  - Congenital lung disease: congenital cystic adenomatoid malformation, bronchogenic cysts, pulmonary hypoplasia.
  - Condition associated with increase intrathoracic pressure: asthma, bronchiolitis, cystic fibrosis, airway foreign body, smoking.
  - Infection: tuberculosis, pneumocystis carinii, pneumatocele, lung abscess, bronchopleural fistula.
  - Lung disease: Langerhans cell histiocytosis, tuberous sclerosis, Marfan syndrome, Ehlers-Danlos syndrome, pulmonary fibrosis, metastatic neoplasm, malignancy.

b. Traumatic

- Non-iatrogenic: penetrating trauma, blunt trauma (non-penetrating trauma)
- Iatrogenic: thoracotomy, thoracoscopy, thoracentesis, tracheostomy, tube or needle puncture, mechanical ventilation.

3. Pathogenesis

In the normal state, the tendency of the lung to collapse or recoil is balanced by the tendency of the chest wall to expand outward, creating negative pressure in the intrapleural space. When the air leaks into pleural space causing the lung to collapse which further induces hypoxia due to alveolar hypoventilation, ventilation-perfusion mismatch and intrapulmonary shunt. If the air continues to leak, it creates more positive pressure in the pleural space causing tension pneumothorax. It compresses to the lung, shifts mediastinum contralaterally, and impairs venous return and cardiac output, ultimately leading to hemodynamic instability. [2]

III. Signs and symptoms

1. Clinical symptoms

- The clinical presentation depends on the volume of air in the pleural space, rapidity of onset, extension of lung collapse, tension within pleural space and patient's age. [4]
- In a small and simple pneumothorax, patient can be asymptomatic, and it is found incidentally on chest radiograph. [4]
- The onset of pneumothorax is usually abrupt. [2]
- Pneumothorax may cause [2]

- Dry cough
- Shortness of breath
- Pleuritic chest pain that is usually sudden in onset and localized to apices (referred pain to shoulders)
- Respiratory distress (cyanosis, increased respiratory rate, chest indrawing, accessory muscles use, nasal flaring, abnormal airway noise).

2. **Physical examination** [5]
   - May be normal
   - Decreased breath sounds on the affected side
   - Decreased vocal fremitus
   - Hyperresonance to percussion on the affected side
   - Tachypnea
   - Tachycardia
   - Shortness of breath
   - Respiratory distress
   - Shifting of the cardiac point of maximal impulse away from the affected side
   - Shifting of the trachea away from the affected side
   - Subcutaneous emphysema
   - cyanosis
   - Shock and severe respiratory distress with tracheal deviation are typically present in tension pneumothorax
   - Areas of contusion or abrasions on the chest wall are usually seen in patients with trauma
   - Flail chest can also be seen in traumatic patients.
3. **Investigations**
   - Pulse oximetry: should be used to monitor oxygen level. However, it is not accurate in child with poor perfusion such as in tension pneumothorax. [4]
   - Arterial Blood Gas (ABG): Retention of CO2 and low blood oxygen level can cause respiratory acidosis. [5]
     - PH decrease
     - PO2 decrease
     - PCO2 elevate
4. **Imaging**
   - Chest x-ray: [4] [5]
     - Radiolucency of the affected lung
     - Lack of lung markings in the periphery of the affected lung
     - Collapsed lung on the affected side
     - Possible pneumomediastinum with subcutaneous emphysema
     - Contralateral mediastinal displacement in tension pneumothorax
     - Flattening or inversion of ipsilateral diaphragm in tension pneumothorax
     - Flattening of ipsilateral heart border in tension pneumothorax.
   - Bedside ultrasound is useful to detect pneumothorax and also evaluation for lung re-expansion after chest tube placement in emergency room. [6]
   - Chest CT: is not always necessary unless abnormalities are noted on the chest x-ray that requires further assessment. [5]
     - Useful for finding small pneumothoraxes
     - Can help distinguish a pneumothorax from a bleb or cyst
     - Helpful for locating small apical blebs associated with spontaneous pneumothoraxes
   - Estimation of size of pneumothorax: The British Thoracic Society uses the plain chest x-ray in an erect position to estimate the size of the pneumothorax. [7]

- Measurement of the distance between the lateral lung edge and chest wall at the level of hilum; Large >2cm at least 50% of pneumothorax (Figure 2.b, Picture 1. B) or
- Measurement of the vertical distance between the lung and thoracic cage at the apex (Figure 2.a) If >3 cm, pneumothorax is large.

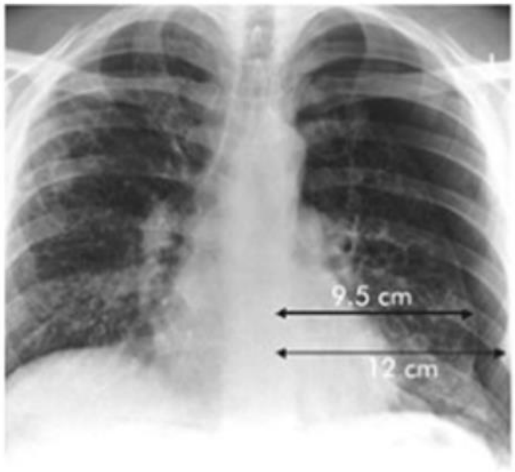


Fig 1. *Measurement of the distance between the lateral lung edge and chest wall.*

B(12cm)-A(9.5cm): 2.5cm (large)

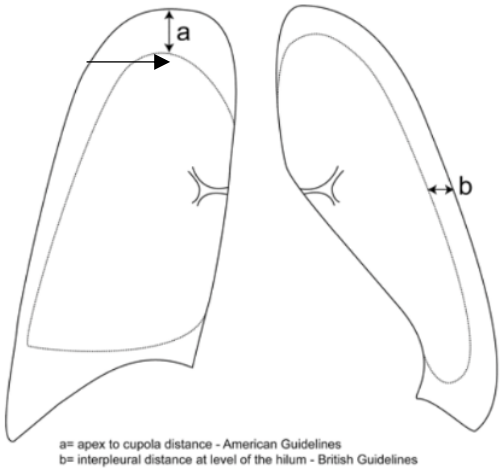


Fig 2. *Measurement of the vertical distance between the lung and thoracic cage at the apex; >3cm (large*)

5. Differential diagnosis [5]

a. Pulmonary

- Congenital lung malformations
  - Cysts (e.g., bronchogenic cysts)
  - Cystic adenomatoid malformation
  - Congenital lobar emphysema
- Acquired emphysema
- Hyperinflation of the lung
- Postinfectious pneumatocele1.
- Bullae formation.

b. Miscellaneous

- Diaphragmatic hernia
- Infections (e.g., pulmonary abscess)
- Muscle strain
- Pleurisy
- Rib fracture

IV. Treatment

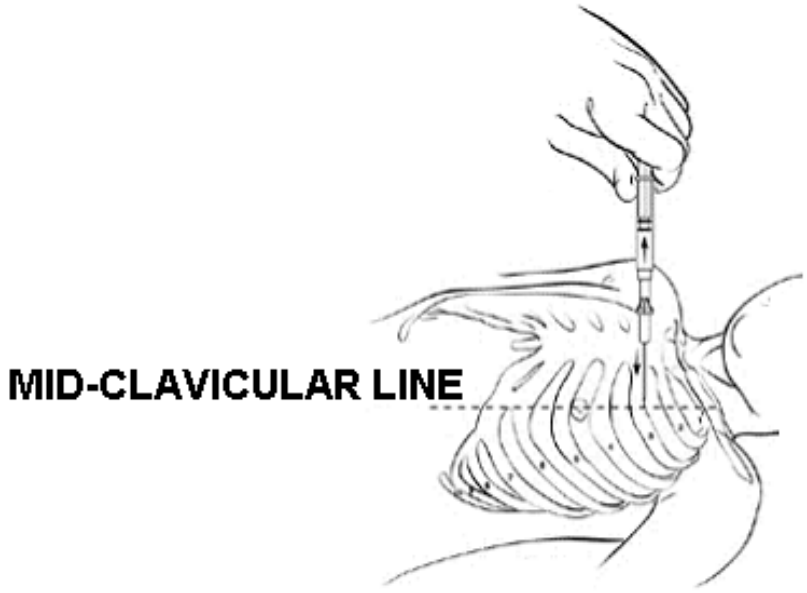
- Stabilize patient's Airway, Breathing and Circulation is the priority [5]
- Treat the underlying condition predisposing for the pneumothorax: [5]
- Antibiotics for infection
- Bronchodilators and anti-inflammatory agents for asthma exacerbation
- Patients with small primary pneumothorax (<2cm) without breathlessness can be managed with observation for 24-48 hours in the hospital. Oxygen therapy is given to

keep oxygen saturation >95%. The pneumothorax can be assessed by chest radiograph in 6-12 hours (level of recommendation B). [7]

- Supplement 100% oxygen via non-rebreathing facemask or high flow-nasal cannula (10 to 15 litters/mn) to hospitalization patients with duration <48 hours (or <72 hours) is found to increase the rate of reabsorption of air within the pleural space because the increased alveolar oxygen tension creates a steep gradient between the partial pressures of nitrogen in the pleural gas collection and the capillaries. [4][5][7]
- Unstable patients with significant dyspnea, hypoxia or pain requires chest drain for air evacuation (level of evidence A). [4][5][7]
- Needle aspiration: Aspiration is the first line treatment for all primary pneumothoraxes requiring intervention (level of recommendation B). [7]
    - Simple aspiration is less likely to succeed in secondary pneumothoraxes
    - Patients with secondary pneumothoraxes treated successfully with simple aspiration should be admitted to hospital and observed for at least 24hr.

1. **Simple aspiration technique:** [5]
    - Infiltrate local anesthetic down to the pleura, in the second intercostal space in the mid-clavicular line.
    - Using a cannula, enter the pleural cavity and withdraw the needle.
    - Connect both the cannula and a 50 ml syringe (Luer lock) to a three-way tap, so that aspirated air can be voided.
    - Aspiration should be discontinued if resistance is felt.
    - Repeat chest radiography in inspiration (an expiration film is unnecessary) in the x-ray department.
    - If pneumothorax is now only small, or resolved, the procedure has been successful.

Fig 3. *Pleural punction*



2. **Chest tube Drainage**
    - If simple aspiration or catheter aspiration drainage of any pneumothorax is unsuccessful in controlling symptoms. (level of recommendation A). [7]
    - Chest tube drainage is recommended in secondary pneumothorax except in patients who are not breathless and have very small pneumothorax (<1cm or apical pneumothorax)
    - A bubbling chest tube should never be clamped.
    - If a chest tube is clamped, this should be under the supervision of a respiratory physician or thoracic surgeon.

- If a patient with a clamped drain becomes breathless or develops subcutaneous emphysema, the drain must be immediately unclamped and medical advice sought.
- Suction to an intercostal tube should not be applied directly after tube insertion but can be added after 48 hours for persistent air leak or failure of pneumothorax to re-expand.
- High volume, low pressure (-10 to -20cmH2O) suction is recommended.
- It should be left until majority of air is reabsorbed and no re-accumulation of air is seen on the sealing of the chest tube.

Recommended Chest Tube Size:

AGE	Tube Size
Newborn	8-12FG
Infant	12-16FG
Child	16-24FG
Adolescent	20-32FG

Drainage system

- One bottle system is acceptable in pneumothorax alone without fluid collection.
- Three bottle drainage system is used in patient with pleural effusion or pneumothorax.

Figure 4. *bottles chest drains System*

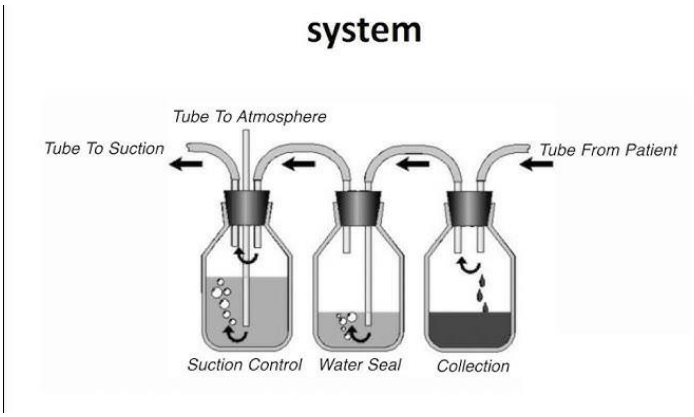
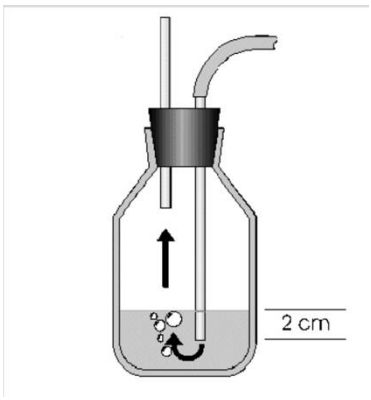
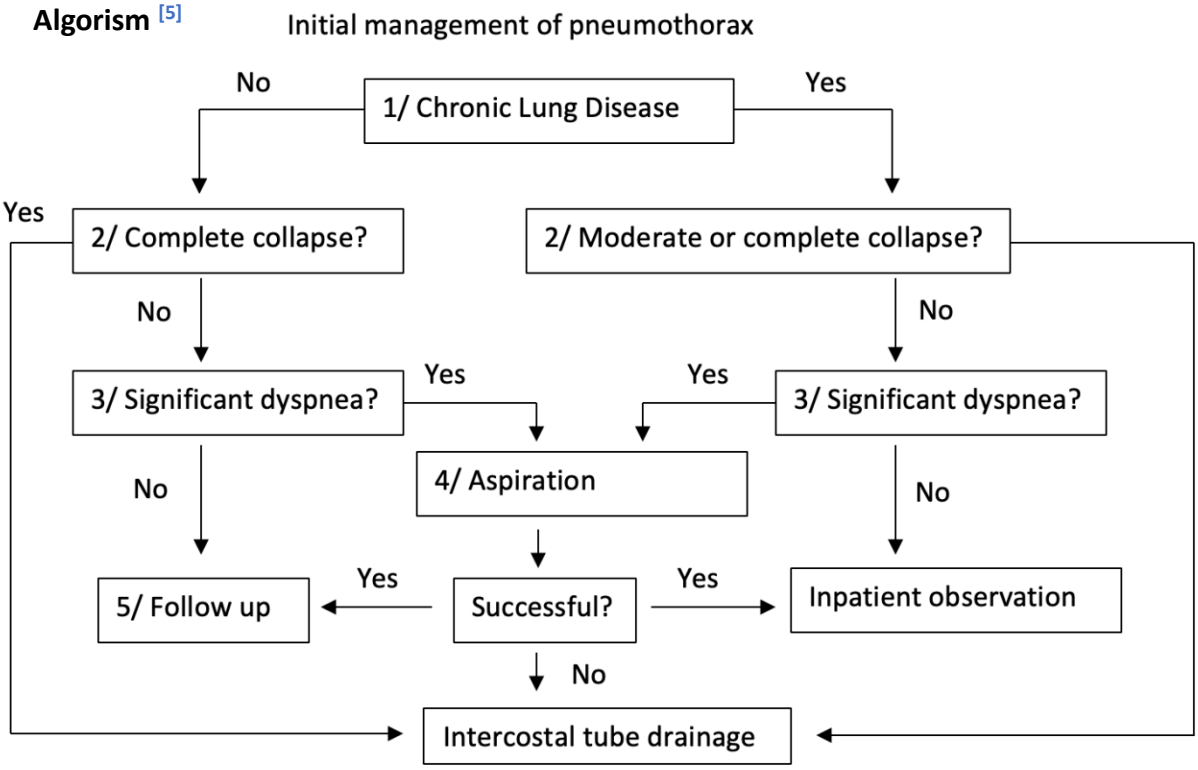


Figure 5. *bottles chest drains System*



2. **Referral to thoracic surgeon** [7]
   - In cases of persistent air leak or failure of the lung to re-expand, respiratory specialist should seek an early (3-5 days) thoracic surgical opinion. [C]
   - Open thoracotomy with plication of blebs, closure of the fistula, stripping of the pleura (apical of the lung) and basilar pleural abrasion is effective for recurrent pneumothorax [A]
   - Pleurodesis uses chemical agents such as talc, fibrin glue, and doxycycline to attach the lung to the intrathoracic chest wall. It can be used during chest tube insertion. [A]
   - Video-assisted thoracoscopic surgery (VATS) is the preferred therapy for blebectomy, pleural stripping, pleural brushing and installation of sclerosing agents with less morbidity than open thoracotomy [A]

Algorism [5]



3. **Tension pneumothorax** [2][4][7]
    - Patient should be given a high concentration of Oxygen
    - A cannula should be introduced into the pleural space at the second anterior intercostal space mid-clavicular line.
    - Chest tube is inserted after the air has been removed and the patient is no longer compromised.

V. Prognosis [5]

- Depend on the underlying etiology of pneumothorax.
- If simple spontaneous pneumothorax recovery is excellent.

VI. Education and Education [7]

- Smokers should be advised to quit.
- Flying should be avoided for at least a week after a chest radiograph has confirmed complete resolution of their spontaneous pneumothorax. Changing in atmospheric pressure can rapidly convert simple pneumothoraxes to tension pneumothoraxes.
- Primary pneumothorax patients treated successfully by simple aspiration should be observed to ensure clinical stability before discharge.
- Secondary pneumothorax patients who successfully treated with simple aspiration should be admitted for 24hours before discharge to ensure no recurrence.

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Strength of recommendation	Interpretation
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh of risk or the disadvantages (adverse event, costs…), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended

CHILDHOOD ASTHMA

KITH Daronic, SENG Soputhirith, LEK Yat, KIM Ang

I. Key Facts [1]

- There are an estimated 300 million people who have asthma worldwide.
- Childhood asthma is the leading cause of chronic disease and missed school days in children.
- All that wheezes are not asthma.
- Reactive airway disease or recurrent wheezing associated respiratory infections often precede a formal diagnosis of asthma in children.
- Asthma will commonly start before school age in children.
- Diagnosis of asthma in preschool years does not mean the child will have asthma forever. Only half of the children who wheeze during preschool years will have asthma at school age.

II. Overview

1. Definition [1]

Asthma is a chronic inflammatory disease of the airways, characterized by recurrent episodes of airflow obstruction resulting from edema, bronchospasm, and increased of mucus production.

2. Physiopathology [1][2]

The pathophysiology of asthma involves the infiltration of inflammatory cells, including neutrophils, eosinophils, and lymphocytes into the airway, activation of mast cells, and damage to the epithelial cells.

These inflammatory responses lead to the classic features:

- Airway swelling
- Increased mucus production
- Bronchial muscle dysfunction

Remodeling is a term to describe persistent changes in the airway structure, can occur, ultimately leading to fibrosis, mucus hypersecretion, epithelial cell injury, smooth muscle hypertrophy, and angiogenesis.

3. Risk factors and triggered factors [1][2]

- Positive family history of atopy
- Multiple environmental exposures, both prenatal (maternal smoking, diet, nutrition, stress, use of antibiotics and C-section delivery) and during childhood.
- Airway allergens exposure: animal, mite, mold, cockroach
- Tobacco smoke and vaping (active and passive)
- Allergic rhinitis
- Obesity
- Obstructive sleep apnea
- Gastro-esophageal reflux
- Exercise
- Stress
- Air pollutants
- Viral respiratory tract infection
- Some drugs: beta-blockers, Aspirin, NSAIDs.

III. Signs and symptoms [1][2]

Acute asthma exacerbation: A flare-up or exacerbation is an acute or sub-acute worsening in symptoms and lung function from the patient's usual status.

Classic symptoms of asthma: cough, wheezing, chest tightness and shortness of breath. Symptoms can be episodic and can become triggered by numerous factors including upper respiratory tract infections, exercise, exposure to allergens, and airway irritants such as tobacco smoke. They may also be worse at night.

Signs of impending respiratory failure in severe acute asthma exacerbation including altered of mental status, appears truly lethargic, becomes unresponsive, is cyanotic or has a silent chest.

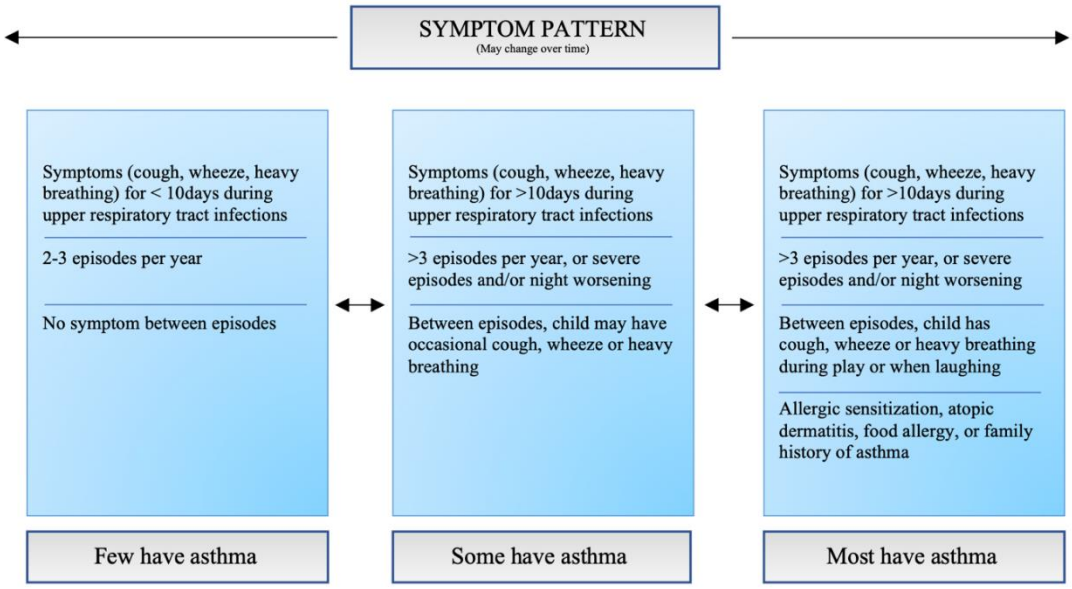
If the child does not have asthma exacerbation, the physical examination may be completely normal. Other associated symptoms including symptoms of allergic rhinitis (nasal secretion, mucosal swelling, nasal polyps) or symptoms of atopic dermatitis.

IV. Diagnosis [1]

1. Clinical diagnostic

- In most adolescents and children, the diagnosis can be made clinically based on symptoms and response to treatment
- History of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough, that vary over time and in intensity, occur and worse at night or on waking, often triggered by exercise, laughter, allergens or cold air and viral infections.
- Look for signs of comorbidity: Allergic rhinitis, eczema, food allergy
- Confirming the diagnosis of asthma is more difficult after treatment has been started.

Probability of asthma diagnosis in children 5 years and younger is challenging.



2. Investigations

a. Spirometry for lung function test

- Spirometry can be performed in bigger child who follow correctly the instruction. It should include bronchodilator respond and may include exercise or other challenge tests if required, with the variable expiratory flow.
- Variable expiratory flow limitation: FEV1 increase >12% of predictive value after inhaling bronchodilator or after 4 weeks of anti-inflammatory treatment (outside respiratory infections).

b. Peak flow: for monitoring asthma.

- A decline of 20-30% or more from patient's personal best may be indicative of an impending or current exacerbation.

- A peak flow of less than 40% of their best is indicative of severe exacerbation.
- Can be used to identify variable expiratory airflow limitation in case of limited access of spirometry: >20% of PEF improvement 15minutes after 2puffs of Salbutamol or after 4 weeks therapeutic trial with ICS.

c. Allergy testing:

- Atopic status can be identified by skin prick testing or by specific IgE testing in serum [1]
- The presence of a positive skin test or positive sIgE does not mean that the allergen is causing symptoms [1]
- Should not be performed if there is no history of an immediate reaction to the potential allergen.
- A clear relationship between allergen and asthma symptoms does not require testing, rather this should be treated as an allergic trigger and avoided where possible.[2]

V. Complications

- Limit ability to engage in normal daily activities including sports and outdoor activities
- Side effects of drugs: fungal infection, hoarse voice, Cushing syndrome (OCS)
- Airway remodeling and chronic obstruction
- Increase risk of obstructive sleep apnea, pneumonia or gastro-esophageal reflux.

VI. Treatment

Asthma cannot be cured but we can control it and live with asthma.

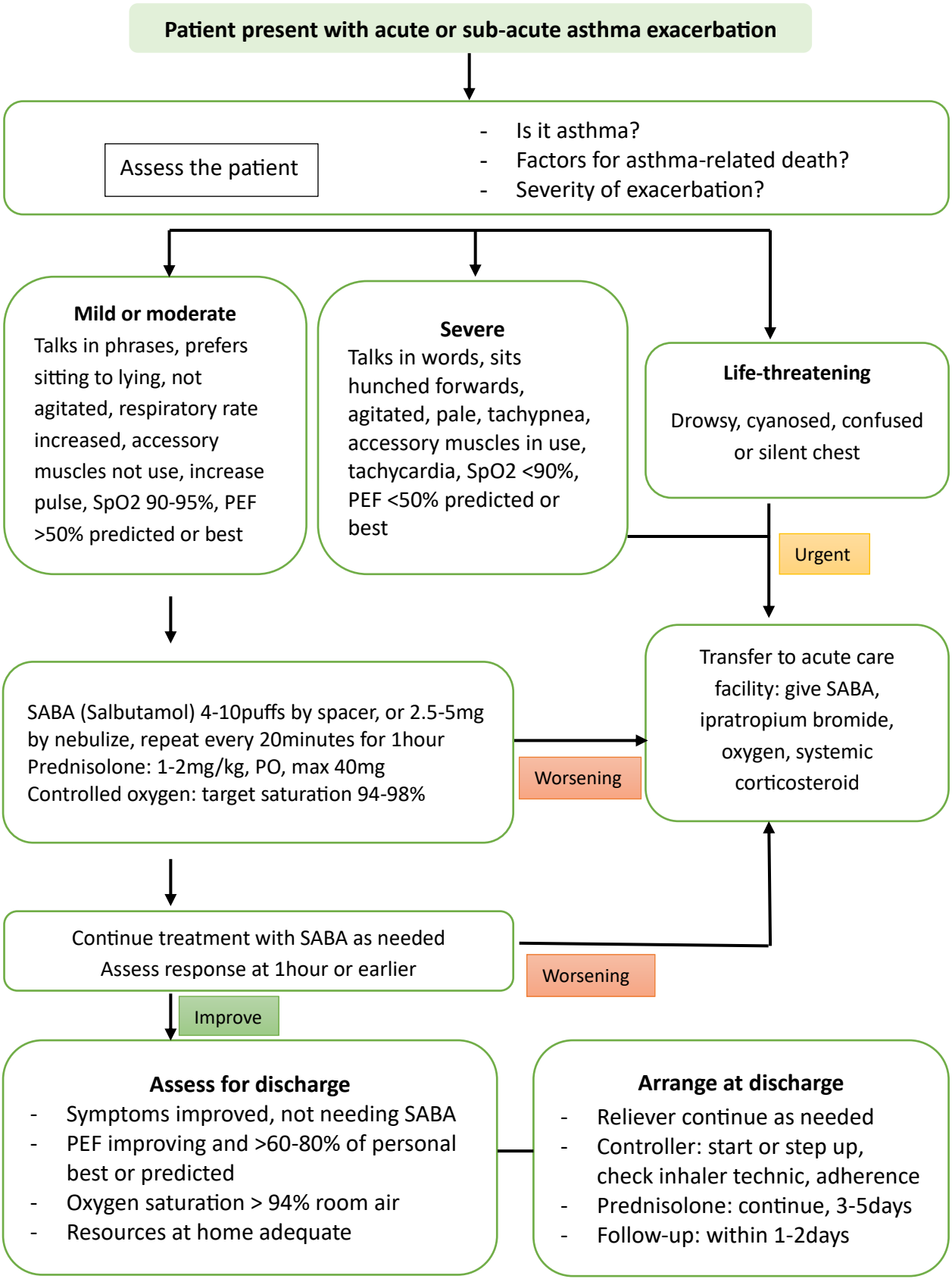
Goals of asthma treatment are [1]

- Avoid troublesome symptoms during day and night
- No sleep disturbance
- Need little or no reliever medication with minimize medication side effects
- Have productive, physically active lives, no exercise limitation
- Have normal or near normal lung function
- Avoid serious asthma flare-ups (exacerbations, or attacks) and asthma death.

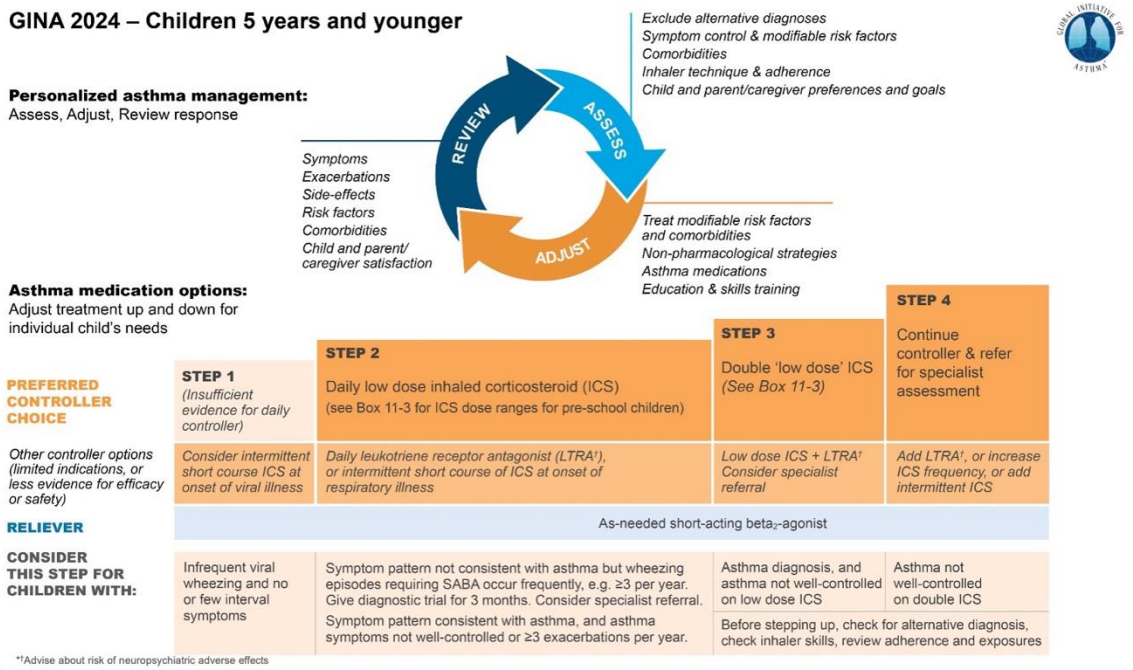
1. Asthma exacerbation management [1][2][3][4]

- Oral corticosteroids (OCS): Short course of OCS is used when
- Worsening symptoms fail to respond to an increase in reliever +/- ICS containing maintenance medication for 2-3days
- Deteriorates rapidly or has PEF or FEV1 < 60% of their personal best or predictive value
- Worsening asthma with history of sudden severe exacerbations
- Dose: Prednisolone 1-2mg/kg/day, up to 40mg, usually 3-5days, preferably taken in the morning. Other medications are Methylprednisolone, hydrocortisone and dexamethasone.
- Tapering is not needed if duration is less than 2 weeks.
- Severe asthma exacerbation
- Inhaled bronchodilators: Salbutamol MDI (metered-dose inhaler) via spacer and mask every 20minutes or reserve nebulization for children unable to tolerate MDI. No evidence of clinically significant arrhythmias following treatment with bronchodilators.
- IV corticosteroids: Methylprednisolone 1mg/kg (max 60mg) IV 6 hourly or Hydrocortisone 4mg/kg (max 100mg) IV 6hourly or Dexamethasone 0.6mg/kg (max 16mg) IV 24-48 hourly
- Second line IV treatment option if no improvement: Magnesium sulphate 0.2mmol/kg (max 8mmol) IV administered over 20minutes.
- Adrenaline IM is indicated in addition to standard therapy for acute asthma associated with anaphylaxis and angioedema, dose 10microg/kg or 0.01ml/kg of 1:1000 into lateral thigh and repeat every 5min as required.

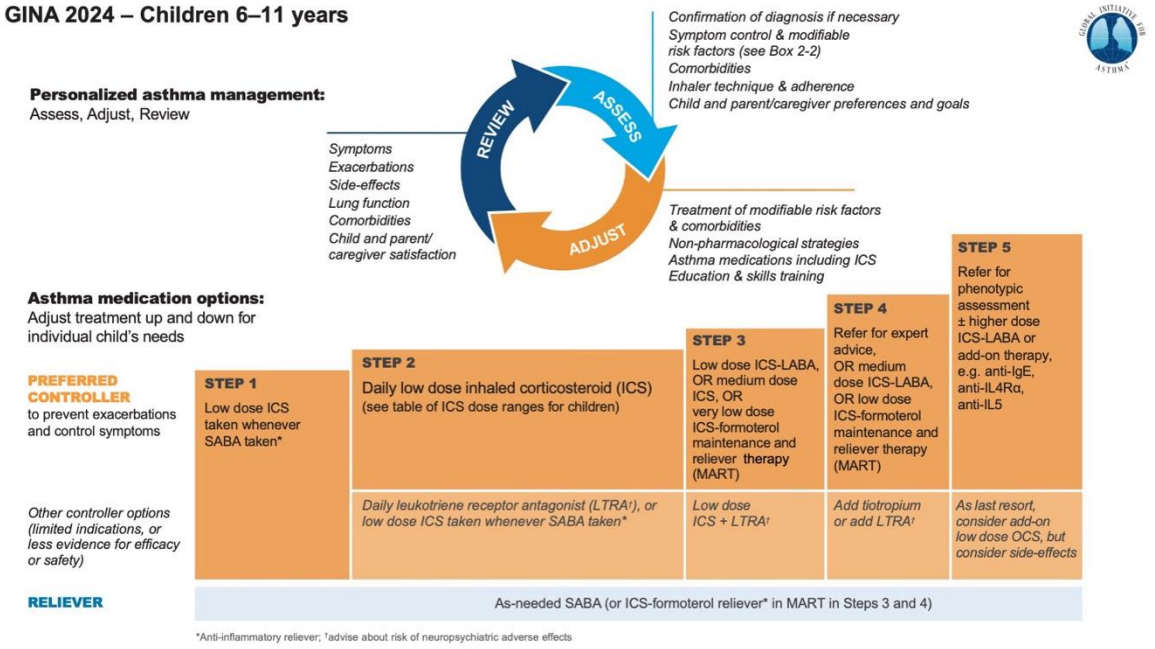
Algorithm of management in asthma exacerbation



2. Asthma preventer and reliever management [1]



GINA 2024 Box 11-2



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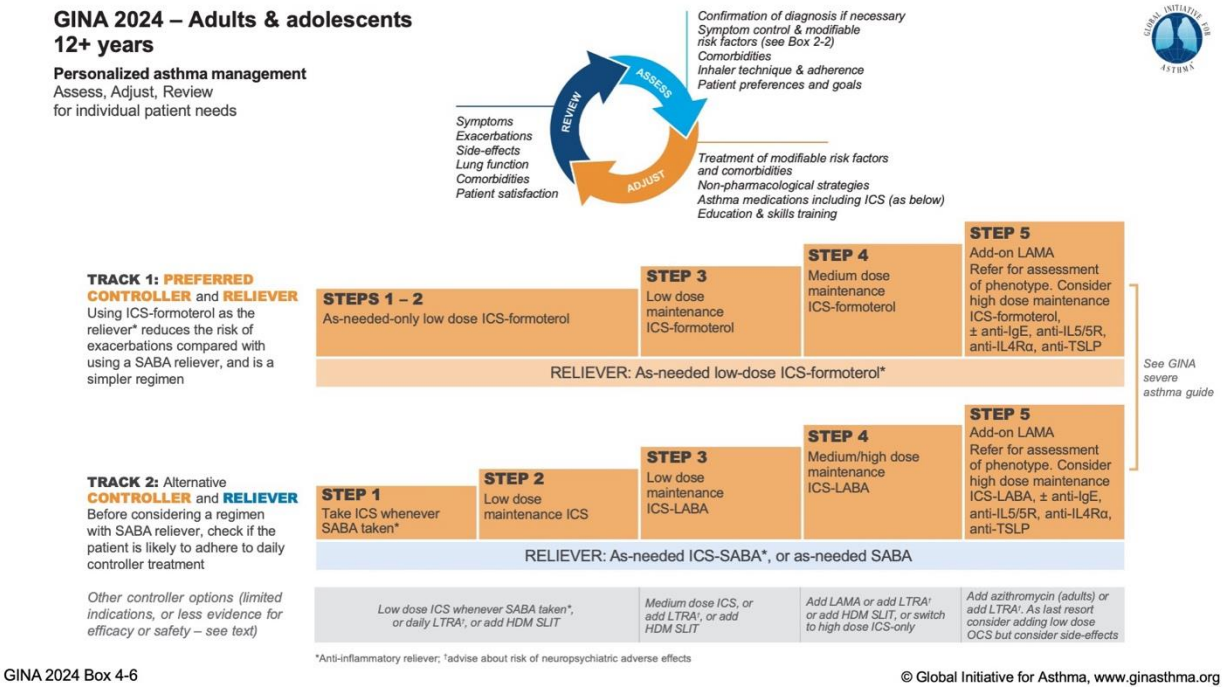
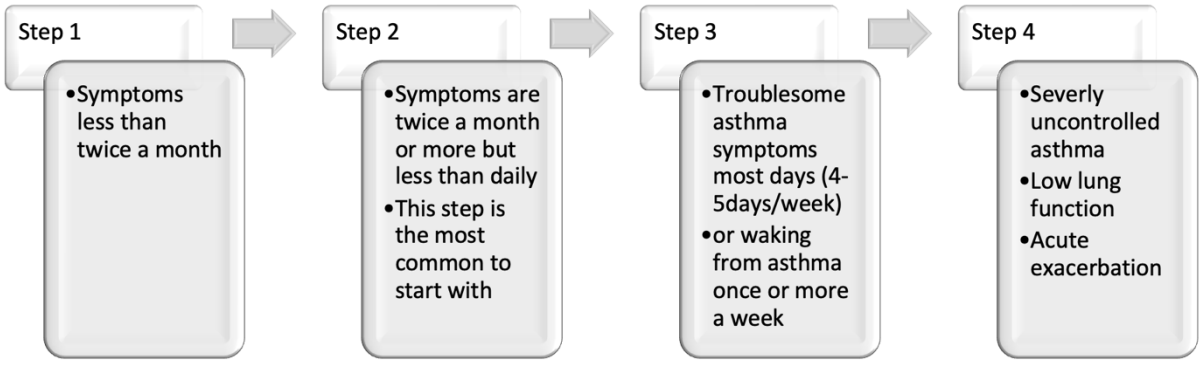


GINA 2024 Box 4-6

- **Evaluation on which step to start the preventer for children > 5 years**

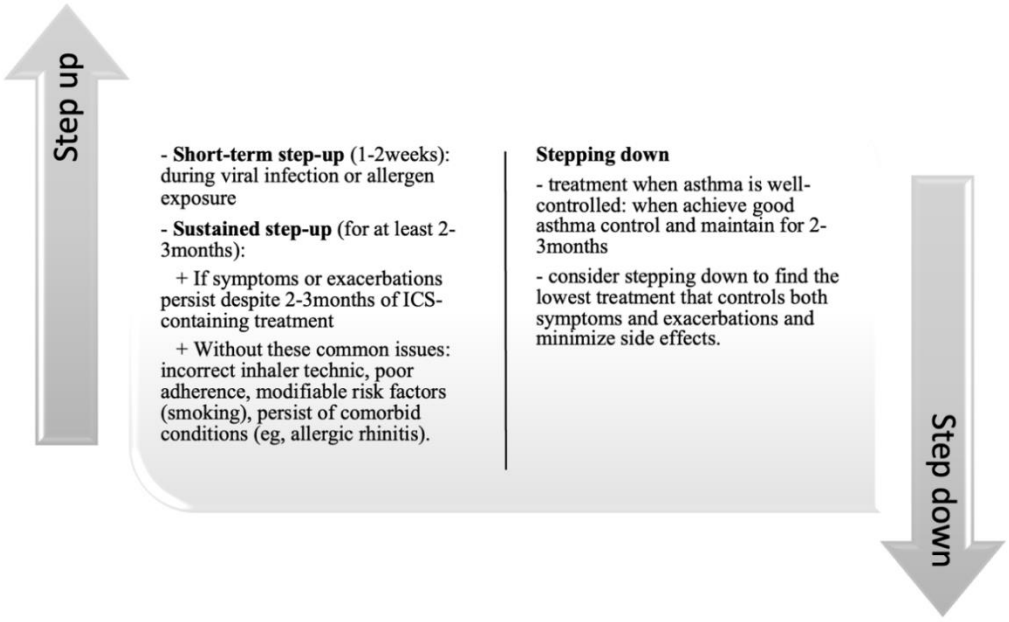


- **Low, medium, and high daily dose of inhaled corticosteroids**

Inhaled corticosteroid		Total daily ICU dose (mcg)		
		Low	Medium	High
Adult and adolescent	Beclomethasone Dipropionate (BDP) HFA	200-500	>500-1000	>1000
	Budesonide HFA or DPI	200-400	>400-800	>800
	Fluticasone propionate HFA	100-250	>250-500	>500
Children 6-11 years	Beclomethasone Dipropionate (BDP) HFA	100-200	>200-400	>400
	Budesonide HFA or DPI	100-200	>200-400	>400
	Budesonide nebules	250-500	>500-1000	>1000
	Fluticasone propionate HFA	50-100	>100-200	>200

- Anti-leukotriene receptor antagonist (LTRA): less effective than daily ICS, particularly in preventing exacerbations. When added to ICS, it is less effective than ICS-LABA. Risk of mental health effects (behavior and mood changes) with Montelukast.
- SABA-only treatment is not recommended:
  - Associated with increased risk of exacerbation and lower lung function and asthma related death.
  - Regular use of SABA increases allergic responses and airway inflammation and reduces the bronchodilator response to SABA when it is needed.
  - Over-use of SABA: more than 3 canisters of SABA yearly are associated risk of severe exacerbation. Home use of nebulized SABA is also associated with an increased risk of asthma death.
- **Assessment of symptom control**

Assessment of symptom control		**Level of asthma symptom control**		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
Daytime symptoms more than twice/week	Yes ☐ No ☐	None of these	1-2 of these	3-4 of these
Any night waking due to asthma?	Yes ☐ No ☐			
SABA reliever needed more than twice/week	Yes ☐ No ☐			
Any activity limitation due to asthma	Yes ☐ No ☐			



VII. Prevention and education [1]

- Engaging patient and family regarding the disease process and triggers, symptoms recognition, when to seek medical attention or emergency.
- Behavioral modification including weight loss, avoiding exposure to tobacco or environmental allergens

- Understand the use of controller and preventer, importance of drug adherence, inhaler technic
- Essential check point to provide to patient with asthma and the family
- Inhaler skills: provide skills training for effective use of inhaler devices
- Check and improve adherence with asthma medications
- Treating modifiable risk factors: smoking, exercise-induced bronchoconstriction, occupational asthma, drugs consumptions (NSAIDs, Aspirin)
- Engage daily physical activity for general health benefits and lung function with advice on management of exercise-induced bronchoconstriction.
- Asthma action plan
- Vaccination: National program of vaccinations, especially annual influenza vaccine

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BRONCHIECTASIS

UM Khemuoy, Michael WALL, KONG Sokchinda

I. Key Facts

- Bronchiectasis is more common than generally recognized and very often has been misdiagnosed as recurrent pneumonia or asthma.
- Bronchiectasis is a chronic airways disease characterized by airway dilation, scarring, mucous plugging, and chronic infection. In most cases it is not fully reversible.
- The symptoms include daily wet cough and sputum production and, with exacerbations, low grade fever, malaise, weight loss, increased cough with darker sputum, increased dyspnea, and hypoxemia.
- The physical exam will show thick crackles over the affected areas of the lung at all times.
- The areas of the lungs affected with bronchiectasis are always colonized with bacteria even after antibiotic treatment.
- The diagnosis requires a high index of suspicion and a thorough past history related to any previous lung symptoms, hospitalizations, etc. the definitive diagnosis is made by chest CT scan.
- The therapy of bronchiectasis includes daily maintenance treatments to help keep patients at their own best baseline plus aggressive and early intervention for exacerbations.

II. Overview

1. Introduction

Bronchiectasis is one of the more common but under-recognized causes of chronic lung disease in children. Prior to establishing a definitive diagnosis of bronchiectasis, most children with this lung condition have been misdiagnosed as having recurrent pneumonia or asthma. Bronchiectasis is characterized by abnormally dilated airways, variable degrees of damage to the epithelial cells that line the airways, decreased clearance of mucous from the airways, and chronic infection in the affected airways. Once fully established, bronchiectasis is irreversible although there is some evidence that early in the process some healing and/or improvement may be possible.

2. Natural history and pathophysiology

Bronchiectasis is usually a result of a previous injury to the airways of the lung. The most common cause is a severe infection that causes airway damage in a previously healthy child. Chronic aspiration of oral or gastric contents or an acute aspiration of a toxic substance can also lead to bronchiectasis. An underlying genetic mutation causing abnormal clearance of mucous from the lungs (cystic fibrosis, ciliary dyskinesia) or an inherited immune defect may be the underlying cause in some patients. Chronic lung infection in patients with HIV/AIDS can lead to bronchiectasis, and symptoms of bronchiectasis can be the first presentation HIV/AIDS in children. Localized bronchiectasis may result from retention of a foreign body in a bronchus.

The unifying problem in all causes of bronchiectasis is damage to the epithelium that lines the lumen of airways. This damage then leads to retention of mucous and subsequent chronic infection in the affected areas of the lung. The infection is permanent and cannot be completely eradicated with any treatment. The chronic infection leads to airway inflammation which causes localized recruitment of inflammatory cells and release of inflammatory mediators. This leads to further epithelial cell damage, increased mucous

production, and eventually destruction of the airway structure. This process becomes a cycle of inflammation, infection, and ongoing airway damage. In some cases, the process of bronchiectasis seems to progress from mild airway dilation (cylindrical stage) with no loss of the airway epithelium to more progressive dilation, development of cyst-like changes, and complete loss of normal epithelium (varicose or cystic stages). In the cylindrical stage there have been reports of reversal of the process with early aggressive treatment.

Figureures 1 and 2 show the gross anatomy of severe bronchiectasis.

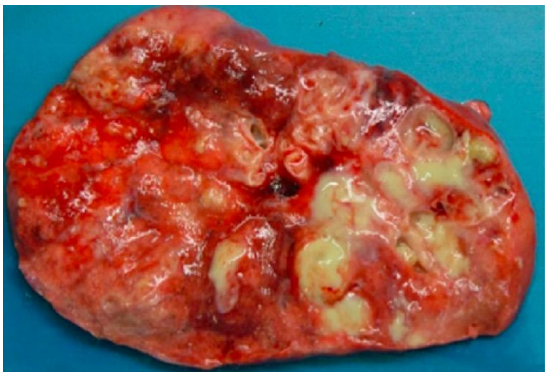

Figure 1. Gross anatomy of severe bronchiectasis. Note Inflammation, hemorrhage, and infected mucous.

Figure 2. Mucous has been removed from specimens. Severe saccular (varicose) bronchiectasis on left and cystic bronchiectasis on right.

- ❖ *Note:* that the pathology and pathophysiology of bronchiectasis is quite different than that of pneumonia which is mostly an alveolar process or asthma.

2. Potential underlying causes of bronchiectasis in children in Cambodia

- Preceding severe lung infection in a previously healthy child. This is the most common cause of childhood bronchiectasis in Cambodia and can precede the onset of symptoms by weeks to years. The most frequent preceding infection is viral with adenovirus being a well-known cause. However, any common respiratory virus such as RSV, influenza, measles, or varicella, can lead to airway damage and bronchiectasis. Any severe bacterial infection including the common causes of community acquired pneumonia, *Staphylococcus aureus*, gram negatives such as *Pseudomonas aeruginosa* or *Burkholderia pseudomallei*, and *Bordetella pertussis* can cause the condition. Tuberculosis can be a cause of bronchiectasis especially if associated with airway obstruction.
- Acute or Chronic aspiration. Acute aspiration of a toxic substance such as a petroleum product or chronic aspiration of oral or gastric contents may cause airway inflammation and bronchiectasis. The latter is especially common in children with severe neurologic conditions that cause loss of normal upper airway protective mechanisms.
- Retained foreign body. A foreign body that causes airway obstruction can cause localized infection and bronchiectasis.
- HIV/AIDS. Bronchiectasis can be a late manifestation of HIV/AIDS in children who acquire the infection at birth. These children usually present beyond early childhood and bronchiectasis may be the first manifestation that brings them to medical attention.

- Congenital disorders of immune function. These are rare conditions that can lead to recurrent lung infections and bronchiectasis. Most of these patients will have sites of infection in addition to the lungs depending upon the specific gene mutation.
- Ciliary dyskinesia. Airway epithelial cells have cilia on their luminal side that are important in normal clearance of mucous, bacteria, etc. from the airways. There are rare genetic conditions that can cause abnormal ciliary function leading to chronic airway infection. Kartagener's Syndrome (situs inversus, sinusitis, bronchiectasis) is one example of an inherited cause of bronchiectasis and should be suspected if the patient has the three manifestations.
- Allergic bronchopulmonary aspergillosis. This is an allergic, immunoglobulin type E reaction to the growth of the fungus Aspergillus in the lungs of patients with severe asthma. The reaction causes severe mucous obstruction in airways that can lead to bronchiectasis.

❖ *Note: The most common cause of bronchiectasis in many parts of the world is the genetic condition of cystic fibrosis. This disease is most common in children of Caucasian background but has been found in numerous others. At present it has not been described in children from Cambodia but it is possible that may change in the future. The concentration of this guideline is on non-cystic fibrosis bronchiectasis.*

3. Bacteriology of bronchiectasis

One of the major features of bronchiectasis is that the lungs of patients are always infected with bacteria. Even during periods of time when the patient is clinically stable a sputum culture will always grow bacteria, and treatment with antibiotic will not totally sterilize the lungs. Various bacteria can chronically inhabit the lungs of these patients, but some are rather common. In patients whose bronchiectasis is caused by a previous severe infection but who do not have an unusual underlying genetic condition, the bacteria found in the sputum often mirror those found in the oropharynx. For example, the sputum culture of these patients often grows non-type b Hemophilus, *Streptococcus pneumoniae*, or *Moraxella catarrhalis*. *Staphylococcus aureus* is also common. The sputum of some patients may grow gram negative organisms such as E. *coli*, P. *aeruginosa*, or K. *pneumoniae*. It should be noted that a sputum culture from patients with bronchiectasis may grow more than one organism. As a general rule, patients with bronchiectasis will grow the same bacteria from their sputum over a long period of time although one may see a change over time related to antibiotic pressure.

Anaerobic bacteria may have a role in the bacteriology of bronchiectasis although this is not clear since these bacteria are not isolated from a routine sputum culture.

Organisms other than bacteria may be isolated from the sputum of patients with bronchiectasis. Two examples include Aspergillus species and non-tuberculous mycobacteria.

III. Signs and Symptoms

The most common symptoms of bronchiectasis include a daily wet cough, chronic sputum production, and dyspnea either with exertion or at rest. These symptoms will increase during exacerbation of the disease (see below, Exacerbations). Hemoptysis may occur.

The physical exam will show thick crackles over the affected areas of the lungs. These crackles will always be present and do not go away with treatment. Wheeze may be present but is not the characteristic high-pitched wheeze of asthma. Wheeze related to bronchiectasis is caused by air moving through and around mucous plugs and therefore

will usually be associated with rhonchi and/or coarse crackles. The wheeze will not improve significantly following inhalation of salbutamol (unlike asthma). Failure to thrive may be present. Nailbed clubbing is also common.

IV. Diagnosis

The first step in diagnosis is a high index of suspicion and a thorough history. Many if not most children with bronchiectasis have had symptoms for months to years and have been diagnosed with recurrent pneumonia, asthma, or bronchitis. A good past history, going back to early infancy, related to the onset of symptoms is required. When did the symptoms first begin? Was there a severe lung infection prior to the onset of symptoms? Was the child ever hospitalized for a severe pneumonia? What previous diagnoses have been made? What response to therapy has been noted? Often the patient has had antibiotic therapy if they had an exacerbation with increased cough, increased mucous production, and perhaps a low-grade fever. Did the patient improve after antibiotic? How long did the improvement last?

A plain chest radiograph should be performed in a patient in whom bronchiectasis is suspected. The x-ray may show evidence of diffuse or localized airway thickening, mucous plugging, and perhaps some cystic changes. Frequently, however, the plain chest x-ray may not be sensitive enough to make a definitive diagnosis of bronchiectasis or reveal the total extent of the process. A chest ct scan (without contrast) will be needed to make a definitive diagnosis of bronchiectasis and should be performed in any patient in whom the condition is suspected.

Figureures 3,4, and 5 show ct scans of various types of bronchiectasis.

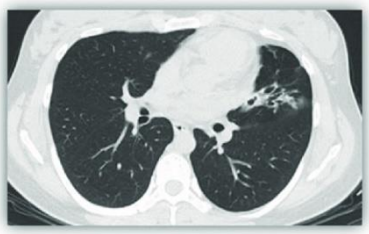

Figure 3

Early cylindrical bronchiectasis

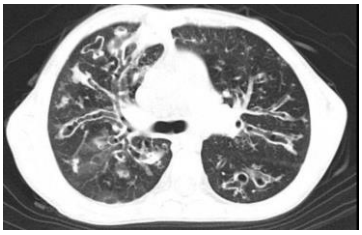

Figure 4.

Severe saccular bronchiectasis

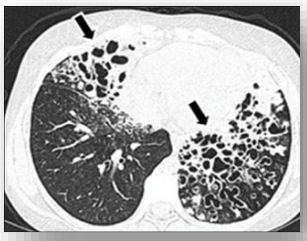

Figure.5

Severe *cystic bronchiectasis*

If the CT scan shows bronchiectasis, then other testing for an underlying cause will often be needed, depending upon the clinical situation. Most children should have HIV testing. If the child has had infections in other parts of the body, then an immune work-up would be indicated. If the child has a clear history of severe asthma as well as bronchiectasis then a blood sample for serum IgE. would be indicated to rule out allergic bronchopulmonary aspergillosis.

All children with bronchiectasis should have an initial sputum culture performed. The rationale for this is that all patients will have chronic airway infection, and one wants to know the predominant organism in order to think about appropriate antibiotic therapy. (See above Bacteriology and below, Treatment).

❖ **What is an exacerbation of bronchiectasis?**

Patients with bronchiectasis will usually have daily symptoms of cough and sputum production. The severity of daily symptoms in these patients can vary considerably from one patient to another. They will have periods of time during which their daily symptoms

are stable and they are at their own clinical best baseline. The length of time for these periods of stability can be quite different from one patient to another and may vary from weeks to many months.

After a period of stability, however, and over the course of days to weeks, patients with bronchiectasis will have an exacerbation of their symptoms. During an exacerbation patients will have increased cough, increased sputum production, a change in sputum color (usually from clear or yellow to green or gray), low grade fever, fatigue, and weight loss. The chest x-ray often shows little or no change from baseline, but spirometry will show a decrease in FEV1. If patients have not already been diagnosed with bronchiectasis and they present to an ED or outpatient clinic during an exacerbation, they are often misdiagnosed with "pneumonia" even though the chest x-ray of bronchiectasis is different than that of a typical community acquired pneumonia.

What causes an exacerbation? Most of the time there is no specific cause that can be identified although sometimes an exacerbation is preceded by an upper viral respiratory infection.

The goal of treatment for an exacerbation is therapy directed at returning the patient to their own best baseline in terms of symptoms and spirometry. (See below, Treatment of Exacerbations).

V. Treatment

Bronchiectasis is generally thought to be a permanent condition. This means that once bronchiectasis is firmly established there is no treatment that will lead to complete reversal of the affected airways to a normal state. While this remains true to a significant extent, there is evidence that very early in the onset of bronchiectasis treatment may lead to at least some reversal of the process. There are two major goals of treatment for bronchiectasis. One is treatment directed at helping patients maintain their own best baseline for as long as possible. The other is aggressive treatment of exacerbations in order to get patients back to their own best baseline and to prevent advancement of the disease.

1. Maintenance treatment of bronchiectasis.

Various maintenance therapies have been proposed for children with bronchiectasis and are discussed below. The overall evidence for the efficacy of the various potential maintenance therapies for this disease vary from weak to strong. It should also be noted that not all families of children with bronchiectasis will be able to adopt all of these therapies due to socioeconomic issues, time constraints, etc.

a. Airway clearance techniques (ACT), also known as chest physiotherapy

There are various modalities for performing ACT in children with bronchiectasis. These basically include manual chest percussion followed by cough or the use of mechanical devices to vibrate the chest followed by cough. The evidence for home use of these techniques to help maintain patients at their best baseline is not strong, but the consensus is that if patients and their families can be taught to do one of these techniques at home then it may be helpful. ACT would need to be done 2-3 times daily and each session would take about 15 minutes. Patients and their families would need to be taught how to perform ACT, preferably by a physiotherapist with training in the various techniques.

b. Oral and Inhale mucolytic agents

None of the available oral so-called expectorants or decongestants have ever been demonstrated to have any efficacy in the treatment of bronchiectasis. Various inhaled mucolytics have been developed over the course of many years. Their use in a home setting would require that the family obtain a nebulizer device. Some of these medications include:

- *N*-acetylcysteine. There is no evidence that this medication helps prevent exacerbations of bronchiectasis. In addition, this medication is an airway irritant and has a bad smell.
- DNase. This medication is used for patients with cystic fibrosis bronchiectasis, but has not been shown to be helpful in non-cystic fibrosis bronchiectasis.
- Hypertonic *saline (HTS).* Inhalation of 6% HTS may promote mucous clearance in some patients, especially those with copious, thick secretions. It is usually administered prior to ACT. HTS can be an airway irritant and inhalation of salbutamol prior to HTS nebulization is recommended.

c. Asthma type medications

These would include a short acting bronchodilator such as salbutamol and inhaled corticosteroids.

Salbutamol. The routine use of inhaled or oral salbutamol for maintenance therapy in bronchiectasis has not been studied. Its use should be confined to those patients with bronchiectasis who have objective evidence of a positive bronchodilator response such as improvement in FEV1 pre/post spirometry or observer-based reduction of wheeze. Inhaled salbutamol can also be used prior to inhalation of hypertonic saline to prevent bronchoconstriction.

Inhaled corticosteroid (ICS). There is no evidence in the literature that ICS help patients maintain their baseline or prevent exacerbations. Thus, their routine use in bronchiectasis is not recommended.

d. Antibiotics

In this section the use of antibiotics for daily, routine maintenance is discussed. Their use for exacerbations is discussed below (see Treatment of exacerbations).

Macrolides. Macrolide antibiotics such as erythromycin and azithromycin have anti-inflammatory as well as anti-bacterial properties. Chronic administration of azithromycin in patients who have recurrent exacerbations has been shown to reduce the exacerbation rate in some patients by approximately 50%. Since not all patients with bronchiectasis have frequent exacerbations, the recommendation is to start azithromycin in those who have had 3 or more exacerbations in the preceding year. One then continues the medication for 6-24 months in order to reassess efficacy. The dose in children is 10 mg/kg 3 times per week.

Other antibiotics for maintenance therapy. The choice of whether to utilize daily, long term antibiotics other than a macrolide as a maintenance therapy and the choice of antibiotic to use depends on two major factors: the frequency of exacerbations and the result of sputum cultures. Patients whose sputum grow the most common bronchiectasis organisms such a normal mouth flora, S. *aureus*, or E. *coli* and who do not have frequent exacerbations should probably not be treated with a maintenance antibiotic. However, a minority of such patients begin to have increased cough and sputum within a very short time after treatment for every exacerbation. This becomes a difficult life quality situation and a trial of long-term treatment with an oral antibiotic matched by sensitivity testing to the relevant sputum culture bacteria may be indicated. However, one may anticipate the

eventual development of antibiotic resistance or a change in sputum bacteria to a new bacterium with inherent resistance to the antibiotic being used.

The situation is somewhat different for those patients whose sputum chronically grows P. aeruginosa. For these patients, inhalation of a nebulized aminoglycoside, e.g., gentamicin or tobramycin, may be a very effective method of decreasing the frequency of exacerbations. While this has not been studied extensively in non-cystic fibrosis bronchiectasis it is a highly efficacious approach in cystic fibrosis patients. After a long period of time the P. aeruginosa in the sputum of these patients may develop resistance to the aminoglycoside, but this is not a uniform issue. An oral fluoroquinolone such as ciprofloxacin is not a good choice for long term maintenance therapy in patients with chronic P. *aeruginosa* infection because resistance tends to occur sooner than with an inhaled aminoglycoside.

2. Treatment of exacerbations

Early recognition of an exacerbation by the patient, family, and health care provider and early initiation of treatment are important factors in preserving residual lung function and improving quality of life. Families should be educated about the early warning signs of an exacerbation and should be encouraged to obtain health care as soon as possible. In general, the earlier an exacerbation is recognized and definitive treatment is begun the faster the patient will return to best baseline. The definitive treatment for a significant exacerbation is admission to a hospital for at least 10-14 days of intravenous antibiotic(s) relevant to the most recent sputum culture. On admission a sputum culture should usually be obtained to ensure that the bacteria in the sputum have not changed. On occasion a patient experiencing a mild exacerbation may be started on an oral antibiotic for 2-3 weeks but only if the provider can be assured that if the patient is not improving, he/she will be brought to the hospital for admission.

Inpatient treatment,

- Airway clearance therapy (ACT). ACT should be performed 2-3 times per day followed by voluntary cough if possible. A physiotherapist with ACT training should perform the ACT if possible.
- Inhalation therapy prior to ACT. While various regimens may be possible, inhalation of salbutamol via metered dose inhaler or nebulization followed by nebulized 6% hypertonic saline just prior to ACT is a good regimen.
- Antibiotic. Parenteral administration of one or more antibiotics relevant to the most recent sputum culture should be initiated until the results of an admission sputum culture are available.
- Nutritional support. Most children with an exacerbation of bronchiectasis will lose weight. Efforts to deliver age-appropriate nutritional support should be initiated.
- Determining the end of antibiotic treatment. It usually takes about 10-14 days for
- patients to return to their previous baseline following inpatient treatment for an exacerbation. The determining factors for end of antibiotic treatment include: clinical improvement of symptoms, return of oxygen saturation to previous baseline, lack of fever, weight gain, improvement in fatigue. If patients have had previous spirometry such that their best baseline values are known, then a return to baseline is a good outcome measure. The provider should not expect any change in the chest x-ray or sputum culture during a 10 -14 days admission so these tests would not be useful in determining if the patient can be discharged.

3. Surgery

The typical child with bronchiectasis has involvement in more than one lobe of the lung and surgery would not be expected to yield any long-lasting benefit. However, a small minority of patients might be candidates for a lobectomy if the involvement is localized to only one lobe. One example may be a child who has had a retained foreign body and has developed bronchiectasis as a result.

VI. Follow up

Bronchiectasis is a chronic, long term lung condition that requires ongoing medical follow up for the lifetime of the patient. The patients may be stable for many months but can be expected to have recurrent exacerbations requiring a step up in intensity of their maintenance therapy. If exacerbations can be recognized early in their course and appropriate treatment started then progression of the condition may be largely prevented. Even if patients are stable for periods of time, they should be seen on a regular basis by a health care provider with experience in treating bronchiectasis. Some elements of an ideal system for managing children with bronchiectasis would include:

- Education of the parents about bronchiectasis including the cause and long-term expectations. It is especially important that parents are taught about the early warning signs of an exacerbation so that specific therapy can be started.
- Appropriate and early treatment of exacerbations that continues until the child has returned to his/her best baseline.
- Long term follow-up by a physician trained in the management of children with bronchiectasis. Ideally this would be in a child specific Chest Clinic type of facility.
- Establishment of a communication system between the parents and the physician so that exacerbation treatment can be started as soon as possible.
- Surveillance sputum culture 1-2 times per year on a maintenance basis and during exacerbations as indicated clinically.

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CONGENITAL CYSTIC LUNG LESIONS

KONG Sokchinda; UM Khemuoy, Michael WALL

I. Key Facts

- Congenital cystic lung lesions are rare but often underdiagnosed
- The pathologies include Congenital Lobar Emphysema (CLE), Bronchogenic cyst, Pulmonary sequestration, Congenital Polycystic Adenomatoid Malformation (CPAM**)**
- Incidence of congenital cystic lung lesions is 1 per 8300 to 35 000 lives birth
- They occur sporadically and slightly male predominant

II. Overview

1. **Definition:** congenital lung lesions are Developmental abnormalities of the lower respiratory tract.
2. **Pathophysiology:**

a. CPAM: there are 5 types. However, type 0 is very rare and type 4 is classified in pleuropulmonary blastoma, therefore this section will concentrate on 3 types:

- CPAM type 1:
  - Represent 70% of all CPAM cases.
  - one or more large cysts, about 2-10 cm in size.
  - The cysts are lined with normal appearing airway epithelium and about 30% contain mucous producing structures.
  - not associated with other congenital malformations. Malignant transformation in this type of CPAM has been reported but is rare.
- CPAM type 2:
  - represents about 15-20%
  - multiple small cysts that are less than 2 cm in size.
  - often associated with other congenital lesions of the lungs, kidneys, intestines, or bones. CPAM type 2 is not associated with malignancy.
- CPAM type 3:
  - represents about 5-10% of CPAMS.
  - The lesions tend to be large, involving an entire lobe or lung, and consists of multiple small cysts.
  - may be partially or completely solid in appearance.

b. CLE: abnormal development of the bronchial cartilage of the proximal airway that leads into the affected lobe. The cartilage abnormality causes internal collapse of the airway such that air can enter the lobe but has difficulty exiting. This then leads to hyperexpansion of the lobe. The affected lobe has a reduced number of alveoli and blood vessels and is non-functional in terms of gas exchange. The major physiologic impact of CLE is not so much related to the affected lobe itself, but rather to the hyperexpansion that can cause atelectasis of other lobes in both the same and opposite lungs. In CLE only one lobe is affected, most often the left upper or right middle lobe.

c. Bronchogenic cyst: abnormal budding of the fetal bronchial tree. The cyst is lined with normal, secretory, bronchial epithelium, and the outer wall of the cyst contains elements normal airways such as cartilage, mucous glands, and smooth muscle. Thus, these cysts are non-malignant. Bronchial cysts are almost always filled with fluid. Most bronchogenic cysts are located near or below the carina with some being paratracheal or retrocardiac. A small percentage of bronchogenic cysts can be found in the lung parenchyma, typically near the hilum. If a patient has symptoms related to a bronchogenic cyst, they are not related to the cyst itself but rather their size and/or location.

d. Bronchopulmonary sequestration (BPS) is a non-functioning mass of embryologic lung tissue, usually located in a lower lobe, that has no airway connection to normal lung. The arterial blood supply for BPS comes directly from the aorta (as opposed to the normal pulmonary arterial supply) and the venous drainage may be to the pulmonary or systemic veins depending upon the type of BPS. Two types of BPS have been described: intralobar and extralobar.

- Intralobar BPS:
  - the most common type accounting for about 80% of BPS.
  - located within normal lung tissue and does not have its own visceral pleura.
  - Its arterial blood supply comes directly from the aorta and its venous drainage usually goes into the pulmonary veins and then left atrium.
  - Most intralobar BPS are located in one of the lower lobes with the left lower lobe being most common.
  - not usually associated with other congenital lesions and does not have a bronchus that connects directly to the normal tracheobronchial tree.
  - may become infected via its arterial blood supply or anomalous connections to the gut or the lung parenchyma. The pathology of intralobar BPS includes primitive airway tissue filled with mucous, microcysts, and abnormal parenchymal tissue
- Extralobar BPS
  - lie outside of the normal lung tissue and are encased in their own visceral pleura.
  - Most are located between the left lower lobe and the hemidiaphragm below.
  - Their arterial blood supply comes from the aorta and the venous drainage goes into the right atrium, one of the vena cava, or the azygous vein.
  - There is no connection to normal lung tissue and thus infection is rare. The pathology of extralobar BPS may look similar to normal lung or have the cyst appearance of a CPAM.
  - About 50% of extralobar BPS are associated with other congenital lesions such as CPAM, diaphragmatic hernia, congenital heart disease, or tracheoesophageal fistula.

III. Signs and symptoms

Newborns can present with respiratory distress similar to features of tension pneumothorax if the lesion is large which makes the mass effect, especially in CLE and CPAM.

Children with congenital lung lesions can be asymptomatic until accidental findings on chest radiography during normal screening or any respiratory symptoms when the lesions become infected.

Some children with large Bronchogenic cyst can present with dysphagia because of external compression to the esophagus

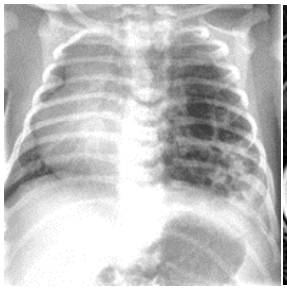
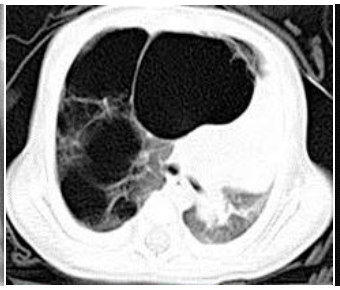
On physical exam: reduce breath sound on the affected lobe or biphasic wheeze if external compression to the lower airways.

IV. Diagnosis

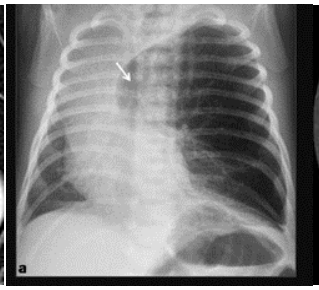
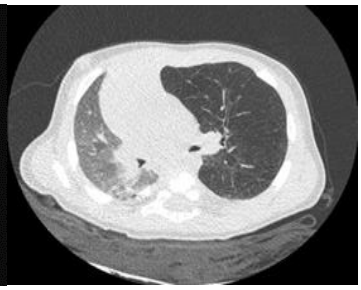
- Prenatal ultrasound
- Chest radiography
- CT with contrast for confirming the diagnosis and helping in anatomic involvement for surgical intervention
- CT angiogram in case of Bronchopulmonary sequestration for confirmation of lesion and helping blood vessel supply to the lesion for both diagnostic and intervention if surgery needed.

❖ Differential Diagnosis

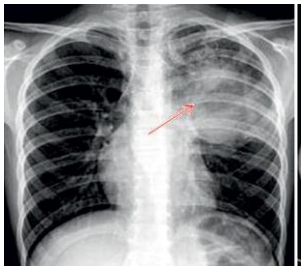
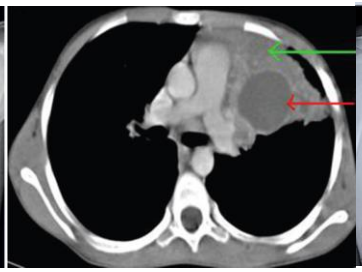
- CLE and CPAM often confuse with each other by ultrasound prenatally or chest radiography if no CT scan
- CPAM and Congenital diaphragmatic hernia
- BPS and pulmonary sequestration can be confused with lung abscess or round pneumonia
- Lung abscess to all the small lesions with infection.

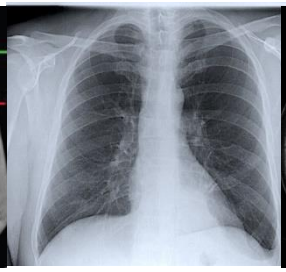
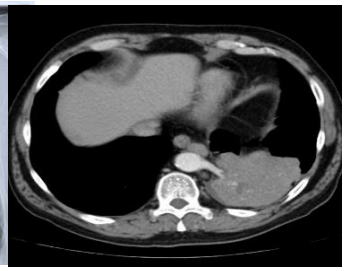
CPAM

CLE

Bronchogenic cyst

Bronchopulmonary Sequestration

V. Complications

- secondary pneumothorax
- mass effect: tension pneumothorax feature, external compression to surrounding tissue
- recurrent lower respiratory tract infection leading to airway or lung tissue damage permanently and affecting quality of life.

VI. Treatment

- If child presents with respiratory symptoms:
  - Evaluation on ABC
  - Treat infection if associated
  - Mainstay of treatment: Surgical removal. Timing of surgical removal is based on clinical presentation, child growth.
- If asymptomatic and small lesion: follow up regularly.
- If symptomatic and having complication: indication for urgent or elective lobectomy. However, multidisciplinary team is required from pediatric respiratory specialist, pediatrician, thoracic surgeon and PICU teams.

VII. Preventions and education

- Parental explanation about nature of disease and complications which might be occurred is the best way to approach.
- There is no prevention for the occurrence of congenital lung lesion. However, if the lesion is found, close monitoring, respiratory support, clearing of superbacterial infection and removal of the affected lesion can prevent life threatening conditions and improve quality of life.

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Chapter III: Infectious diseases

Find out more:

- Dengue Fever (National Program)
- Malaria (National Program)
- Parasitosis (National Program)

HAND FOOT AND MOUTH DISEASE (HFMD)

TEK Lyvannara, NGOURN Yanet, VA Sreyleak, HENG Sothy

I. Key Facts

Over the last decade, many outbreaks of HFMD have been reported in countries of the Western Pacific Region, including Australia, Brunei Darussalam, China, Japan, Malaysia, Mongolia, the Republic of Korea, Singapore, and Viet Nam. In temperate climates, cases occur more often in summer and early autumn. Since 1997, outbreaks of HFMD caused by Enterovirus 71 have been reported in Asia and Australia [6]. In 2012, there was an outbreak of HFMD in Cambodia and about 98 cases died [4].

II. Overview

HFMD	
Etiology	Human Enteroviruses species A (HEV-A): Coxsackie virus A 16(CA16), Enterovirus (EV71) has been associated with neurological disease and mortality
Reservoir	EV replicates in upper respiratory tract (recovered from throat swabs for up to two weeks post-infection) and intestinal tract (shed for between two and four weeks, and sometimes for as long as 12 weeks post-infection)
Route of infection	Respiratory droplet, contact with fluid in the blisters or contact with infected faces. HFMD is not transmitted to/ transmitted from pets or other animals [11].
Infectivity	-Incubation period is normally 3-7 days -Small epidemics in nursery schools or kindergartens, usually during the summer and autumn months - Infected persons are most contagious during the first week of the illness. They can still pass the infection to other people even though he/she appears well. -Some persons who are infected and excreting the virus, including most adults, may have no symptoms.
Age group	Occurs mainly in children under 10 years of age. But it can occur in adults too.
Risk Assessment	Young children under 5 years of age are most susceptible

III. Signs and Symptoms

1. Case definition

- **Hand, foot and mouth disease** is characterized by a brief febrile illness in children and typical skin rash, with or without mouth ulcers. Typically, the rash is papulovesicular and affects the palms or soles of the feet, or both. In some cases, the rash may be maculopapular without vesicles and may also involve the buttocks, knees or elbows, particularly in younger children and infants [6, 12].
- **Herpangina** is also characterized by fever and multiple, painful mouth ulcers, predominantly affecting the posterior oral cavity, including the anterior pharyngeal folds, uvula, tonsils and soft palate and tongue [12].
- **Fatal-case** children typically experience a brief febrile illness and present with only subtle neurological signs before succumbing dramatically to acute refractory myocardial dysfunction and fulminant pulmonary oedema within hours of developing tachycardia, poor peripheral perfusion and tachypnea.

- The exact disease mechanism of cardiopulmonary failure is still not well defined, although it has been linked to brainstem encephalitis following a number of clinical and pathological studies [20,21,24]. CSF pleocytosis, an objective marker for CNS involvement, has been universally observed among fatal-case children, despite the absence of obvious neurological signs before sudden cardiopulmonary collapse, indicating that CNS involvement precedes the onset of cardiopulmonary failure. CNS involvement may therefore be considered a harbinger of acute systemic complication in HFMD.
- *Early recognition of children with CNS involvement will enable doctors to focus special attention on those children and provide timely intervention before the onset of fulminant, intractable cardiopulmonary failure*.
- In resource-limited settings, the diagnosis of **brainstem encephalitis** can be made in children with:
  - Frequent myoclonic jerks
  - Other clinical features associated CNS involvement includes body temperature of 38.5ºC or higher longer than three days with lethargy, recurrent vomiting, limb weakness and myoclonic jerks [20, 22, 23]
  - CSF pleocytosis.

Figure 1: *Skin lesion and mouth ulcer of HFMD*

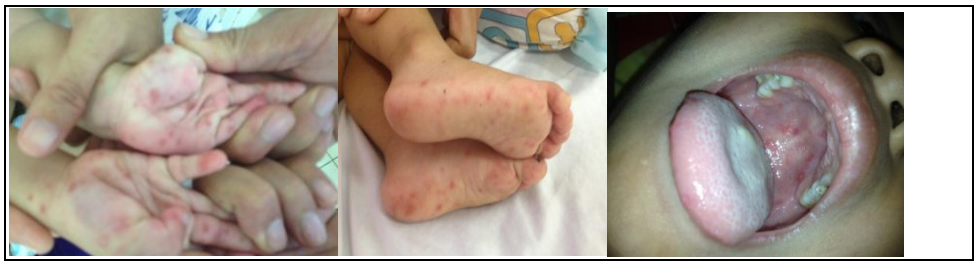
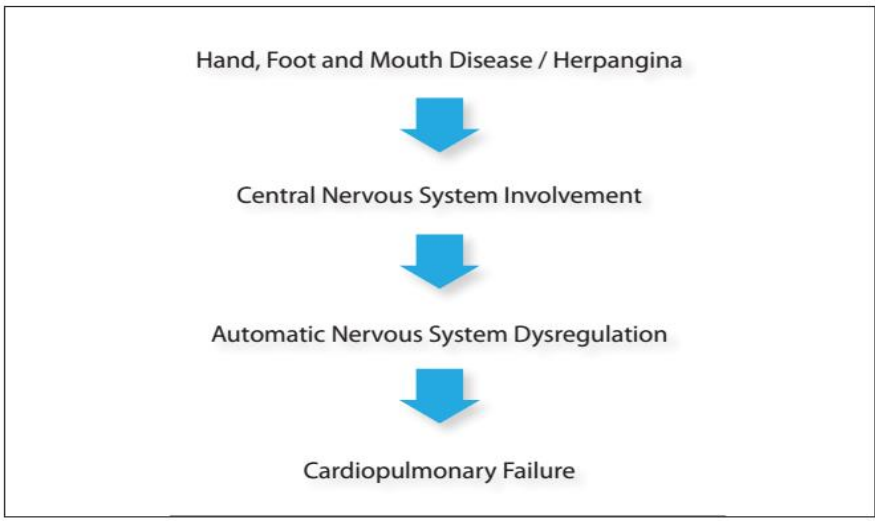


Figure 2: *Clinical course of fulminant EV71-associated HFMD*



- Ordinary case of HFMD is defined as HFMD without Complications.
- Severe cases of HFMD are defined as HFMD with CNS involvement stage (Aseptic Meningitis/Brainstem Encephalitis/ Encephalomyelitis), HFMD with autonomic Nervous System (ANS) dysregulation Stage, HFMD with Cardiopulmonary Failure Stage:
  - Aseptic meningitis: Febrile illness with headache, vomiting and meningism associated with presence of more than 5 – 10 white cells per cubic millimeter in cerebrospinal (CSF) fluid, and negative results on CSF bacterial culture.

- Brainstem encephalitis: Myoclonus, ataxia, nystagmus, oculomotor palsies, and bulbar palsy in various combinations, with or without MRI and CSF pleocytosis.

IV. Diagnosis

1. Signs and symptoms:

- Brief febrile illness
- Typical skin rash: papulovesicular, maculopapular without vesicles on palms or
- soles of the feet, or both or the buttocks, knees or elbows.
- With or without mouth ulcers.

2. Laboratory test:

- Samples from the throat or stool or skin lesion should be collected within 48 hours of illness and sent to a laboratory to test for the virus involved in causing the illness. The testing should be done for investigation of an outbreak, so that preventive measures can be initiated.
- For Serology: 4-fold rise in level of neutralizing antibody in paired blood sample collected at an interval of 14 days. i.e. one acute sample at the onset of illness and second sample after ten days of illness.
- In severe case:
- CBC: Raised white cell count with relative neutrophilia
- Hyperglycemia [13, 14]
- Abnormal CSF (> 5 – 10 white cells/mm3, with elevated lactate [14]. and negative results on CSF bacterial culture)
- Elevated creatine kinase is sometimes seen in patients with cardiac involvement [15]
- Chest X-ray: Pulmonary edema, heart size is always normal
- Echocardiography: Cardiac dysfunction, poorly contractile heart, particularly the left ventricle [16, 17].
- Computed tomography (CT) scans of the brain are not useful because the primary site of CNS pathology is located at the brainstem.
- Magnetic resonance imaging (MRI) shows characteristic high signal intensities on T2 weighted images in the dorsal pons and medulla, most of the midbrain, and the dentate nuclei of the cerebellum. Similar high signal lesions may also be found in the anterior horn cells of the cervical spinal cord [18, 19].

❖ Differential diagnosis

Diseases	Symptoms
Herpetic gingivostomatitis	Febrile and look toxic, gingival erythema, swelling or bleeding, cervical lymphadenopathy and no extremity involvement.
Aphthous stomatitis	larger, ulcerative lesions of the lips, tongue and buccal mucosa that are exquisitely painful.
Scabies infestation	An intense itch and interdigital space
Chickenpox (varicella)	varicella lesions are centrifugal in distribution and involve a larger skin area, including the scalp, but spare the palms and soles. Lesions heal by formation of crusts, while vesicles of HFMD resolve by reabsorption of vesicular fluid
Measles	Cough, coryza and conjunctivitis, and koplik spots may be found on examination of the mouth
Rubella	the skin rash has centripetal distribution and occipital lymphadenopathy [12].

V. Clinical assessment and Management

Table 2: *Stage-base therapeutic strategy*

Stage	Management
Stage 1: *Patients with any of the following and* no warning signs: - Skin rash. - Oral ulcers. *Warning Signs of CNS Involvement:* (one or more of the following): - Fever ≥ 39°C or ≥ 48 hours - Limb weakness - Truncal ataxia - Myoclonic jerks - Agitation/irritability - Lethargy - Wandering eyes - Vomiting - Dyspnea/tachypnea - Mottled skin - Hyperglycemia (>8.3 mmol/L) - Leukocytosis (WBC >15×109/L)	- Paracetamol - Adequate fluid intake Monitoring: - Educate parents to watch out for warning signs - Clinic follow up every 1 – 2 days for the next 7 days (if possible)
Stage 2: *HFMD with CNS Involvement Stage* **(**Aseptic Meningitis / Brainstem Encephalitis / Encephalomyelitis). Patients with HFMD/Herpangina and any of the following: - Meningism - Lethargy - Myoclonic jerks - Limb weakness - Ataxia, tremors * Patients with aseptic meningitis generally have a good prognosis.	- Oxygen - Fluid restriction: 60-80 ml/kg/day - Intubate patient and provide mechanical ventilator for GCS < 9 - Intravenous immunoglobulin (IVIG): indicated in encephalitis (brainstem encephalitis, rhombencephalitis). IVIG is not indicated in patient with aseptic meningitis - Corticosteroids: o Methylprednisolone: 1-2mg/(kg·d) i.v o Hydrocortisone: 3-5 mg/(kg·d) i.v o Dexamethasone: 0.2-0.5 mg/(kg·d) i.v
Stage 3 (early stage of cardiorespiratory failure): HFMD with autonomic nervous system, dysregulation Stage. Patients with CNS involvement and any of the following: - Resting Heart rate 150- 170/min - Hypertension - Profuse sweating - Respiratory abnormalities (tachypnea, labored breathing).	- I.V fluid therapy: Use NSS if glycemia > 20mmol/l and D5 1/2 S if glycemia < 20mmol/l - Consider early intubation - IVIG - Dobutamine 5-20 µg /kg/min - Furosemide (1-2mg/kg) i.v - Corticosteroid -
Stage 4 *(stage of cardio-respiratory failure):* HFMD with Cardio-pulmonary Failure Stage Patients with ANS dysregulation and any of the following: - Hypotension/Shock - Pulmonary oedema/haemorrhage	- I.V fluid therapy: for shock patients, normal saline 10-20 ml/kg within 30-60mn, colloidal fluid can be transfused for those patients whose symptoms still cannot be corrected (fluid replacement based on central venous pressure: CVP) - Mechanical ventilation

Stage	Management
- Heart failure	- Inotropes: Dopamine (5-15 µg/kg/min), dobutamine (2-20 µg/kg/min), Adrenaline (0.05-2 µg/kg/min), Noradrenaline (0.05-2 µg/kg/min). - 20% mannitol at 0.5-1.0 g/(kg·time), q4-8h, rapid I.V within 30 min in case of severe intracranial hypertension or cerebral hernia, the dose can be increased to 1.5-2.0 g/(kg·time), once per 2-4h - Furosemide (1-2mg/kg) i.v - Human serum albumin to alleviate cerebral edema 0.4 g/(kg·time) + furosemide - Corticosteroid - IVIG may be considered if not previously used
Stage 5 *(recovery stage):* - The body temperature gradually returns to a normal level - Symptoms of involved nervous system gradually disappear - Cardiorespiratory function gradually recovered. - Only a minority of patients has neurologic sequelae.	- Maintenance therapy - Rehabilitative treatment

VI. Complications

- Complications from the viral infections that cause HFMD are not common, but if they do occur, medical care should be sought:
- Viral or "aseptic" meningitis rarely occurs with HFMD. Viral meningitis causes fever, headache, stiff neck, or back pain. The condition is usually mild and clears without treatment; however, some patients may need to be hospitalized for a short time.
- Encephalitis or a polio-like paralysis may occur very rarely but encephalitis can be fatal. [6]

VII. Prevention

1. Specific preventive tools for HFMD are not available, but the risk of infection can be lowered by following good hygiene practices. Preventive measures include:

- Washing hands frequently and correctly especially after changing diapers and after using the toilet.
- Children should be kept away from crowded public places (such as schools, preschools, play groups, markets and public transport) if they show signs of infection.
- Cleaning dirty surfaces and soiled items, including toys with soap
- Avoiding close contact (kissing, hugging, sharing eating utensils and cups, etc.) with persons with HFMD. [6]

2. Advice for parents (Education):

- Parents are advised to consult a doctor early if their child has symptoms of HFMD. They should also be alert to any change in their child's normal behavior, e.g. irritation and sleepiness. If they refuse to eat or drink, have persistent vomiting or drowsiness, parents should bring their child immediately to hospital.
- It is important to make sure that all children and adults wash their hands frequently and thoroughly, especially after changing diapers or using the toilet. Contaminated

items and surfaces should be thoroughly washed and disinfected using a diluted solution of chlorine-containing bleach

3. Vaccination: No vaccine is available to protect against the enteroviruses that cause HFMD. [6]

❖ **HFMD and Pregnancy**

In adults, including pregnant women, the risk of infection is higher among those who do not have protective antibodies from earlier exposures to these viruses and for those who are constantly exposed to young children–the main spreaders of the infection [6].

Most enterovirus infections during pregnancy cause mild or no illness in the mother. Currently, there is no clear evidence that maternal enterovirus infection causes adverse outcomes of pregnancy, such as abortion, stillbirth, or congenital defects. However, mothers infected shortly before delivery may pass the virus to the newborn. Babies born to mothers who have symptoms of enteroviral illness around the time of delivery are more likely to be infected.

Most newborns infected with an enterovirus have mild illness, but, in rare cases, they may develop an overwhelming infection of many organs, including liver and heart, and die from the infection. The risk of this severe illness in newborns is higher during the first two weeks of life. Strict adherence to good hygiene practices by pregnant women may decrease the risk of infection during pregnancy and around the time of delivery.

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BACTERIAL MENINGITIS

TE Haypheng, EANG Kim-Ean, CHOEUNG Chea, KIM Ang

I. Key Facts

- Bacterial meningitis in children is a severe form of central nervous system infection that could cause death or permanent neuro complications.
- The ages of children with meningoencephalitis in different regions are different distributions, but infected children in Cambodia are frequently from 1-5 years old.
- Streptococcus pneumoniae is the most common cause of meningoencephalitis and is followed by E. coli, Neisseria meningitidis, or Hib in Cambodia. Interestingly, many confirmed cases in Kantha Bopha Hospital were Scrub typhus and were also reported.
- The classic triad of meningeal signs like neck stiffness, kerning sign or abnormal mental status may present minority in young children.
- Empirical treatments shouldn't wait in all suspected cases and cultures of sample collection from CSF and/or blood should be done before giving antibiotic.
- Most of finding bacterial meningitis in Cambodia are vaccine preventable diseases, thus every child is strongly encouraged to get immunization based on their ages.

II. Overview

1. Definition

Bacterial Meningitis is an inflammation of the meninges from bacteria. It is a life-threatening disease and is an important cause of morbidities and mortality in children. In Cambodia, it represented 4.6% of total admissions with 2.5 % of mortalities rate [2].

2. Epidemiology

In a systemic review in 2019, the estimate incidence of global meningitis was 2.51 million cases and half of the cases (1.28 million) were children younger than 5-year-olds. The mortality rate of age-standardized was 3.3/100 000 population in 2019 [3]. In Cambodia anyway, the median age was 6-year-old or the most common age group was children from1–5-year-olds based on the published study in 2017 of Kantha Bopha hospital which included 1160 patients from 2010-13. Younger children from 1 month to 11 months had only 4%. [4] Anyway, there is no statistical difference between male and female distribution in all age. [2]

3. Causative agents in Cambodia

In Cambodia, a pathogen (virus/bacteria) from CSF or blood can be identified between 20.8% to 35% of clinical cases. Additionally, the major proportion of confirmed cases is still by virus (JE/enterovirus) [2,4]. The two bacterial organisms that were most frequently found are Strep. Pneumo and E. coli in AHC and these were also supported by NPH data from 2018-22. Anyway, Orientia Tsutsugamushi was oppositely found the most common bacterial case in KBH from 2010-13. Others finding bacteria are N. meningitidis, Hib, and Staph Aureus. Even though there is limited data in neonate cases. [1]

4. Risk factors

Some factor of impact immunity from both congenital and acquire cause are known of predisposing factors includes asplenia, hypogammaglobulinemia, HIV infection, chronic steroid use etc.

Others could be anatomic defects of the spinal cord or recurrent para-meningeal infection (Ex: sinusitis, mastoiditis) [6]

III. Signs and symptoms

In younger children, the classic triad of meningitis signs besides fever, neck stiffness and abnormal mental status occurs in a minority [4]. The median duration of clinic is 4 days that patients come and admit in hospital and the common clinical presentations are [2]:

- Fever (100%)

- Headache 93.5% from 5-15 years (unknown in case <5 years)
- Reduced feeding (62.3%)
- Vomit (53.2%)
- Seizure (53.2%, mostly generalized)
- Respiratory symptoms (51.9%)
- Lethargic (51.6%)
- Bulging anterior fontanelle (26.6%, age 1-11 months)
- Diarrhea (25.7%)
- Kernig's sign positive (16.9%)
- Reduce consciousness level (10.7%)
- Photophobia (8.7%, age 5-15 years)
- Limb weakness (4.9%)
- Rash (0.2%)

IV. Diagnosis

1. Investigations

Lumbar Puncture should be done in all cases except of having contraindications, and CSF is tested for cell count, biochemistry, gram stain and culture. The profiles of bacterial meningitis in CSF are. [1]

- Pleocytosis with a predominance of neutrophils (typically >1000 WBC/microL but early course of infection could be less).
- Elevate CSF pressure (the left lateral decubitus position is 150mm of water)
- Low glucose (typically <60% of the blood glucose level)
- Increase Protein (typically ranges from 100 to 500 mg/dL)

Note: the contraindication of lumbar puncture is sign of raise ICP, Cardiorespiratory instability, infection in the area through which the LP needle will pass, and evidence of coagulopathy [1].

- In special circumstances (ex: HIV), additional testing for unusual pathogens may be considered
- Other tests: Blood examination: CBC, CRP, Procalcitonin, serum electrolyte, glucose etc may give additional information for clinical decisions.

-Blood culture should be done in all resource available before empirical treatments

2. Differential diagnosis:

Viral meningoencephalitis, febrile seizure, Brain tumor or abscess, intracerebral hematoma.

V. Complications

Sensorineural hearing loss is the most common sequelae. It occurs in 20–30% of patients after S. pneumoniae meningitis and in 5–10% of cases after meningitis due to Hib or N. meningitidis. Hearing should be tested within one month of discharge to detect hearing loss as early as possible. [1]

VI. Treatment

1. Antibiotic therapy

a. Empirical antibiotics [8]:

- >1 month old: Ceftriaxone 50mg/kg/dose Q12h IV (Max. 4g/day)
- < 1 month old: Ampicillin + Cefotaxime 50mg/k/dose IV Q12h if 1-7day old, and Q8h if 7-28 day old (alternate choice of cefotaxime is ceftriaxone, but ceftriaxone could cause biliary sought in neonate and clinic could worse with kernicterus).

b. Duration [7,8].

- If CSF and/or blood culture positive, duration depends on specific pathogen (as below)
- If CSF and/or blood culture negative with CSF pleocytosis, consult with hospital expert.
- Specific organisms:

- Streptococcus Pneumoniae: Ceftriaxone 10-14 days
- Haemophilus influenzae type b: Ceftriaxone 10 days
- Neisseria meningitidis: Ceftriaxone 7-10 days
- Group B Streptococcus: Penicillin G IV 14 days
- Staphylcoccus aureus: Cloxacillin IV 14- 21 day (MRSA: Vancomycin 21 days)
- Scrub Typhus: Doxycycline IV/PO 7-15 days
- Listeria monocytogenes: Ampicillin 21 to 28 days
- Gram Negative Bacillus: Ceftriaxone > 14 days.

c. In case of specific- therapy:

- Penicillin Resistance Pneumococcal: add Vancomycin (60mg/kg/day) IV Q6h
- Rickettsia and Scrub typhus: Doxycycline (4mg/kg/day) Q12h IV/PO
- Gram Negative Bacillus/ESBL bacteria: Meropenem (40mg/kg/dose) Q8h [1m to 12 y]
- If TB meningitis is suspected, follow national TB guideline.

2. Steroid

- May be good to reduce complication like haring loss to children with Hib meningitis (OR 0.34, 95% CI 0.20-0.59), but the mortality in the group of giving dexamethasone and placebo was similar (OR 0.89; 95% CI 0.74-1.07) according to a systemic review 2015. the efficacy of dexamethasone for children with meningitis caused by other organisms, including pneumococcus are still debated [7].
- Timing: Dexamethasone (0.15mg/kg/dose) Q6h IV 2-4 days, and should be administered before or at the same time as the first dose of antibiotics. It is probably of no benefit if given more than one hour later.

3. Supportive therapies

- Airway, Breathing, and Circulation resuscitations in case of emergency condition
- Fluid management: Isotonic IV fluid, and just 2/3 of fluid maintenance if SIADH.
- Antipyretic: Acetaminophen, - Correct Electrolyte imbalance if present
- Hypoglycemia: D10% 5ml/kg/dos bolus IV, and re-check glycemia
- Increase ICP: 30 degree sleeping position, IV Furosemide or Mannitol 0.25-0.5g/kg/dose
- Other aspects: Seizure, or ventilation supports [1].

VII. Prevention

- Many of bacteria induce meningitis are vaccine preventable diseases like Hip, Stret. Pneumo, N. Meningitidis.
- Therefore, routine vaccine from National Immunization Program is very important that every child is encouraged to get based on their age.

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ACUTE POLIOMYELITIS

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I. Key Facts

- Polio (poliomyelitis) mainly affects children under 5 years of age.
- 1 in 200 infections leads to irreversible paralysis. Among those paralyzed, 5–10% die when their breathing muscles become immobilized.
- Wild poliovirus cases have decreased by over 99% since 1988, from an estimated 350 000 cases in more than 125 endemic countries to 6 reported cases in 2021. (1)
- As long as a single child remains infected, children in all countries are at risk of contracting polio. Failure to eradicate polio from these last remaining strongholds could result in a global resurgence of the disease. (1)

II. Overview

1. Definition

Acute poliomyelitis often called polio or infantile paralysis is a disease of the anterior horn motor neurons of the spinal cord and brain stem caused by poliovirus. [1]

2. Causes

- Poliovirus is a member of genus Enterovirus, family Picornaviridae. which damages the anterior horn cells of the spinal cord.
- There are three poliovirus serotypes (type1, type 2, and type 3); Wild polio types 2 and 3 have been eradicated (no longer exist), and wild polio type 1 only exists in a few parts of the world.
- Poliovirus is rapidly inactivated by heat, formaldehyde, chlorine, and ultraviolet light.
- Transmission: fecal-oral route through direct contact.

3. Pathophysiology

- The virus enters via the fecal-oral or respiratory route, then multiplies in oropharyngeal and lower gastrointestinal tract mucosa.
- The virus spreads through the blood stream
- The virus finds its way to the anterior horn cells of the spinal cord. (2)

4. Risk factors

- Child unvaccinated
- Live or travel in endemic zone
- Immunodeficiency
- Malnutrition.

III. Clinical features

The incubation period, is usually 6 to 20 days, with a maximum range of 3 to 35 days.

- Up to 90% of cases are asymptomatic or present mild symptoms
- Abortive poliomyelitis 4 to 8%:
  - Clinically indistinct from many other viral infections (fever, myalgia, malaise)
  - Only suspected to be polio during an epidemic
- Non-paralytic form (1 to 2%):
  - stiffness in the neck and along the spine
  - headache, vomiting, backache;
  - no neurological involvement. As spontaneous recovery usually occurs within 10 days, diagnosis is rarely made outside epidemic contexts
- Paralytic poliomyelitis 0.1 to 0.5 % which is further subdivided:
  - o Spinal paralytic poliomyelitis (frank polio 79%)
  - Bulbar paralytic poliomyelitis: paralysis of muscle groups innervated by cranial nerves; involves the circulatory and respiratory centers of the medulla with high mortality (19%)

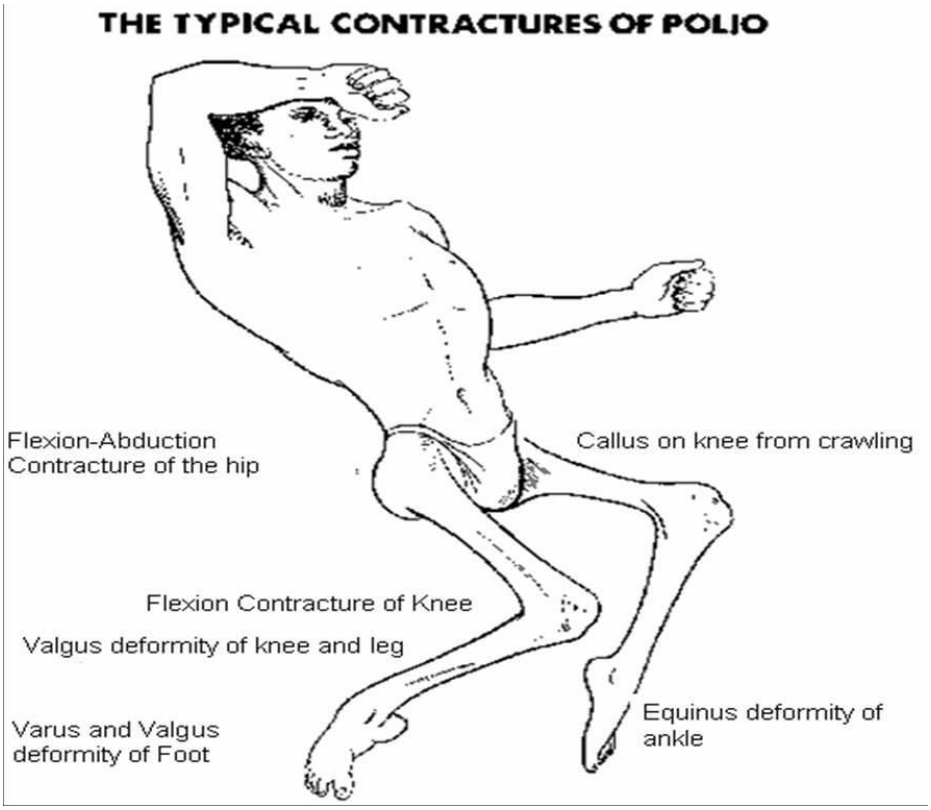
- Mixed bulbospinal poliomyelitis (2%). [3]

❖ Outcomes of poliovirus infection

Outcome	Proportion of cases
Asymptomatic	90%-95%
Minor illness	4%-8%
Non-paralytic aseptic meningitis	1%-2%
Paralytic Poliomyelitis	0.1%-0.5%
Spinal Polio	79% of paralytic cases
Bulbospinal Polio	19% of paralytic cases
Bulbar polio	2% of paralytic cases

❖ Practice Essentials [1]

Flaccid asymmetrical weakness and muscle atrophy are the hallmarks of its clinical manifestations, due to loss of motor neurons and denervation of their associated skeletal muscles. Because of the success of poliovirus vaccine, poliomyelitis, once one of the most feared human infectious diseases, is now almost entirely preventable by proper immunization (see image below).



IV. Diagnosis

1. Laboratory test:

- Two stool samples are taken at 48 hours interval.
  - 1st specimen taken 24 hours after case reported.
  - 2nd specimen taken 48 hours after case reported.
- Lumbar puncture
- Viral culture (stool, throat, and cerebrospinal fluid)

- PCR of cerebrospinal fluid
- Serologic testing for poliovirus serotypes, other enteroviruses, fold increase in the immunoglobulin G (IgG) antibody titers or a positive, anti-immunoglobulin M (IgM) titer during the acute stage is diagnostic.

2. Differential Diagnosis

- Enteroviral Meningitis – Coxsackie virus, myocarditis, hand-foot-and-mouth disease; difference is made serologically.
- Acute Flaccid Paralysis (AFP) (myelitis)– a variety of neurologic illnesses including and mimicking poliomyelitis; distinguished by increased frequency of fevers and asymmetric neurologic signs in poliomyelitis AFP.
- Guillain-Barre Syndrome – weakness is more symmetric and ascending and CSF often is normal in the first week of the illness and then shows elevated protein levels without pleocytosis.

V. Complications

Poliomyelitis mortality in children is about 2 to 5%.

- Breathing muscles: difficulty in breathing. Recurrent lung infection
- Nerves: That control the muscles of the face, the eye, the tongue, etc. The paralysis makes it difficult for the patient to use their mouth properly, it may affect their speech and it also affects their vision.
- Swallowing muscles: difficult to feed and increase risk of choking sometime require naso-gastric tube
- Digestive system: can be constipation.
- Urinary system: can be incontinence or urinary retention sometime require cystotomy and recurrent urinary tract infection.
- Arms / legs: paralysis and muscular atrophy. (4)

VI. Treatment

- No specific treatment is available.
- Only supportive care for non-paralytic forms: rest and analgesics (paracetamol: oral, rectal: Children: 60mg/kg/day divided in 4-6 time as needed).
- Hospitalize patients with the paralytic form:
  - Rest
  - Prevent bed sores in bedridden patients
  - Give analgesics (do not give IM injections to patients in the febrile phase)
  - Ventilate patients with respiratory paralysis
  - Physiotherapy once the lesions are stable to prevent muscle atrophy and contractures
  - Care for sequelae: physiotherapy, surgery and prosthetics

VII. Prevention

- In Cambodia, oral polio vaccine composed of live attenuated viruses is used within EPI program
- Eradication program (National Immunization Day. [5]

Immunization schedule: [5]

Age / vaccine	6 weeks	10 weeks	14 weeks
bOPV	☑	☑	☑
IPV			☑

**bOPV: bivalent oral polio vaccine *IPV: inactivated polio vaccine* [6]

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KAWASAKI DISEASE

HU SokHeng, SRENG Limheng, KHUN Leangchhun, YAY Chantana

I. Key Facts

- Kawasaki disease (KD), also known as muco-cutaneous lymph node syndrome, and Kawasaki syndrome, is an acute febrile illness of early childhood characterized by vasculitis of the medium-sized arteries. [1]
- KD was first described in a 1967 report by Japanese pediatrician Tomisaku Kawasaki. The cardiac sequelae were later documented in 1970 following investigation of 10 autopsy cases of sudden cardiac death following diagnosis of KD. The first reported case outside Japan were in Hawaii in the early 1970s, KD cases have since been reported in more than 60 countries worldwide. [2]
- Affect children <5 years (peak onset between 18 and 24 months).
- It's the leading cause of childhood acquired heart disease in the developed world.
- It's the second most common vasculitis of childhood after Henoch-Schönlein purpura.
- The incidence in USA is approximately 25/100,000 in children < 5 years while those in Japan is approximately 250/100,000 in children < 5 years. [1]
- Male and female ratio is about 1.5/1. [3]
- Rate of recurrence is approximately 3600 per 100,000 while acute mortality occurred in just one of the 23,730 cases (Nakamura analyzed in 2009 to 2010 period). [4]

II. Overview

1. Definition

KD is an acute, self-resolving systemic vasculitis including blood vessels throughout the body, which has a predilection for the coronary arteries (CAs) leading to the coronary artery aneurysms (CAAs) in around 25% of patients without proper treatment. Aneurysm may occur in other extra-parenchymal muscular arteries, such as the celiac, mesenteric, femoral, iliac, renal, axillary and brachial arteries. [5,6,7]

2. Etiopathogenesis

- The etiology of KD remains unknown, many theories have been proposed based on genetic, infectious and immune dysregulation.
- The concept of an underlying genetic predisposition to KD is based on 2 keys observations. Firstly, there is an increased risk of KD in patients who have a first degree relative with a history of KD. Similarly, parents of a child with KD are twice as likely to have a history of KD compared to the general population. Secondly, KD has a significantly higher incidence in certain ethnicities, which persist even after their relocation to other regions of the world.
- The concept of an infection triggers is supported by symptomatology of KD which resembles common childhood infections, region-specific incidence rates, seasonality, the occurrence of epidemics and the low incidence of recurrence. Bacterial and viral infections like retrovirus, Epstein Barr virus, coronavirus, staphylococcal, streptococcal superantigens act like infection trigger of KD.
- The fact that 80% of KD occurs in those < 5 years of age could be due to the immature immune system failing to protect from this agent.
- From the pathophysiological point of view: arteritis develops around the eighth-ninth day after KD onset, and CAA starts with edema formation of the intima and media of arteries and partial rupture of the internal and external elastic lamina. The arterial wall does not support the internal pressure, especially diastolic and under goes distension and deformation, leading to the formation of aneurysm. When aneurysm begins to calcify a further pathological distension may develop within 2-3 years. [7, 8]
- From the pathological point of view:
  There are 3 phases in KD

- Acute phase: it has a mean duration of 2 weeks and is characterized by a necrotizing vasculitis with a predominance of neutrophils and macrophages, while platelets display a pro-coagulant phenotype in the second week.
- Subacute/Chronic phase: it starts after 15 days and is characterized by the presence of lymphocytes, plasma-cells and eosinophils, which migrate to the lumen and alter the adventitia.
- Convalescence phase: it is characterized by the proliferation of myofibroblasts that form a concentric mass, which progressively obliterate the lumen. [8,9,10]

III. Signs and symptoms

Most children with KD are brought to medical attention because of prolonged fever. The typical presentation of KD is an infant or young child who has a high spiking fever (often >39˚c) for 5 or more days that often persists despites antibiotic and/or antipyretic treatment. [2]

The other principles clinical presentations including

1. Mucosal changes

- Erythema and cracking lips
- "Strawberry tongue" erythema and prominent fungiform papillae and/or erythema of the oral and pharyngeal mucosa.

2. Conjunctivitis

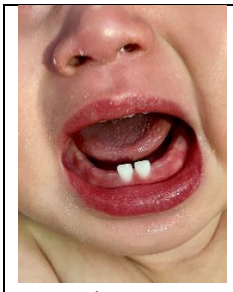
Bilateral bulbar non-exudative conjunctival injection, often limbic sparing.

3. Polymorphous rash

- Maculopapular diffuse, erythema or erythema multiforme-like, less commonly urticaria or fine micro-pustular eruptions.

4. Extremities changes

- Acute phase: erythema and edema of the hands and feet.
- Subacute phase: periungual desquamation.

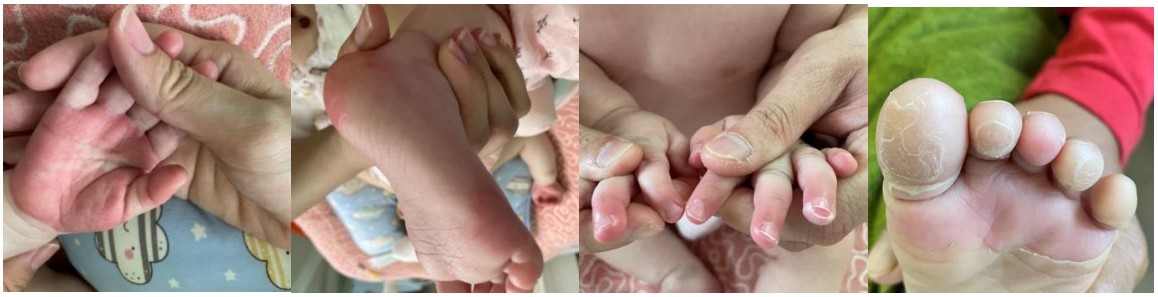


Strawberry tongue Erythema, dryness of the lips

Bilateral non-exudative Conjunctivitis

Erythema polymorphous rash involving trunk and limbs

Erythema maculous rash on the back



Palmar and plantar erythema with swelling, resolves with subsequent periungual desquamation in the subacute phase

Figure 1. *Courtesy's cases of KD in Jayavarman VII Hospital*

5. Lymphadenopathy

- Acute, non-suppurative, cervical lymphadenopathy ≥1.5cm of diameter, typically unilateral. [2,3,6]

Other (less common) clinical manifestations of KD

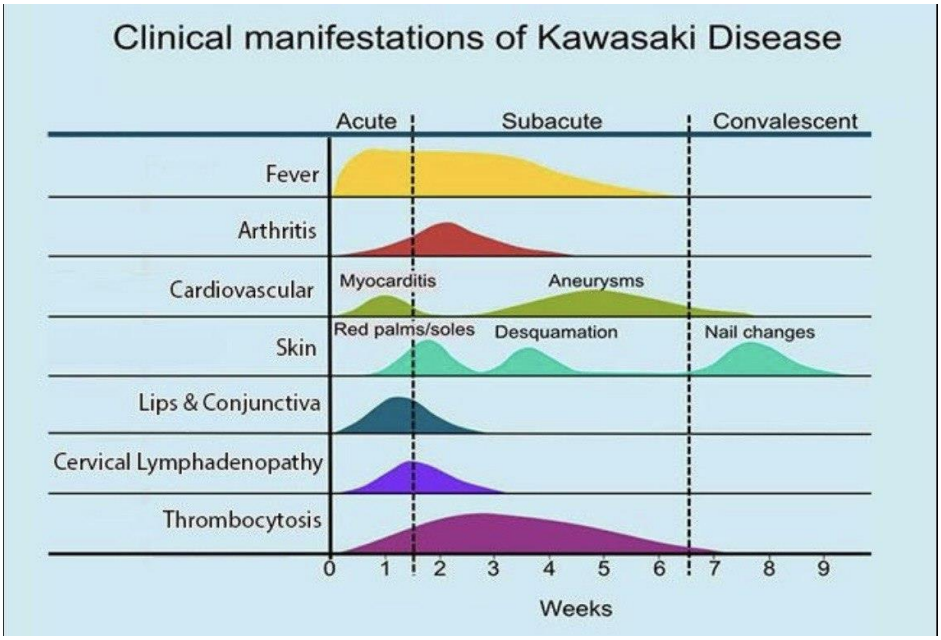
- Arthralgias and arthritis.
- Abdominal pain.
- Vomiting, diarrhea. [2]
-

❖ **Clinical course of KD**

KD clinical course can be divided into 3 clinical phases: acute, subacute and convalescence phase.

- Acute phase: (1st and 2nd week)
  - High spiking fever (>39˚c).
  - Principal features.
- Subacute phase (3rd and 4th week)
  - Often an asymptomatic period after the febrile episode subsides.
  - Desquamation of the digits.
  - Arthralgia.
  - Abnormal lab finding (thrombocytosis).
  - Time for greatest risk of developing cardiac sequelae (CAAs).
  - There is a risk of sudden death.
- Convalescence (fifth to eighth week).
  - All disease signs and symptoms disappear. Inflammatory indexes return completely to normal.
  - Endothelial disfunction might cause cardiovascular acute events. [8]

Figure 2. *Clinical Manifestations and time course of Kawasaki Disease* [1]



IV. Diagnosis

Due to a lack of pathognomonic diagnosis tests, the characteristic clinic manifestations of KD have formed the basis of its diagnosis.

The main diagnosis criteria of KD are based on the guidelines of the American Heart Association in 2017 and the Japanese diagnostic guideline.

To be diagnosed with:

- Classic KD, the patient must have ≥5 days of fever + ≥4 of 5 principles clinic features.
- Incomplete KD, the patient needs 4 of the following criteria.
  - Fever lasting 5 days or more.
  - Presence of 2 or 3 clinical KD symptoms.
  - Elevated CRP level exceeding 3.0mg/dl or ESR surpassing 40mm/h.
  - Fulfillment of at least 3 of the supplementary laboratory criteria (age-appropriate anemia, platelets count ≥450 000/mm^3 after 7 days of fever, albumin level <3.0g/dl, increased Alanine transferase, WBC≥15 000/mm^3, urine WC ≥10WBC per high power field or a positive echocardiography. [11]

1. **Lab analysis [2]**

Table 1. *Lab analysis*

White blood cell	>15 000/mm^3 with neutrophilic in immature form
Hemoglobin	Anemia (for age)
Platelets	>450 000/mm^3 (peak in the 3rd week)
Sedimentation rate	>40mm/h
CRP	>3.0g/dl
Albumin	>3.0g/dl
Ferritin	Elevation above normal range
ALT	Elevation about normal range
GGT	Elevation about normal range
Urine WBCs	>10WBCs per high power field
Cerebral spinal fluid	Mononuclear pleocytosis without hypoglycorrhachia and/or elevated protein

2. **Imaging**

a. Echocardiography

The echocardiography remains the standard imaging modality to evaluate for both coronary artery dimension as well as other cardiac abnormalities. The 2D echocardiography imaging of left main coronary artery (LMCA), left anterior descending artery (LAD), left circumflex artery (LCx) and right coronary artery (RCA) on multiple imaging plan and transducer position are required for optimal visualization. [5]

Several factors associated with increased risk of developing CALs (lesions).

- Male sex.
- Age <12 months or >8 years.
- Fever duration >10 days.
- Leukocytosis >15 000/mm3.
- Thrombocytopenia.
- Hypoalbuminemia.
- Hyponatremia.
- Persistent fever or occurrence of fever >36h after IVIG administration. [2]

The Japanese ministry of health criteria is widely used to classify coronary artery sizes according to age. In children <5 years, coronary artery lumen diameter is abnormal, if

> 3mm. In children 5 years of age and older, a lumen diameter > 4mm is considered abnormal.

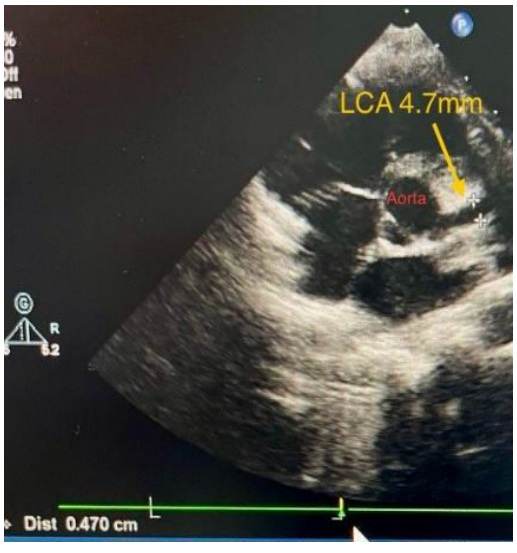
In addition to absolute lumen dimensions, both the Japanese minister of health and American heart association also utilize Z scores when classify CALs. Z scores are coronary artery dimensions that are adjusted for body surface area, as coronary artery dimension will change with the size of the child. [2]

❖ **Classification of coronary abnormalities in American heart association and Japanese Circulation Society guidelines.** [5]

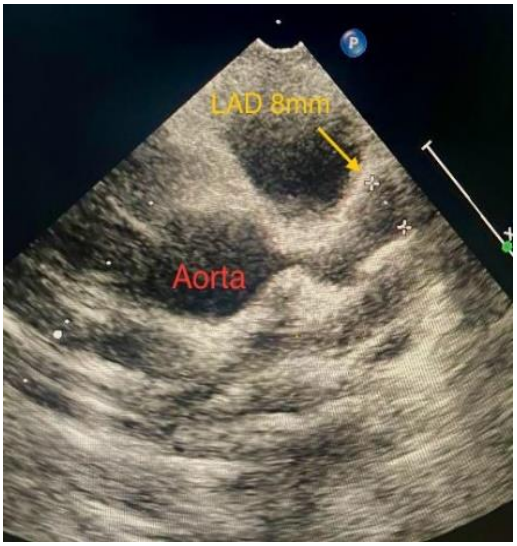
Table 2.

Guideline	Classification of Coronary Abnormalities
American Heart Association Guideline	1. No involvement: Always *z* score <2 2. Dilation only: 2 to <2.5; or if initially <2, a decrease in *z* score during follow-up ≥1 3. Small aneurysm: ≥2.5 to <5 4. Medium aneurysm: ≥5 to <10, and absolute dimension <8 mm 5. Large or giant aneurysm: ≥10, or absolute dimension ≥8 mm
Japanese Circulation Society guideline Acute phase (<30 days)	1. Small aneurysm: z score ≥2.5 to <5 2. Medium aneurysm: ≥5 to <10 3. Giant aneurysm: ≥10 ***Notes*** If it is difficult to evaluate by z score, evaluating by absolute value of inner diameter may be used in patients under 5 years old - Small aneurysm: 3 mm ≤ inner diameter <4 mm - Medium aneurysm: 4 mm ≤ inner diameter <8 mm - Giant aneurysm: 8 mm ≤ inner diameter

Figure 3. *Courtesy's Sonography of KD in Jayavarman VII Hospital*



2D echocardiogram showed aneurysm of LMCA 4.7 mm in 2-year-old boy



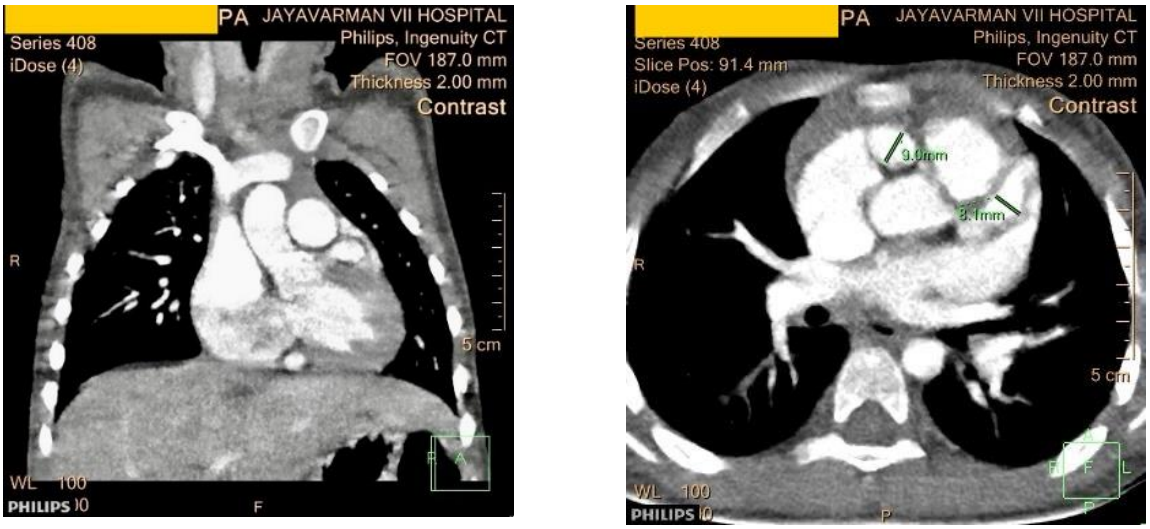
2D echocardiogram showed coronary ectasia LCA multiple sacciform dilatation (4mm, 7mm, 8mm from proximal into distal end) in 3-year-old boy

b. Computed Tomography Scan Angiography (CTA)

Coronary CT angiography (CTCA) is a useful modality for better characterization and delineation of coronary artery dilatations, ectasia and aneurysm especially in the mid

and distal segments. It also provides precise details of aneurysm size, morphology, and thrombus. [9]

Figure 4. *Courtesy's CT scan angiogram of KD in Jayavarman VII Hospital*



Coronary CT angiogram demonstrating ectasia of the LAD and the RCA in 3-year-old boy

3. Differential diagnosis

a. Viral

- Measles can present with similar clinical features, however a presence of a viral prodrome, exudative conjunctivitis, and Koplik spots will help to differentiate measles from KD.
- Adenovirus.
- Enterovirus.
- Epstein-Barr virus.

Table3: *the comparison table of Measle and KD*

Measle	KD
Viral prodrome	No viral prodrome
Exudative conjunctivitis	Non- exudative conjunctivitis
Koplik spot	Erythema of the oral cavity
Lymphocytic leukocytosis	Polymorphonuclear leukocytosis

b. Bacteria

- Scalet fever.
  - Absence of eyes changes and lip changes.
  - Presence of sand paper rash.
  - Elevated anti-streptolysin O titers.
  - A brisk response to antimicrobial.
- Acute rheumatic fever.
- Rocky mountain spotted fever.
- Leptospirosis.
- Cervical lymphadenitis.

c. Hypersensitivity reactions

- Drug hypersensitivity reaction.
- Steven-Johnson syndrome.

d. Toxin-mediated

- Staphylococcal scaled skin syndrome.
- Toxic shock syndrome. [5]

V. Complications

- CAAs.
- Pericarditis, Myocarditis.
- Valvular dysfunction (most commonly involve in mitral valve).
- Myocardial infarction.
- Death due to complete thrombotic occlusion of CAAs with myocardial infarction, rupture of a large CA. [7,8]

VI. Treatment

The goal of the management in the acute phase of KD is to stop the inflammation as early as possible in order to limit the risk and severity of CALs and to prevent CA thrombosis.

The initial treatment of KD acute phase included the combined use of IVIG and ASA. [1,8]

1. Intravenous Immunoglobulin (IVIG)

- Most effective when administered within 10 days of onset of fever.
- Decrease risk of CAA formation from 20-25% to 3-5% in those who are appropriately treated.
- Dose: 2g/kg in single dose over 12h infusion. [1,2]
- Side effect (rare).
    - Chills.
    - Hypotension.
    - Anaphylactic reaction.
    - Aseptic meningitis.
    - Hemolytic anemia.
    - Abnormal liver function test.
    - Jaundice.
    - Acute renal failure.
    - Thrombocytopenia.
    - Pulmonary edema.
- Contraindication: Active vaccination (MMR and Varicella). These vaccinations should be administered at 11 months after administration of IVIG. [12]

2. Acetylsalicylic Acid (ASA)

- Acute phase: Moderate dose (30-50mg/kg/d, QID) or high dose (80-100mg/kg/d, QID) for 14 days or until the patient is afebrile for 48-72h.
- After acute phase: Children are transitioned to low dose ASA for antiplatelet effect (3-5mg/kg/d, QD).
- The decision to continue or discontinue therapy is usually made around 6-8 weeks pending any CALs on the echocardiography.
- Contraindication: NSAIDs which utilize the cyclooxygenase pathway, may interfere with the antiplatelet effect of ASA and should be avoid. [2]

3. Adjuvant therapy and treatment options for cases refractory to IVIG and ASA

- Refractory KD or IVIG resistance is defined as:
    - Persistent fever of any magnitude 24-36h after completion of initial IVIG therapy.
    - Return of fever of any magnitude after an afebrile period not explained by any cause other than KD (up to two weeks after the start of treatment).
    - Other signs of failed initial therapy such as progressive CA dilatation or other manifestations of inflammation associated with KD, e.g. Non exudative conjunctivitis. [13]
- In refractory KD, the second infusion of IVIG is required. In case of failure, pulses of methylprednisolone for 3 consecutive days followed by oral prednisolone or modified methyl prednisone are used.
- For IVIG and corticosteroid resistant patient, infliximab is used as rescue therapy. [14]

- Corticosteroid
  - Methyl prednisolone 30mg/kg/d infusion over 2hours.
  - Prednisone 2mg/kg/d IV or orally in 3 divided doses for 10days, then 1mg/kg/d for 5days. [7]
  - Modified methyl prednisolone: (IV) 2-4mg/kg/d divided into 2-3 doses for 3-5days then 1mg/kg/d once a day for 3-5days then oral prednisolone was tapered over 3-5 weeks in 5-7days. [15]
- TNF inhibition: single dose of Infliximab 5mg/kg giving in 2h.
- Interleukin 1 inhibition: Anakinra. [7]

4. Primary prevention of thrombosis

- Patients with no evidence of CALs are maintained on low dose ASA therapy throughout the acute phase of illness. At 6-8 weeks follow up appointment, ASA may be discontinued as long as no adverse changes are seen in the final cardiac finding.
- Patients with small CALs are typically continued on low dose ASA monotherapy past this period.
- Patients with moderate-sized aneurysms are managed with ASA and ADP receptor antagonist (e.g. Clopidogrel).
- Child with persistent large or giant aneurysms internal lumen diameter ≥8mm may be treated with antiplatelet agent plus anticoagulant therapy (Warfarin or Low-molecular-weight heparins (LMWH) [2] with international normalized ratio of PT targeted of 1.5-2.0 (2.0-3.0 for white people). [16]

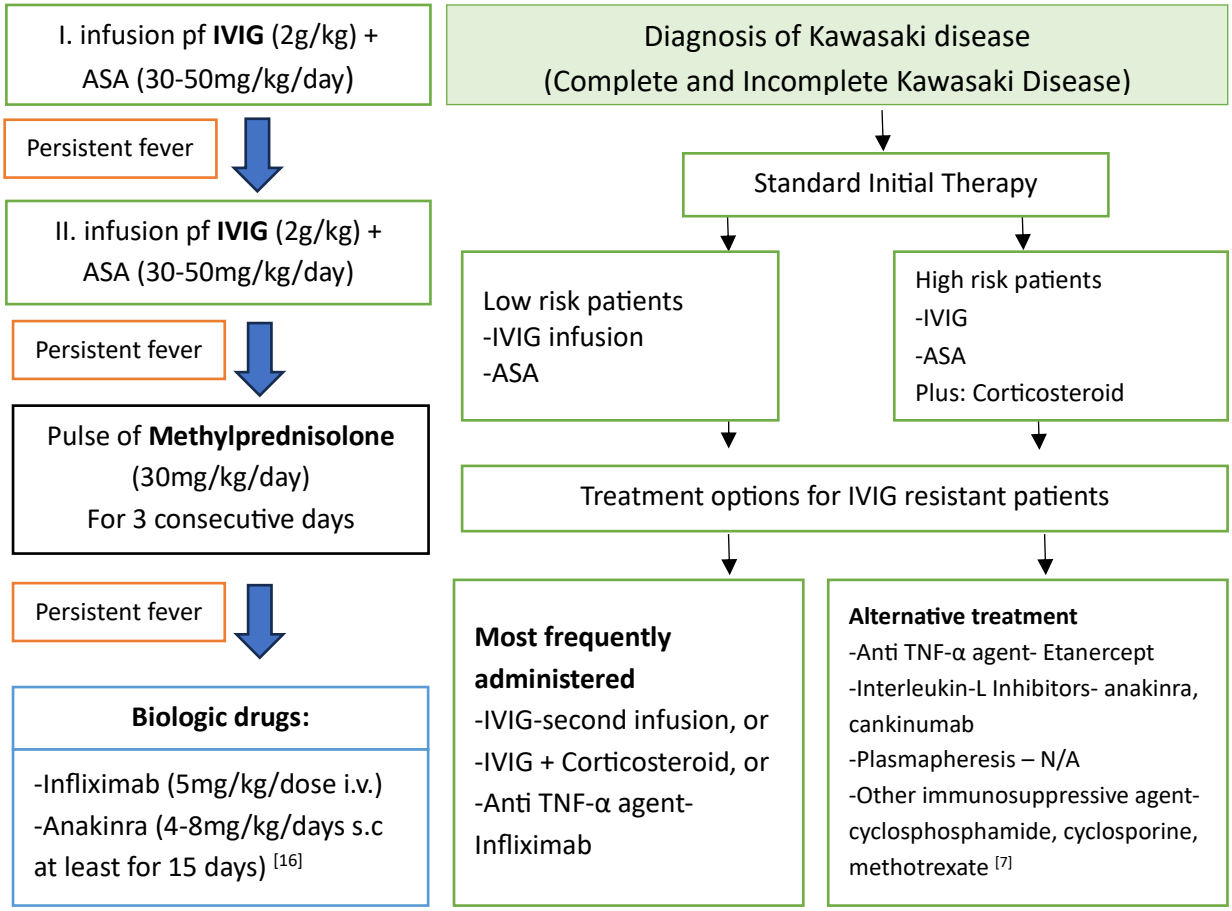
5. Monitoring and assessment after initial therapy

- Patients should receive regular follow up during the convalescent period regardless of whether there are any signs of smoldering vasculitis. Patients are monitored for persistent or recurrent fever after starting initial therapy. The frequency of repeat echocardiograms depends up on the degree of initial CA involvement and Risk factors for CA dilatation. [1]
  - No or transient dilatation: should be done at 1-2-6-12 months and 5 years (or yearly) until 5 years of age.
  - No or transient dilatation: should be done at 1-2-6-12 months and 5 years (or yearly) until 5 years of age.
  - Patient with remaining giant aneurism: every 6-12 months. [5]
  - Coronary Z score classification and timing of echocardiography [18]

Table 4.

Severity of coronary artery abnormal	Z score or diameter	Timing of echocardiography
No involvement	Z score<+2	1-2 weeks and 4-6 weeks after treatment
Dilatation only	Z score ≥+2 to < +2.5, or Initial Z score < +2, decrement of Z score ≥ +1 during follow-up	1-2 weeks and 4-6 weeks after treatment
Small aneurysm	Z score ≥ +2.5 to < +5	Twice per week till no progression
Medium aneurysm	Z score ≥ +5 to < +10 and absolute diameter < 8 mm	Twice per week till no progression
Large/Giant aneurysm	Z score ≥ +10 or absolute diameter ≥ 8 mm	Twice per week, at least once weekly in first 1.5 month, then monthly until the 3rd month

6. Summarized algorithm for treatment of KD



7. Long term treatment plan according to Z score system modified from the 2017 American heart association guidelines [5]

Table 5.

Risk level	Frequency of cardiology assessment	Assessment for inducible myocardial ischemia	Low-dose aspirin	Anticoagulation (Warfarin or LMWH)	Dual antiplatelet therapy ASA+Clopidogrel
No involvement	May discharge between 4w and 12m	None	4–6w then discontinue	Not indicated	Not indicated
Dilation only	If decreased to normal, discharge between 4w to 12m; if persistent dilation, reassess every 2–5y	None	Indicated until regression to normal	Not indicated	Not indicated

Risk level	Frequency of cardiology assessment	Assessment for inducible myocardial ischemia	Low-dose aspirin	Anticoagulation (Warfarin or LMWH)	Dual antiplatelet therapy ASA+Clopidogrel
Small aneurysm, current or persistent	Assess at 6m, then yearly	Assess every 2–3y	indicated	Not indicated	Not indicated
Small aneurysm, regressed to normal to dilation only	Assess every 1–3y (may omit echocardiography)	Assess every 3–5y	May be considered	Not indicated	Not indicated
Medium aneurysm, current or persistent	Assess at 3, 6, and 12m, then every 6–12m	Assess every 1–3y	indicated	Not indicated	May be considered
Medium aneurysm, regressed to small aneurysm	Assess yearly	Assess every 2–3y	indicated	Not indicated	May be considered
Medium aneurysm, regressed to normal or dilation only	Assess every 1–2y (may omit echocardiography)	Assess every 2–5y	Reasonably indicated	Not indicated	Not recommended except in the presence of inducible myocardial ischemia
Large or giant aneurysm, current or persistent	Assess at 3, 6, 9, and 12m, then every 3–6m	Assess every 6–12m	Indicated	Reasonably indicate	May be considered in addition to anticoagulation
Large or giant aneurysms, regressed to medium aneurysm	Assess every 6–12m	Assess yearly	Indicated	Not indicated	Reasonably indicated
Large to giant aneurysm, regressed to small aneurysm	Assess every 6–12m	Assess every 1–2y	Indicated	Not indicated	Not indicated
Large or giant aneurysm, regressed to normal or dilation only	Assess every 1–2y (may omit echocardiography)	Assess every 2–5y	Reasonably indicated	Not indicated	Not indicated

VII. Patient education

Family education on KD should include the following key points.

- KD causes swelling and damage to the blood vessels in the body.

- The cause is unknown, but it is not believed to spread from person to person.
- KD is treated with an IVIG which is infused over 12h and also with aspirin, if the patient still has fever 36h after IVIG, the patient will receive a second dose and other medication as well.
- CALs and other heart abnormalities are dangerous complications of KD. With treatment with IVIG, the risk is low. If heart problems are not present 6-8 weeks after symptoms began, it is very likely that the patient will have a full recovery with no complications.
- The patient will need to follow up with a primary care doctor and a cardiologist after discharge from the hospital. [1]

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INFECTIVE ENDOCARDITIS

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I. Key Facts

Unlike in adult, infective endocarditis (IE) in children is uncommon. The incidence of IE in children range between 0.43–0.69 cases per 100,000 children-year[1,2] with mortality rate of 3 to 7 percents. [1,3,4]

Diagnosis is complex, although it has improved with the use of multimodal imaging techniques. Antibiotic treatment should be started early, according to causative microorganism and risk factors. Despite treatment, complications are frequent and continue to cause significant morbidity.[7]

II. Overview

1. Definition:

Infective endocarditis is an infection of the endocardial surface of the heart. It usually involves heart valves, but it can occur on the endocardium or intracardiac devices.[5]

2. Causes

Common causes of infective endocarditis include (the list starts from most to least common): *Staphylococcus aureus*, *Oral (viridans) streptococci*, *Coagulase-negative staphylococcus*, *Group A streptococcus* (GAS), *Group B streptococcus* (GBS), *Enterococcus* spp., *Streptococcus pneumoniae*, *Escherichia coli*, *Coxiella burnetiid*, HACEK organisms (***H****aemophilus* spp., ***A****ggregatibacter actinomycetemcomitans*, ***C****ardiobacterium hominis*, ***E****ikenella corrodens*, ***K****ingella kingae)*, Candida spp.

3. Physiopathology:

Endothelial injury allows for either direct infection by virulent organisms or the development of uninfected platelet-fibrin thrombus which becomes a nidus for transient bacteremia, except in the case of S. aureus, which can infect intact endothelium.

These organisms enter the bloodstream from the skin, mucosal surfaces or previously infected sites and adhere to nonbacterial thrombus due to valvular damage or turbulent blood flow as in congenital heart defects. In the absence of host defenses, this organism is allowed to proliferate forming small colonies and shed in the bloodstream. Left-sided infection is much more common than right-sided infection.[5]

4. Risk factors

Table 3. *Risk factors for Infective endocarditis*

Congenital heart disease	Acquired risk factors	Previously healthy
a. Cyanotic disease **b.** Recent cardiac surgery **c.** Left-sided lesion **d.** Endocardial cushion defects	**a.** Immunodeficiency **b.** Cancer **c.** Homolysis **d.** Intravenous drug use	**a.** Dental procedures **b.** Skin infections /lacerations

III. Signs and symptoms

Clinical presentation of IE can be classified as acute and subacute. These, however, vary between different age groups. IE in older children is usually presented as seen in adult patients: fever, loss of appetite, and malaise as evidence of a systemic infectious process. A new murmur or a change in a previous murmur may be heard.

In cases of subacute onset, it is common to find progressive deterioration in functional class, with persistent fatigue, malaise, or growth retardation. Patients with IE may present evidence of acute heart failure due to valve destruction.

Regarding systemic manifestations, there may be renal immunological involvement (glomerulonephritis), seizures, or cerebral infarction due to cerebral embolisms. Immunological phenomena (Osler nodes, Janeway spots) are less common in children than in adults.

IV. Diagnosis

Table 1. *The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria*[6]

Definite Endocarditis	1. 2 Major Criteria, or 2. 1 Major Criterion AND 3 Minor Criteria, or 3. 5 Minor Criteria
Possible Endocarditis	1. 1 Major Criterion AND 1 Minor Criterion, or 2. 3 Minor Criteria
Rejected Endocarditis	1. Firm alternative diagnosis explaining the clinical syndrome, or 2. Lack of recurrent despite antibiotic therapy less than 4 days, or 3. No pathologic or macroscopic evidence of IE at surgery with antibiotic for less than 4 days, or 4. Does not meet criteria for definite or possible IE

Table 2. *Major and minor criteria for diagnosis of Infective Endocarditis*

Major Criteria	1. Microbiologic Major Criteria, Positive blood cultures: a. Microorganisms that commonly cause IE* isolated from 2 or more separate blood culture sets. Or b. Microorganisms that occasionally or rarely cause IE isolated from 3 or more separated blood culture sets. or c. *Coxiella burnetii* isolated from a single blood culture 2. Imaging Major Criteria a. Echocardiography and/or cardiac CT show vegetation, valvular/leaflet perforation, valvular/leaflet aneurysm, abscess or intracardiac fistula. or b. Significant new valvular regurgitation on echocardio-graphy as compared with previous imaging. c. New partial dehiscence of prosthetic valve as compare with previous imaging. 3. Surgical Major Criteria Evidence of IE by direct inspection during heart surgery.

Minor Criteria	1. Predisposition - Previous history of IE - Prosthetic valve - Previous valve repair - Congenital heart disease - More than mild regurgitation or stenosis of any etiology - Hypertrophic obstructive cardiomyopathy - Injection drug use 2. Documented fever (temperature greater than 38.0 ^{0}C) 3. Vascular phenomena: clinical or radiological evidence of arterial emboli, septic pulmonary infarct, cerebral or splenic abscess, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura 1. Immunologic phenomena: positive rheumatoid factor, Osler nodes, Roth spots, or immune complex-mediated glomerulonephritis 4. Microbiologic evidence a. Positive blood culture for a microorganism consistent with IE but not meeting the requirement for Major criterion. (OR) b. Positive culture or PCR for an organism consistent with IE from a sterile body site other than cardiac tissue or prosthesis. 5. Physical examination criteria: new valvular regurgitation identified on auscultation if echocardiography is not available. Worsening or changing or preexisting murmur not sufficient.

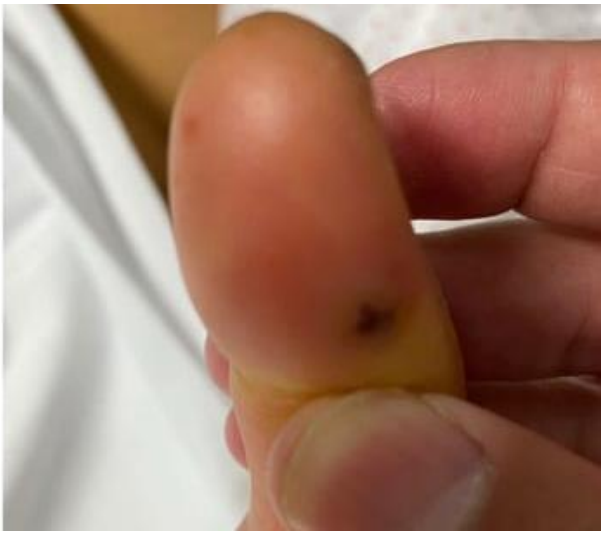

Figure 1.

Janeway lesions in a 15-year-old adolescent with aortic valve infective endocarditis: hemorrhagic macules of the palms and soles that are due to septic emboli.[7]

❖ **Differential diagnosis**

History and/or associated clinical features usually help to distinguish the condition below from infective endocarditis. In some cases, additional laboratory or imaging may be necessary:

1. **Rheumatic fever:** sequela that occurs two to four weeks following group A *Streptococcus* (GAS) pharyngitis and may consist of arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules
2. **Juvenile rheumatoid arthritis:** autoimmune disorder affecting joints for more than 6 weeks in a child age 16 or younger

3. **Acute myocarditis**: inflammatory disease of cardiac muscle which can be of infectious or non-infectious origin.
4. **Pneumonia:** acute infection of the lung parenchyma. Fever, cough and dyspnea are common findings in moderate to severe cases.
5. **Kawasaki disease:** systemic vasculitis that can progress to coronary artery aneurysm and other cardiac complications such as heart failure, myocardial infarction or arrhythmias.
6. **Acute myelocytic leukemia**: Fever and fatigue also present as in IE but these symptoms in AML usually caused by pancytopenia.
7. **Bacterial meningitis:** most patients present with fever and symptoms/signs of meningeal inflammation. Seizure can be present may be confused with brain infarction from septic embolism detached from the heart valve in IE.
8. **Childhood vasculitis:** inflammation of the blood vessel that may occur as a primary or secondary to an underlying condition. Clinical features vary depending on type and location of the vessels involved.
9. **Any infections** complicated with septicemia i.e. soft tissue, bone and joint, urinary, etc.

V. Complications

1. **Predisposing factors for complications in children with IE:**
   - Size of the vegetation > 1cm
   - Younger age, prematurity
   - IE caused by staphylococcus aureus or fungal
   - No known heart disease
   - Left-sided valvular lesion
   - Complex cyanotic congenital heart disease
   - Higher inflammatory marker such as WBC and C-reactive protein
   - Persistent fever.

   Overall, complications are more common in children without known heart diseases especially those <2 years of age. Complications of IE can be classified as cardiac or extracardiac complications.
2. **Cardiac complications**: occur in up to 50% of patients, caused by local destructive effect of the infection on the valve and surrounding structures.

   The cardiac complications include:
   - Heart failure is the most common cause of mortality in patients with I.E.
   - Paravalvular abscess leading to conduction disturbances,
   - Sinus of Valsalva perforation,
   - Suppurative pericarditis or intracardiac fistula.
3. **Extracardiac complications:** are caused by embolic phenomena of the cardiac vegetations, sepsis or immune-mediated mechanism. These include:
   - Embolization,
   - Abscess or mycotic aneurysms,
   - Intracranial hemorrhage or obstruction.

VI. Treatment

If available, pediatric infectious disease specialists, pediatric cardiologists and cardiac surgeons should be consulted.

Patients present with severe manifestations should be treated in facility where intensive care unit with multidisciplinary support are available.

1. **Medical Treatment**

At least 3 blood culture sets should be drawn before starting antibiotics.

Antibiotics should be tailored toward the organism and sensitivity profile when available.

- **Ceftriaxone** 100mg/kg/dose (IV) every 24 hours. Max 2g per dose. Duration: Minimum 4 weeks. The whole treatment course should be IV.
- **Gentamycin** may be added for synergistic purpose
  - in severe cases or Streptococcal infection has been confirmed.
  - Dose: 3mg/kg/dose (IV) every 24 hours.
  - Duration for gentamycin is 7-10days (Max 2 weeks).
  - Renal function must be monitored closely if Gentamycin is used.
- ***Note:*** the study did not show benefit when adding gentamycin for *S. aureus infection* because of potential of side effects, that Gentamycin should not be added (or should be stopped if already added) when IE caused by *S. aureus* has been confirmed.

2. **Surgery Treatment**

There are three main reasons to undergo surgery in the management of acute IE:

a. Heart failure

b. Uncontrolled infection

c. Prevention of septic embolization

Below are indications for surgery:

- Valve dysfunction resulting in symptoms of heart failure
- Left-sided IE caused by S. aureus, fungal or highly resistant microorganisms
- Complications: heart block, annular or aortic abscess, or fistulae
- Persistent bacteremia, fever > 7 days despite appropriate antimicrobial therapy
- Relapsing infection (recurrence of bacteremia after a complete antibiotic course)
- Persistent vegetation and recurrent emboli despite appropriate antimicrobial therapy

VII. Prevention and Education

Prevention of IE requires combination of actions to reduced chance of bacteremia, minimize predisposing factors and improve immune function.

Below are general preventive measures:

- Antibiotic prophylaxis for patients with high risk of IE
- Maintain dental hygiene with daily tooth cleaning and regular dental visits
- Strick cutaneous hygiene, including optimized treatment of chronic skin condition
- Curative antibiotics for any focus of bacterial infection

Antibiotic prophylaxis is recommended for patients with highest risk of IE undergoing at-risk dental procedure such as oral procedures with the manipulation of gingival or periapical dental mucosa or perforation of the oral mucosa.

Patients with below condition are considered at high risk:

- Previous history of IE
- Prosthetic valves
- Previous valve or congenital heart defect repair
- Cyanotic congenital heart disease

- Heart transplant with heart valve disease
- Mechanical circulatory support

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Viral Encephalitis in Children

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I. Key Facts

- Incidence and prevalence: Encephalitis is rare, however viral encephalitis is the most common type of encephalitis reported in children and adolescents [1][2][3]
- The reported annual incidence of viral encephalitis is approximately 16 per 100,000 children worldwide. [4]

II. Overview

1. It may be difficult to distinguish between encephalitis and meningitis:

- **Encephalitis**: inflammation of the brain parenchyma and it manifests with signs of neuro dysfunction.
- **Meningitis**: inflammation of the meninges and typically manifests with fever, headache and neck stiffness. For the clinical characteristics, diagnosis and management refer to bacterial meningitis in children section.
- **Meningoencephalitis** refers to central nervous system (CNS) infection manifesting signs and symptoms consistent with inflammation of brain parenchyma and spinal cord.

2. Causes/etiology

- The are multiple etiologies of encephalitis in children, including bacteria (TB, mycoplasma), parasites (malaria), amoebae, and autoimmune. However, viruses are the predominant cause.
- Several viruses can cause viral encephalitis in children, which may vary depending on demographics and risk factors.

Table1. Common causes of viral encephalitis

Family	Viruses
Herpesviridae	HSV-1, HSV2, VZV, HBV, HHV-6, EBV, and CMV
Flaviviridae	Japanese encephalitis (JEV), Dengue, Chikungunya, Zika
Picornaviridae	Enterovirus, Coxsacki.e. Polio
Retroviridae	HIV
Adenoviridae	Adenovirus
Paramyxoviridae	Mumps, Measles
Orthomyxoviridae	Influenza viruses
Rhabdoviridae	Rabies virus

- In a recent multi-country prospective etiology study, JEV was the most common cause in Greater Mekong region follow by dengue, enterovirus A71, influenza and HSV-1. [5]

3. Risk factors

In young infants, relevant risk information may be obtained from their relatives

- Residence in or travel to endemic areas for specific causative viruses e.g., JEV, Dengue, Chikungunya etc.
- Exposure to animal, tick, and mosquito bites.
- Immunocompromise or immunosuppression

4. Transmission

Transmission depends on the causative virus and may occur by [6]:

- Person-to-person via mucous membranes, injured skin, sexual contact, aerosolized droplets, or vertical transmission.

- Infected blood transfusion or organ transplant.
- Vector transmission such as mosquito bites or animal bites (e.g., dog, cat or another animal)

5. Pathogenesis [7]:

- Infectious agents cause clinical symptoms and signs in the CNS, either by direct invasion or indirectly, without invading the parenchyma. Viruses enter the CNS in two ways: via the bloodstream (most viruses) OR via the peripheral nerves (e.g. HSV, VZV, polio, rabies). Once the virus enters the brain, only certain cells will become infected, this results in variable clinical manifestations, e.g. seizures, demyelination, impaired consciousness, coma, respiratory failure.
- In fatal viral encephalitis an inflammatory reaction is usually prominent in the meninges and in a perivascular distribution in the brain. Neural cells may show degenerative changes and apparent phagocytosis of neural cells by macrophages. Intranuclear inclusion bodies are seen in herpesvirus and adenovirus infections.
- When acute demyelinating disease complicates viral infections outside the brain, damage is thought to be related to induction of an immune response against CNS myelin rather than invasion on the brain.

III. Signs and symptoms

Viral encephalitis typically presents acutely and sub-acutely with neurologic dysfunction and systemic symptoms.

- Neurological signs include irritability, lethargy, loss of interest in feeding, severe headaches, altered consciousness, seizures and focal deficits.
- Systemic symptoms may include fever, lymphadenopathy, respiratory symptoms, nausea, vomiting, diarrhea, sepsis-like illness, arthralgia, oral lesions, and myalgia.

IV. Diagnosis

1. Laboratory tests:

a. The lumbar puncture (LP) and cerebrospinal fluid (CSF) analysis and culture are essential (if no contra-indication for LP). The LP and CSF diagnostic test might be available only in CPA3and National hospital in Cambodia.

b. Interpretation of CSF findings should take into account the epidemiology, history, clinical presentation and other laboratory findings. For details of how to interpret CSF results, refer to the meningitis section.

c. Additional diagnostic tests should be performed based on clinical suspicion and laboratory availability, such as blood count, electrolyte, ALT and AST, PCR, serology (e.g., Dengue, JEV….), nasopharyngeal swab for influenza viruses etc;

2. Imaging:

CT scan, with and without contrast enhancement, should be used to evaluate patients with encephalitis if MRI is unavailable or impractical.

3. Differential diagnosis

- Bacterial meningitis
- Meningoencephalitis
- Epilepsy
- Febrile seizure in infant
- Autoimmune encephalitis (ADAM).

V. Complications

There are several complications, including but not limited to [4]:

- Raised intra-cranial pressure (ICP)
- Respiratory failure
- Coma
- Memory impairment
- Development delay

- Learning disabilities

VI. Prognosis

The prognosis of viral encephalitis and mortality depends on the etiology and availability of supportive and directed treatment. In the US the overall estimated were about 3% mortality. For example, HSV encephalitis can have a mortality rate up to 30% with treatment and up to 70% - 80% without treatment [1] [11].

VII. Treatment [8]

- Supportive care is a critical aspect, including management of raised ICP, seizure control, cardiovascular and respiratory support, and electrolyte and fluid balance.
- Consider herpes simplex virus (HSV) encephalitis in any child with encephalopathy, and in neonates. Treat with aciclovir.
- Intravenous aciclovir should be started if suspected or confirmed HSV or varicella zoster virus (VZV).
- Whole course should be intravenous, because oral aciclovir is not well absorbed and will not treat HSV encephalitis adequately.
- Aciclovir dose varies depending on age.

Table 2.

	Age categories	Dose/frequency	Duration
HSV	<30 weeks gestation [9]	20 mg/ kg per dose IV every 12 hours	Minimum 21 days
	>30 gestation	20 mg/kg per dose IV every 8 hours	Minimum 21 days
	>28 day to < 3 months [10]	20 mg/kg per dose IV every 8 hours	Minimum 21 days
	>3 months to < 12 years	10 to 15 mg/kg per dose IV every 8 hours	Minimum 21 days
	>12 years	10mg/kg per dose IV every 8 hours	Minimum 21 days

VIII. Prevention and Education

Because of limited treatment options for viral encephalitis, prevention is crucial. Key prevention measures include good hand hygiene practice and up-to-date vaccination (e.g., JE, mumps, measles, and influenza).

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CELLULITIS IN CHILDREN

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I. Key Facts

Incidence and burden: Cellulitis is a common skin infection in children, and the incidence and burden of cellulitis in children can be summarized as follows: [8]

- Incidence is between 2006 and 2016, the annual incidence of cellulitis in pediatric emergency departments (EDs) was 1.14 to 2.09 per million patients.
- the most common sites for cellulitis in children are the legs, buttocks, and arms.

II. Overview

1. Definition

Cellulitis is a localized skin infection caused by disruption of the physical barrier allowing pathogen entry [1, 2]. In children it is commonly caused by trauma, insect bites or varicella, predominantly affecting the face or extremities [2, 4]. Common pathogens are *Streptococcus pyogenes* (group A streptococci (GAS) and *Staphylococcus aureus* [1,2,5,7].

2. Etiology, cellulitis is caused by: [9]

- Staphylococcus aureus.
- Group A beta-hemolytic streptococci (Streptococcus pyogenes).
- S.pneumoniae: less common since the advent of childhood vaccination of heptavalent pneumococcal conjugate (Prevenar)
- Group B streptococci, gram-negative bacilli: neonates
- Haemophilus influenzae type b: very rare now as a result of childhood immunization.
- Pseudomonas aeruginosa, anaerobic bacteria: immunocompromised children.
- Pasteurella species: from cat and dog bites.
- Eikenella corrodens: from human bites.

3. Physiopathology [9]

- Most commonly secondary to local trauma, Abrasions, Lacerations, Bite wounds, Excoriated dermatitis, varicella
- Other breaches in the integument
- May develop secondary to local invasion or infection (e.g. sinusitis leading to orbital cellulitis).
- Hematogenous dissemination.

III. Diagnosis

1. Clinical presentations [1]

- Skin: Redness, swelling, pain, tenderness, warmth, bruising, blisters, dimpling, or a rash.
- Temperature: Fever (38°C) or higher
- Swollen lymph nodes: Swollen glands near the affected area
- Red streaks: Red streaks that extend from the original site of the infection
- Other symptoms: Headache, chills, weakness, nausea, vomiting, dizziness, confusion, high heart rate, low blood pressure, difficulty breathing, and fewer wet diapers.

2. Laboratory [1]

- CBC (White blood cell count maybe normal or elevated)
- Erythrocyte sedimentation rate – Elevation of the erythrocyte sedimentation rate (ESR) (≥20 mm/h) occurs in most children with cellulitis.
- C-reactive protein – Elevation of the C-reactive protein occurs in most children with cellulitis.
- Procalcitonine – Elevation.

- Blood culture for finding responsible bacteria.
- Wound culture.

3. **Imaging:** [1]
   - X-ray to rule out complications such as arthritis or osteomyelitis.
   - Head CT scan: important in orbital cellulitis.
4. **Differential diagnosis** [10]
   - Erysipelas: Has raised borders that are sharply defined
   - Stasis dermatitis: Usually affects both lower legs, unlike cellulitis which affects one leg
   - Septic arthritis or bursitis: Consider if the cellulitis is near a relevant structure
   - Gout: Consider if the cellulitis is in a clearly inflamed joint or if the patient has a history of similar symptoms
   - Insect bite: Some bites can cause large local reactions, such as Lyme disease
   - Allergic or contact dermatitis: If the cellulitis is itchy and not tender, it's unlikely to be cellulitis
   - Impetigo: Has well-defined lesions that often crust or discharge
   - Staph scalded skin syndrome: A blistering, exfoliative rash that's more common in young children and neonates
   - Necrotizing fasciitis: A serious infection that progresses rapidly and causes extreme pain
   - Superficial thrombophlebitis: Causes redness, heat, and tenderness that resembles cellulitis, but the inflammation is linear

IV. Treatment

- Antibiotic regimens are effective in more than 90% of patients. However, all but the smallest of abscesses require drainage for resolution, regardless of the microbiology of the infection [9]
  - Most cases of uncomplicated, superficial cellulitis can be treated with oral antibiotics against Staphylococcus and Streptococcus (e.g. Amoxillin-clavulanate dosage:22.5 mg/kg (max 875 mg) oral bd, cephalexin dosage: 33 mg/kg (max 500 mg) oral bd).
  - For more severe infections, in which S aureus is a suspected pathogen, Clindamycin should be considered as empiric therapy (10 mg/kg (max 600 mg) IV 6H), allergic patients should receive Trimethoprim-sulfamethoxazole (8/40 mg/kg (max 320/1600 mg) oral bd)
  - Initial intravenous therapy should be directed against S.auresu and Streptococcus (e.g Oxacillinm (,50 mg/kg (max 2 g) IV 6H), cefazolin (50 mg/kg (max 2g) IV bd), or Ampicillin/sulbactam).
  - As MRSA infection continues to rise, many experts now recommend clindamycin as initial parenteral therapy.
  - Vancomycin should be used as empiric therapy for severe rapidly progressive infections
  - (20 mg/kg IV (max 1 g) 8H).
- If hematogenous dissemination is a strong possibility, an agent active against H.influenzae type B also should be added (e.g ceftriaxone (50 mg/kg (max 2g) IV daily).
- The duration of antibiotics should generally be 7 to 10 days.
- Abscesses should be surgically drained.
- Bite wounds should have tetanus and rabies prophylaxis issues addressed.
- Do not forget to consider the possibility of MRSA in all deep, invasive, or persistent infections (Clindamycin is recommended).

❖ *bd: Twice a day*

V. Complications [1,2]

- Meningitis: An inflammation of the brain and spinal cord
- Septic arthritis: A bacterial infection of a joint
- Glomerulonephritis: An inflammation of the kidneys
- Tissue damage and death: Also known as gangrene, this can lead to amputation
- Infection of other organs: Such as pneumonia, osteomyelitis, or endocarditis
- Necrotizing fasciitis: A serious soft tissue infection that causes severe pain, skin pallor, and loss of sensation
- Abscess: An area of pus in the skin
- Necrosis: An area of dead skin or tissue

VI. Prognosis

The prognosis for complete recovery is good as long as appropriate antimicrobials are administered in a timely fashion.

VII. Follow up

- Rapid, steady improvement should be expected.
- If daily improvement is not noted. inappropriate antimicrobials coverage, deeper infections, or abscess or some other complications should be suspected (e.g foreign body).

VIII. Prevention

- Good wound care can prevent most cases of cellulitis.
- Parents should be instructed to clean all wounds thoroughly with soap and water, then cover with a clean, dry cloth.
- Topical antibiotic ointment is optional.

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INFECTIOUS MYOSITIS

NANG Sreynet, SOM Sereyrith, KHUN Leangchhun, YAY Chantana

I. Key Facts

- Infective myositis may be due to a wide variety of pathogens, including bacteria, viruses, fungi and parasites.
- Bacterial myositis presents as focal muscle infection, while viruses and parasites are more diffuse leading to generalized myalgia or multifocal myositis.
- Fungal myositis is rare, occurs among immunocompromised hosts. Parasitic myositis is most commonly a result of trichinosis or cysticercosis, but other protozoa or helminths may be involved
- 2 most common causes of childhood infective myositis: Benign acute childhood myositis and Pyomyositis.

II. Overview

1. Benign acute childhood myositis

a. Etiology

- Influenza virus type A and B, parainfluenza
- school-aged children at a median age of 8.3 years (range 7.3 to 10.3 years) [1]
- male-to-female ratio of 2:1 [1]
- Self-limited process that can be diagnosed clinically

b. Clinical features

- Self-limited process that can be diagnosed clinically
- Prodromal symptoms: rhinorrhea, low-grade fever, sore throat, cough, and malaise [3]
- symmetric bilateral leg pain (gastrocnemius and soleus complex), Pain is often worse after a period of rest [1,4]
- no sensory or motor deficits, no altered deep tendon reflexes
- CPK levels will peak after 2 weeks. [2]

c. Treatment and evolution

- Spontaneous recovery within 1 week
- Bed rest and hydration
- Analgesic such as Paracetamol
- Rhabdomyolysis is rare (dark urine, poor urine output)

2. Pyomyositis

Pyomyositis is an infection of the muscle, almost always due to Staphylococcus aureus. It most commonly affects the muscles of the limbs and torso. Infections may occur simultaneously in multiple sites.

Pyomyositis, also called “tropical pyomyositis,” Myositis purulent atropica, Pyogenic myositis or Suppurative myositis is an acute inflammation characterized by neutrophil-rich infiltrates. [6]

a. Etiology

- Staphylococcus **aureus is implicated in 90%** of cases. Also, Streptococcus pyogenes, Salmonella, Escherichia coli, and pneumococci are known to cause pyomyositis [7,11]
- Risk factors: immunosuppression, concurrent S. aureus infection, malnutrition, trauma, mortality is significant if treatment is delayed.
- Blood cultures are positive in 5%–30% of patients. [10] Serum creatine kinase concentrations are typically normal.

b. Clinical features

- Invasive Stage (subacute):
  - 1 to 3 weeks
  - Local painful swelling (wooden consistency)

- Low grade fever
- malaise
- Non purulent collection

- Suppurative Stage:
  - High fever
  - extremely painful and tender
  - Regional lymphadenopathy
  - classical characteristics of abscess, such as erythema and fluctuation, are generally absent
  - abscess is recognized by imaging (Ultrasound)
- Late Stage:
  If the suppurative stage remains undiagnosed and untreated, the infection disseminates, leading to multiple abscesses, septicemia, septic shock, and multi-organ system failure.

III. Differential diagnosis

- Deep vein thrombosis: Unilateral pain, swelling and discoloration in limb
- Osteomyelitis: fever and localized, unilateral pain
- Fracture: History of trauma, unilateral symptoms
- Malignancy: Subacute with associated fever, weight loss and bone pain that is worse at night [5]

IV. Management

1. Medical treatment:

A. Adapt analgesics to the pain level

B. Systematic antibiotic therapy

a. ***Communities with relatively little MRSA*** [8,11]

- Nafcillin or Oxacillin or Cloxaxilline150 to 200 mg/kg can be administered intravenously every 6 h OR
- Clindamycin 40 mg/kg/day divided every 8 h (for penicillin hypersensitivity or streptococcal myositis) [9]

b. ***Communities with high incident CA-MRSA***

- Vancomycin ***
  - In children, 60 mg/kg/day divided every 6 h
  - In adolescents, 45 mg/kg/day, divided every 8 h OR
- Teicoplanin loading dosage is 10 mg/kg IV every 12 h for three doses, followed by 10 mg/kg once daily OR
- Linezolid intravenously (alternative to Vancomycin)
  - children younger than 12 years;30 mg/kg/day divided every 8 h
  - children 12 years and older, 20 mg/kg/day divided every 12 h

Treatment options for VRSA (MIC ≥ 16 µg/ml) and VISA (MIC 4–8 µg/ml)

- Vancomycin, loading dose25–30 mg/kg, then continuous infusions

Plus

- Daptomycin 4–6 mg/kg/day for a duration of 6–36 days

c. ***Critically ill child having fulminant sepsis or immunocompromised*** [9]

- **Meropenem** 20mg/kg/day intravenously divided every 8 h plus Vancomycin
- **Clindamycin** 40 mg/kg/day intravenously divided every 8 h plus aminoglycoside **or**
- **Cloxaxilline**150 to 200 mg/kg intravenously every 6 h

+

- **Amikacin** 15mg/kg/day intravenously divided every 12h.

❖ **Note.** ***
- Parenteral therapy is continued until clinical improvement is evident, usually within a few days after surgical drainage. The antibiotics can be given orally for an additional 2 to 3 weeks.
  - For methicillin-sensitive isolates oral cloxacillin, cephalosporin (cephalexin 100 mg/kg/day) or clindamycin 30 to 40 mg/kg/day.
  - For MRSA isolates oral linezolid 30 mg/kg/day divided every 8 h for children younger than 12 years; for children 12 years and older, 20 mg/kg/day divided every 12 h (for 3 to 4 weeks).
- Discontinuing antibiotics; normal levels of C-reactive protein and erythrocyte sedimentation rate.[11]
- Continuation or recurrence of fever after surgical drainage while the patient is receiving appropriate antimicrobials suggests the presence of other foci needing further drainage, development of drug resistance or, less commonly, drug fever.

❖ **Abbreviation:**
- MRSA: Methicillin-resistant Staphylococcus Aureus
- CA-MRSA: Community-associated MRSA
- VRSA/VISA: Vancomycin-intermediate/ resistant Staphylococcal Aureus.

2. Surgical treatment:

Incision and drainage, under aseptic conditions (sterile consumables and instruments, antiseptic skin preparation) following the rules for incision and drainage of abscesses. Muscle abscesses are often deeper than other abscesses. As a result, aspiration with a large bore needle may be necessary to locate the abscess. Needle aspiration is insufficient treatment even if pus is evacuated and should be followed by surgical incision and drainage.

V. Complications

- Osteomyelitis
- Sepsis
- Pneumonia
- Venous thrombosis
- Sepsis causes acute respiratory distress syndrome (ARDS), pericarditis, acute renal failure and even meningitis. [11]

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OSTEOMYELITIS IN CHILDREN

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I. Key Facts

- Incidence rates of osteomyelitis increased by 11.7% from 8.2 - 9.2 cases per 100,000 children in (2009 – 2019)
- The age-specific incidence rate revealed the highest occurrence of osteomyelitis in patients aged 10–15 years (15.3/100,000 children), which increased by 23% over the observation period, followed by the age group 5–10 years (9.7/100,000 children).
- In 2019, out of all diagnoses, 39.2% were classified as acute, 38.4% as chronic, and 22.4% were unspecified.
- The lower extremity was mainly affected, with 58.9% of osteomyelitis diagnoses. [4]

II. Overview

1. Definition

Osteomyelitis is an infection localized to the bone.[5] It is usually caused by microorganisms (predominantly bacteria) that enter the bone hematogenous. Other pathogenic mechanisms include direct inoculation (usually traumatic, but also surgical) or local invasion from a contiguous infection (e.g. sinusitis, decubitus ulcers, deep wound infections, periodontal disease).

2. Etiology, osteomyelitis is caused by:

- The most common pathogens in osteomyelitis depend on the patient's age.
- Staphylococcus aureus is the most common cause of acute and chronic hematogenous osteomyelitis in adults and children.[3]
- Group A streptococcus, Streptococcus pneumoniae, and Kingella kingae are the next most common pathogens in children.
- Group B streptococcal infection occurs primarily in newborns. [4]
- In adults, S. aureus is the most common pathogen in bone and prosthetic joint infections.
- Increasingly, methicillin-resistant S. aureus (MRSA) is isolated from patients with osteomyelitis.
- In some studies, MRSA accounted for more than one-third of staphylococcal isolates.[7]
- In more chronic cases that may be caused by contiguous infection, Staphylococcus epidermidis, Pseudomonas aeruginosa, Serratia marcescens, and Escherichia coli may be isolated.
- Fungal and mycobacterial infections have been reported in patients with osteomyelitis, but these are uncommon and are generally found in patients with impaired immune function

3. Physiopathology

Osteomyelitis tends to occlude local blood vessels, which causes bone necrosis and local spread of infection. Infection may expand through the bone cortex and spread under the periosteum, with formation of subcutaneous abscesses that may drain spontaneously through the skin.[1]

III. Diagnosis

1. Clinical presentation

- The initial symptoms of osteomyelitis can be nonspecific in children of all ages.
- Fever, irritability, decreased appetite or activity
- Focal findings of bone inflammation (e.g. Warmth, Swelling, point tenderness),
- limitation of function (e.g. limp, limited use of extremity). [8][9]

2. **Laboratory**
   - WBC White blood cell counts elevations
   - Erythrocyte sedimentation rate – Elevation of the erythrocyte sedimentation rate (ESR) (≥20 mm/h) occurs in most children with osteomyelitis.
   - C-reactive protein – Elevation of the C-reactive protein occurs in most children with osteomyelitis. In the 2012 systematic review, CRP was elevated in 81% of children at the time of presentation, peaked on day 2, and normalized over one week.
   - Procalcitonine – Elevation.
3. **Imaging**
   - Radiographic findings associated with osteomyelitis include deep soft tissue swelling, periosteal reaction (suggestive of new bone formation or reactive edema), periosteal elevation (suggestive of subperiosteal abscess), and lytic sclerosis (suggestive of subacute/chronic infection).
   - Magnetic resonance imaging
     - Bone marrow inflammation (decreased signal in T1-weighted images; increased signal in T2-weighted images)
     - Edema in marrow and soft tissues
     - Penumbra sign (high-intensity-signal transition zone between abscess and sclerotic bone marrow in T1-weighted images)
     - With gadolinium enhancement: absent blood flow, suggestive of necrosis or abscess.
   - Scintigraphy: Focal uptake of tracer in the third phase of a three-phase bone scan is associated with osteomyelitis.
   - Computed tomography findings of osteomyelitis include increased density of bone marrow, cortex destruction, periosteal reaction (new bone formation), periosteal purulence, and sequestra.
   - Ultrasonography findings compatible with osteomyelitis include fluid collection adjacent to the bone without intervening soft tissue, elevation of the periosteum by more than 2 mm, and thickening of the periosteum.
4. **Confirmed by Histopathologic**

   evidence of inflammation in a surgical specimen of bone or identification of a pathogen by culture or Gram stain in an aspirate or biopsy of bone, or a periosteal fluid collection.
5. **Differential diagnosis** [5]
   - Cellulitis
   - Fracture
   - Bursitis
   - Osteitis
   - Charcot arthropathy
   - Septic arthritis
   - Trauma
   - Malignancy.

IV. Treatment [6]

Osteomyelitis treatment requires a multifaceted approach that may include antibiotics, surgical intervention

1. **Antibiothrapy probability**

Old	1st choice	Posology	Alternative regimen	Posology	Time IV
1-3month	Cefotaxime +Gentamycin	50mg/kg/6h 5mg/kg/24			15day
>3month	Cefamandole	35mg/kg/6h	Augmentin or Cefuroxime	50mg/kg/8h 50mg/kg/8h	5day

2. Antibiothrapy adaptation document of bacteriology [6]

Antibiothrapy / Germe	IV for 5 days		PO for 1 month	
	1st choice	Alternatives	1st choice	Alternative
S. aureus meti S	Cloxacillin 50mg/kg/6h	Or Augmentin Or Clindamycin Or Cefamandole	Augmentin	Clindamycin Cotrimoxazole
S.aureus meti R	Vancomycin 15mg/kg/6h + Rifampicin 10mg/kg/12	Or Clindamycin Or Levofloxacin Or Rifampicin	Clindamycin Rifampicin	Cotrimoxazole Levofloxacin
Kingella kingae	Amoxicillin 40mg/kg/6h	Cefotaxime or ceftriaxone + Rifampicin	Amoxicillin	Ciprofloxacin Cotrimoxazole
Group A streptococcus	Amoxicillin 50mg/kg/6h	Cefotaxime or ceftriaxone + Rifampicin	Amoxicillin	Clindamycin
Group B Streptococcus	Cefotaxime 50mg/kg/6h	Ceftriaxone	Amoxicillin	Cefadroxil

3. Surgery

If any constitutional findings (e.g. fever, malaise, weight loss) persist or if large areas of bone are destroyed, necrotic tissue is debrided surgically. Skin or pedicle grafts may be needed to close large surgical defects. Broad-spectrum antibiotics should be continued for > 3 weeks after surgery. Long-term antibiotic therapy may be needed.

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SEPTIC ARTHRITIS

CHENG Samrech, KIM Ang, CHOEU Hor, ROS Rithyvorn

I. Overview

1. Definition

Septic arthritis is an inflammatory response to the presence of infectious organisms within the joint space.[1]

2. Causes [5]

Table 1. *Types of Organisms infected*

Age	Most common organism	Other organisms
Newborn	S. aureus	Candida albicans Group B streptococcus Gram negative organisms
	Klebsiella, Salmonella	
Infants and children≤5 Years	S. aureus	Haemophilus influenzae* Streptococcus pneumonia
Children >5 years	S. aureus	S. pneumoniae, Neisseria meningitides
Adolescents	N. gonorrhoeae	S. aureus, S. Pneumoniae, N. Meningitidis
* *Less likely in fully immunized children.*		

3. Epidemiology [6]

- Predominant age: 1-5 years old: 70%, adolescent (N. gonorrhea)
- Sex predominance: male/female 2:1
- Most cases of pyogenic arthritis occur in children 2 years old or younger.
- Predominantly affected joints: hip (40%), knee (40%), ankle (14%), elbow (12%), wrist (4%), shoulder (4%)
- Single joint: 95%
- 5% multiple joint

4. Pathology/pathophysiology [5]

- Entry of bacteria into joint space
  - Hematogenous spread
  - Direct inoculation (penetrating trauma) or extension from bone infection (0steomyelitis)
  - Influx of inflammatory cells within the joint capsule
  - Destruction of cartilaginous structures within the joint by bacterial and lysosomal enzymes
  - If left untreated, can progress to necrosis of the intraarticular epiphysis
- Degradation of articular cartilage begins 8 hours after onset of infection (varying 2-5 days)
  - 30% at 48h
  - 50% at 5 days
  - 80% at 3 weeks.

II. Diagnosis

1. History

- History of recent trauma does not rule out septic arthritis.
- Pain of bacterial infection worsens over 1 to 3 days and doses not wax and wane.
- Septic arthritis is rarely polyarticular.

2. Physical examination [5]

- Fever and signs of sepsis(Fever occurs within the first few days of illness in 75% of patients, but less commonly in infants. Only 50% of children with gonococcal arthritis will have fever).
- Antalgic attitude: hip in flexion, abduction and external rotation and knee, elbow in flexion.
- Acute onset of joint pain, swelling, and warmth.
- reluctance to weight bear or to use the affected limb or limited range of motion.
- Irritability, crying with movement, or refusal to use the limb (non-specific signs in infants).

3. Investigation

a. Laboratory:

- WBC, CRP, ESR (elevated)
- ASLO (Antistreptolysine O)
- Other cultures: blood, pharynx, skin, ENT
- Stool exam, urine exam

b. Microbiologic diagnostic

- Blood and joint fluid for aerobic and anaerobic culture
- Synovial fluid analysis: Gram stain, culture, cell count.
    - Joint fluid in septic arthritis [5]
        - The WBC is often greater than 100,000/mm^3, but can be as low as 50,000/mm^3 in early infections.
        - The glucose level in the synovial fluid is less than 50% that of the serum.
        - Culture of the joint reveals an organism in 70% to 80% of cases (except for gonorrhea).
        - A Gram stain of synovial fluid reveals pathogens in 50% of cases.
    - Other Supportive Tests [5]
        - The ESR is elevated (>30 mm/hr) in 95% of cases. Retain suspicion if >20 mm/hr.
        - The C-reactive protein is increased. In one study, a CRP less than 1.0 mg/dL had a negative predictive value of 87% in a population in which the prevalence of septic arthritis in tested patients was 29%.
        - Blood cultures are positive in 30% to 40% of cases.
        - A high peripheral WBC count is neither sensitive nor specific for septic arthritis.

c. Imaging [5]

- Radiography is rarely helpful in diagnosis, can show widening of joint space and/or displacement of the normal fat pads in the knee or elbow, and is less often positive in

the shoulder or hip. Sometime we show a widening of articular space/interline under pressure of pus.

- Ultrasonography is a simple to identify joint effusion in suspected septic arthritis. This test has a greater Highly sensitive than plain radiography and is becoming the modality of choice to reveal hip effusions. Ultrasonography is also used to guide the aspiration needle if an effusion is detected.

4. Differential diagnosis [7]

- Juvenile Rheumatoid Arthritis
- Kawasaki Disease
- Lyme Disease
- Rheumatic Fever
- Serum Sickness
- Transient Synovitis
- Trauma, including non-accidental injury
- Malignancy, including leukemia
- Other infection occurring near a joint, such as osteomyelitis, pyomyositis, septic bursitis, cellulitis, and abscess, can be the clinical presentation of septic arthritis

III. Complications and prognosis [6]

- Permanent limitation of range of motion as a result of tissue destruction and scarring
- Growth disturbance if the epiphysis is involved
- Differentiation between hip septic and transient arthritis: combined clinical and laboratory features.
- Time to diagnose is the most important prognostic factor in septic arthritis. Early institution of therapy helps to prevent degenerative arthritis. Diagnosis may be delayed in young infants, which leads to a poorer outcome.
- Septic arthritis without or uncorrected treatment:
    - Fistulization,
    - Osteitis of the hip.
    - Chondrolysis
    - Growth plate arrest (epiphysiodesis)
    - Hip arthrosis
    - Osteonecrosis
    - Ankylosis
    - Motor handicap

Because of the availability of antibiotics, children rarely die from septic arthritis or its complications. Although chronic arthritis is uncommon, the short-term morbidity and costs, in terms of prolonged antibiotic therapy and hospitalizations, may be substantial.

IV. Treatment

1. Emergency Care

- Kocher's criteria: Hip pain, variable fever, refusal to walk, elevated ESR > 40mm/h, elevated WBC > 12000/mm3 = probability greater than 99%.

- Other recommendation: fever (>37*), ESR>20mn/h, CRP >1mg/dl, WBC > 11 000/mm3, plain x-ray shows widening of joint space (>2mm). – If 4 or 5 of these criteria = septic arthritis (99.1%) – Candidate for joint aspiration
- Drainage of infection: should occur as soon as possible if bacterial cause is suspected
- Indications for open surgical or arthroscopy drainage/irrigation/ DBM
  - Hip involvement
  - Shoulder involvement (controversial)
  - Thick, purulent, or fibrinous exudate unable to pass through 18-gauge needle
  - All other joints not undergoing open drainage should undergo needle aspiration.
- Antibiotic administration as soon as possible after joint aspiration is performed
- Immobilization of extremity (Casting: Spica cast for hip, long leg cast for knee or Traction)
- Pain management.

2. Drugs [5]

Choice of antibiotics depends on age of child as outlined in the tables. In communities in which the prevalence of methicillin-resistant S. aureus is high, vancomycin should be considered. After oral administration, a physician should do re-evaluation to ensure compliance and good clinical response are essential.

Empiric therapy prior to Identification of organism infected

Age	**First choice***	**Second choice**	Duration
Neonatal	Cefotaxime	Ampicillin and Gentamicin	IV for 14 days PO for 14 days
≤5 years	Cefuroxime	O/N/M	IV + PO = 28 days
>5 years	O/N/M, Cefazolin	Clindamycin	IV + PO = 28 days
Adolescent: - Gonococcal	Ceftriaxone	Penicillin	IV + PO = 7 to10 days
- Nongonococcal	O/N/M	Cefazolin	IV + PO = 28 days

O/N/M = oxacillin or nafcillin or methicillin.

* *In communities in which the prevalence of methicillin-resistant S. aureus is high, vancomycin should be considered.*

In general, the duration of antibiotic therapy for most cases of uncomplicated septic arthritis is approximately 4 weeks.

As in the treatment of osteomyelitis, extend the duration of treatment based on clinical response and normalization of the ESR.

a. Oxacillin:

- <u>Susceptible Staphylococcus Infections in Infants & Children</u>
  - 100-200 mg/kg/day divided q6hr IV/IM
  - Maximum 4gm/day for mild to moderate infections
  - Maximum 12gm/day for severe infections
- <u>Susceptible Staphylococcus Infections in Neonates</u>
  - (<7 days old, <2 kg) OR (>7 days old, <1.2 kg): 50 mg/kg/day divided q12hr IV/IM
  - (<7 days old, >2 kg) OR (>7 days old, 1.2-2 kg): 75 mg/kg/day divided q8hr IV/IM

- >7 days old, >2 kg: 100 mg/kg/day divided q6hr IV/IM

b. Gentamicin

- >5 years old: 2-2.5 mg/kg/dose IV/IM q8hr
- <5 years old: 2.5 mg/kg/dose IV/IM q8hr

c. Ceftriaxone

- <12 years old: 50-100 mg/kg IV/IM divided q12hr

d. Clindamycin

8-20 mg/kg/day PO as hydrochloride; 8-25 mg/kg/day as palmitate divided q6-8hr; 37.5 mg q8hr minimum palmitate dose

- <1 month old: 15-20 mg/kg/day divided q6-8hr

  Neonates (<28 days old):
  - <7 days old, <2 kg OR (>7 days old, <1.2 kg): 10 mg/kg/day IV/IM divided q12hr
  - <7 days old, >2 kg OR >7 days old, 1.2-2kg: 15 mg/kg/day IV/IM divided q8hr
  - >7 days old, >2 kg: 20 mg/kg/day IV/IM divided q6hr.
- >1 month old: 20-40 mg/kg/day divided q6-8hr.

e. Vancomycin

- 40 mg/kg/day divided q6hours IV
- Neonatal Dosing
  - (<7 days old, >2 kg) OR (>7 days old, 1.2-2 kg): 10-15 mg/kg q8-12hours IV
  - (>7 days old, >2 kg): 45-60 mg/kg/day divided q8hours IV.

f. Penicillin:

- Neonatal Bacterial Infection General Dosing Guidelines
  - <7 days & <2000 g: 50,000 units/kg/day IV divided q12hr
  - <7 days & >2000 g: 75,000 units/kg/day IV divided q8hr
  - >7 days & <1200 g: 50,000 units/kg/day IV divided q12hr
  - >7 days & 1200-2000 g: 75,000 units/kg/day IV divided q8hr
  - >7 days & >2000 g: 100,000 units/kg/day IV divided q6hr
  - Infant & Children Bacterial Infection General Dosing Guidelines
- Moderate Infection: 25,000-50,000 units/kg/day IV/IM divided q6hr
- Severe Infection: 250,000-400,000 units/kg/day IV/IM divided q4-6hr

  Not to exceed 24 million units/day.

3. Duration of therapy (IV and PO) for various organisms

- Treat for at least 2 weeks after resolution of fever and joint effusion.
- 28 days: S. aureus, gram-negative organisms, group B streptococcus
- 14 days: H. influenzae, N. meningitidis, streptococci
- 7 days: N. gonorrhoeae.

4. Follow-Up

- Involve orthopedic surgery and physical therapy services in follow-up.
- When to expect improvement
  - With appropriate antibacterial therapy, one should see improvement of symptoms
  - with 2 days of initial administration.
- Signs to watch for

- Continued pain, fever, or lack of improvement of range of motion after 3 to 4 days of appropriate antibiotic treatment.
- Rising ESR or CRP in the face of antibiotic treatment.

V. Patient education

Nontraumatic joint pain with evidence of arthritis, such as swelling, warmth, or redness, requires emergency medical attention.

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TYPHOID FEVER

TE Haypheng, KDAN Yuvathana, EANG Kim-Ean

I. Key Facts

- Typhoid Fever is a complex disease due to the increasing antimicrobial resistance. There have been reported strains of Ciprofloxacin and Multiple Drug Resistance in Cambodia [2-3].
- The disease is transmitted through the ingestion of Salmonella Typhi or Paratyphi via contaminated food or water.
- It is common among children under 5 years old, with the majority of cases caused by Salmonella Typhi or Salmonella Paratyphi-A [2-3].
- Treatment and outcomes are dependent on drug susceptibility or antimicrobial resistance.

II. Overview

1. Introduction

- Typhoid fever, also known as enteric fever, is caused by the bacteria Salmonella enterica serovar Typhi and Paratyphi (A, B, and C), and these bacteria are gram-negative bacilli transmitted through contaminated food and water. [1-2]
- The majority of cases are caused by S. Typhi and S. Paratyphi-A, especially a shift from S. Typhi to S. Paratyphi as the primary typhoid was noted recently in Thailand. [2-3]

2. Asian Epidemiology and Cambodia Situation

- In Asia, it is estimated that there are 267.6 cases of enteric fever per 100,000 people per year, as indicated by a systematic review in 2019. [4]
- Enteric fever is common among children under 5 years of age, with a case fatality risk of dramatically less than 1% when antimicrobials are introduced. Meanwhile, antimicrobial resistance of Salmonella Typhi has gradually became majority of global concern, and poor patient outcomes are associated with this resistance. [2-3]
- In Cambodia, the peak incidence of typhoid fever occurs from May to October, and it is widespread in both rural and urban areas. [6]
- Multiple Drug Resistance (MDR) such as Ampicillin, Co-trimoxazole as well as Ciprofloxacin are another significant challenge in confirmed cases of Cambodian children, especially 151/154 cases or 98.1% aren't susceptible to Ciprofloxacin for Salmonella Typhi but is only 15.8% for Salmonella Paratyphi. [7]

3. Pathogenesis

- The organisms enter the mucosa of the small intestine and then travel through the reticuloendothelial cell system, where they multiply before entering the bloodstream in large numbers, which is the start of the fever. During this time, the Peyer's patches of the ileum also become infected, leading to inflammation.
- In the second or third week of the illness, the patches may ulcerate, causing hemorrhage and perforation of the small bowel. The liver and gallbladder are also affected. After recovery, symptomless biliary infection may persist indefinitely, leading to chronic fecal or urinary carriage. [1]

III. Signs and symptoms

1. Clinical features

The incubation period ranges from 5 to 21 days. The clinical manifestations could be divided into the classic presentations (untreated case), gastrointestinal, neurological, and extraintestinal manifestations.[8]

- Classic Presentations (Untreated Individual):
  - First week: fever and bacteremia. Others: Malaise, anorexia, abdominal pain,

diarrhea/constipation, hepatomegaly. Relative bradycardia or pulse-temperature dissociation may be observed. [1]

- *Second week:* abdominal pain increases and develops "rose spots". Patients appear acutely ill, disoriented, and lethargic.
- *Third week:* intestinal bleeding, perforation, with secondary bacteremia, peritonitis, and septic shock. [8]

- Signs and Symptoms of 192 confirmed cases in Cambodian children.[7]

History Characteristic	Number (Frequency)	Physical Examination	Number (Frequency)
- Fever	192 (100%)	Mean temperature	38.6 ^{0}C
- Abdominal Pain	102 (53.1%)	- Abdominal soft	161 (83.9%)
- Headache	66 (34.4%)	- Abdominal Tenderness	36 (18.8%)
- Cough,	64 (33.3%	- Hepatomegaly	32 (16.7%)
- Vomiting	53 (27.6%)	- Splenomegaly	4 (2.1%)
- Diarrhea	40 (20.8%)	- Abnormal lung sound,	8 (4.2%)
- Chill	32 (16.7%)	- Rose spot	0 (0)
- Constipation	12 (6.7%)		

❖ Note: *association of Pneumonia and febrile seizures occur commonly in children.* [8]

2. Laboratory tests

- Complete blood count: WBC is often low, Neutrophil and Platelet mild increase [13]
- Malaria smear: to exclude malaria
- Lumbar puncture: if necessary to exclude meningitis. [1]

IV. Diagnosis

1. Culture: for confirm diagnostic

- Blood Culture: 50-70% positive (First-week).
- Stool Culture: 30-40 % positive (Second-week).
- Bone Marrow: >90% positive, but rarely indicate. [8]

2. Serology:

- Rapid *Diagnostic Tests:*
  Detect IgM Antibody against the lipopolysaccharide of Salmonella Typhi within 15-30 min. This test has been evaluated in Cambodian and Bangladeshi Children with Sensitive and Specificity 59% and 98%, respectively. [9]
- Widal *Test*: Non-specific and unreliable, may represent the previous infection. Positive results need to compare serum with 2 weeks interval of raising fourfold Antibody titer. [1,8]

3. Classification of Disease Severity [1]

	Mild	Moderate	Severe	Very Severe
General	fever +/- chills	Typhoid facies	Pre-Shock	Septic Shock
Neuro	headaches	Drowsiness +/- Neck stiffness	delirium confusion +/- Meningeal reaction	Coma +/- Meningitis
Liver	hepatomegaly	Tender hepatomegaly	with jaundice	with abscess
Intestine	soft abdomen cramps	Tenderness Constipation or diarrhea	Abdominal distension melaena	signs of Ileus or perforation

	Mild	Moderate	Severe	Very Severe
		(+/- blood)		
Spleen	none	Palpable	Tenderness	Abscess
Renal	normal	Proteinuria	pyuria Pyelonephritis	hematuria Glomerulo-nephritis
Lungs	Dry cough	Bronchitis	Pneumonia	Severe pneumonia +/- emphysema

4. Differential Diagnosis

- Malaria
- Gastro-enteritis and dysentery
- Septicemia or septic shock
- Meningitis
- Dengue Hemorrhagic Fever [1]

V. Complications

- Intestinal hemorrhage/Perforation
- Peritonitis (intestinal perforation)
- Septicemia with or without shock
- Myocarditis
- Encephalitis. [1]

VI. Management

Treatments of enteric fever has been complicated and challenging due to the emergence of multiple drug resistances, including resistance to ampicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, and cephalosporins. [8]

1. Antibiotic therapy [10-11]

a. Uncomplicated typhoid fever

Uncomplicated typhoid fever	Antibiotic	Daily dose in mg/kg	Total days
First line	Cefixime	15-20	14
Second-line	Azithromycin	10	7
	Ceftriaxone IV	75	7

b. Severe typhoid fever

Severe typhoid fever	Antibiotic	Daily dose in mg/kg	Total days
First line	Ceftriaxone IV	75	10
Oral Switch	Azithromycin	10	10

❖ **Notes:**

- Ciprofloxacin may be used only if an organism is isolated and reported as sensitive but rare in Cambodia for Salmonella Typhi. [11]

- If isolated organism is Multiple Drug Resistant (MDR) or extensively drug-Resistant (XDR) strain, please discuss the case with the Hospital Microbiology Team and use antibiotics according to drug susceptibility.
- In severe cases (delirium, obtundation, stupor, coma, or shock), should adjunctive with dexamethasone (3 mg/kg followed by 1 mg/kg every 6 hours for a total of 48 hours) [10]
- Persistent fever or Defervescence could be observed with mean time 4-6 days after successful treatment, so continuing fever does not imply therapeutic failure [10].
- Relapse case could be occurred 4-8 % after 2 to 3 weeks treatment, but is usually milder and of shorter duration. [1]
- Chronic carrier stage with continue bacterial shedding in stool or urine could be 5-10 % of cases.

2. Supportive Treatment:

- Fever: Paracetamol (60mg/kg/day, divided in 4 times per day).
- Fluid: ensure adequate hydration PO (ORS, water,) or IV (Ringer Lactate/dextrose 10%) for severe complicated cases. [1]
- Intestinal Perforation: Surgical intervention.

VII. Prevention

- **Food and water safety:** clean hand properly, drink only fresh water, and any raw or unclean food should be avoided.
- **Vaccination:** effective against *Salmonella* Typhi but none S. Paratyphi.
  Currently, there are 3 types of typhoid vaccine [10]

a. Conjugate *vaccine:*

- Suitable from 6 months to 45 years
- Formulation: Typbar-TCV (a Vi-TT; Vi Polysaccharide TT conjugate)
- Dose and Route: Single Dose IM
- Immunogenicity: higher seroconversion rates and higher antibody titer than Polysaccharide vaccine
- Efficacy: 78.3%-85% over 2-4 years protection

b. Polysaccharide vaccine (Available in Cambodia)

- Suitable for 2 years up
- Formulation: Vi polysaccharide vaccine (Inactivated Vaccine).
- Dose and Route: Single dose IM or Subcutaneous.
- Efficacy: 55%-69% over 1-3 years protection

c. Live attenuated vaccine

- Suitable for 6 years up
- Formulation: Consist of attenuated S. Typhi strain Ty21a
- Dosage and Route: Oral, 1 capsule taken every other day for total 4 capsule. One hour before meal
- Efficacy: 45%-56% over 1-3 years protection
- Contraindication: Immunocompromised group.

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VIRAL HEPATITIS

NANG Sreynet, KHUN Leangchhun, YAY Chantana

I. Key Facts

- Hepatitis is an inflammation of the liver that is caused by a variety of infectious viruses and noninfectious agents leading to a range of health problems, some of which can be fatal. [1]
- There are five main strains of the hepatitis virus, referred to as types A, B, C, D and E. [1,2]
- In particular, types B and C lead to chronic disease in hundreds of millions of people and together are the most common cause of liver cirrhosis, liver cancer and viral hepatitis-related deaths. [1]
- WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year. [1]

II. Overview

1. Definition

- Viral Hepatitis is an inflammation of the liver caused by the hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV). [1,5]
- Almost everyone recovers fully from hepatitis A with a lifelong immunity. However, a very small proportion of people infected with hepatitis A could die from fulminant hepatitis. [1]
- Hepatitis D is an inflammation of the liver caused by the hepatitis D virus (HDV), which requires HBV for its replication. Hepatitis D infection cannot occur in the absence of hepatitis B virus. [1,5]

2. Transmission [1,5,7]

- Hepatitis A and E are transmitted primarily by the fecal-oral route (contaminated food and water, dirty hand, inadequate sanitation, poor personal hygiene) and through close physical contact (such as oral-anal sex) with an infectious person.
- Hepatitis B, C and D are most commonly spread from mother to child at birth (perinatal transmission) or through horizontal transmission (exposure to infected blood) and sexual transmission. They are also spread by needlestick injury, tattooing, piercing and exposure to infected blood and body fluids, such as saliva and menstrual, vaginal and seminal fluids.

3. Physiopathology [2,3]

- Hepatocyte injury can be due to:
  - Cytopathic effects
  - Immune mediated cell lysis (by HBV & HCV)
- Cholestatic jaundice with elevated both direct and indirect bilirubin
- In perinatal HBV infection: markers of infection and antigenemia appear 1-3 months after birth.

4. Risk factors [1,3,7]

- Poor sanitation, lack of safe water
- Living in a household with an infected person
- Travelling to areas of high endemicity without being immunized
- Perinatal exposure to an infected mother (The most important risk factor for acquisition of HBV in children)
- Post transfusion, Hemodialysis patients, Drug abusers, Sexual with multiple partner
- Health care worker.

III. Signs and symptoms

- Many cases of viral hepatitis pass asymptomatic
- Symptomatic cases pass in following phases: [2,3]
  - Pre-icteric phase (2-4 weeks): Fever, malaise, anorexia, nausea, vomiting, abdominal pain, diarrhea is frequent in children while constipation predominates in adults
  - Icteric phase (2-4 weeks): Improved previous symptoms with appearance of: Jaundice, Tender hepatomegaly, dark urine and pale stool
  - Convalescent phase
    - Most patients achieve full recovery in hepatitis A and E

  - Some patients evolute complications (Acute liver failure and Prolonged cholestatic syndrome)
  - Pregnant women with hepatitis E, particularly those in the second or third trimester, are at increased risk of acute liver failure, fetal loss and mortality. Up to 20–25% of pregnant women can die if they get hepatitis E in third trimester. [1]
- Extrahepatic manifestations due to circulating immune complexes; mainly in HBV & HCV: [2]
- Serum sickness like prodrome marked by arthralgia or skin lesions e.g: urticarial, purpuric, macular, or maculopapular rashes
- Aplastic anemia
- Glomerulonephritis
- Vasculitis.

Fig.1- *Characteristics of viral hepatitis* [3]

Table 113-1 Characteristics of Agents Causing Acute Viral Hepatitis

	HEPATITIS VIRUSES				
FEATURE	**HAV***	**HBV**	**HCV†**	**HDV**	**HEV‡**
Viral structure	27-nm ssRNA virus	42-nm dsDNA virus	30- to 60-nm ssRNA virus	36-nm circular ssRNA hybrid particle with HB_sAg coat	27–34 nm ssRNA virus
Family	Picornavirus	Hepadnavirus	Flavivirus	Satellite	Flavivirus
Transmission	Fecal-oral, rarely parenteral	Transfusion, sexual, inoculation, perinatal	Parenteral, transfusion, perinatal	Similar to HBV	Fecal-oral (endemic and epidemic)
Incubation period	15–30 days	60–180 days	30–60 days	Coinfection with HBV	35–60 days
Serum markers	Anti-HAV	HBsAg, HBcAg, HB_eAg, anti-HB_s, anti-HBc	Anti-HCV (IgG, IgM), RIBA, PCR assay for HCV RNA	Anti-HDV, RNA	Anti-HEV
Fulminant liver failure	Rare	<1% unless coinfection with HDV	Uncommon	2%–20%	20%
Persistent infection	No	5%–10% (90% with perinatal infection)	85%	2%–70%	No
Increased risk of hepatocellular carcinoma	No	Yes	Yes	No	No
Prophylaxis	Vaccine: immune serum globulin	Vaccine: hepatitis B immunoglobulin (HBIG)			

IV. Diagnosis

1. Laboratory test [2,3,5]

A. To prove acute hepatitis:

- Liver function tests:
  - Aminotransferase levels (ALT & AST): Markedly elevated (The elevation level does not correlate with the extent of hepatocellular necrosis nor to the prognosis)
  - Serum bilirubin: Moderately elevated (mainly conjugated)
  - Albumin and prothrombin time: usually normal.

In acute liver failure: [2]

  - Aminotransferases rise initially then rapidly decline with rising bilirubin
  - Altered synthetic function: (The most important marker of liver injury and defining severity)
    - Abnormal protein synthesis (prolonged prothrombin time, low serum albumin levels)

- Metabolic disturbances (hypoglycemia, lactic acidosis, hyperammonemia)

- Urine: Dark color due to increase cholebilirubin and bile salts
- Stool: Pale color due to decrease stercobilinogen.

B. Viral serology for etiology

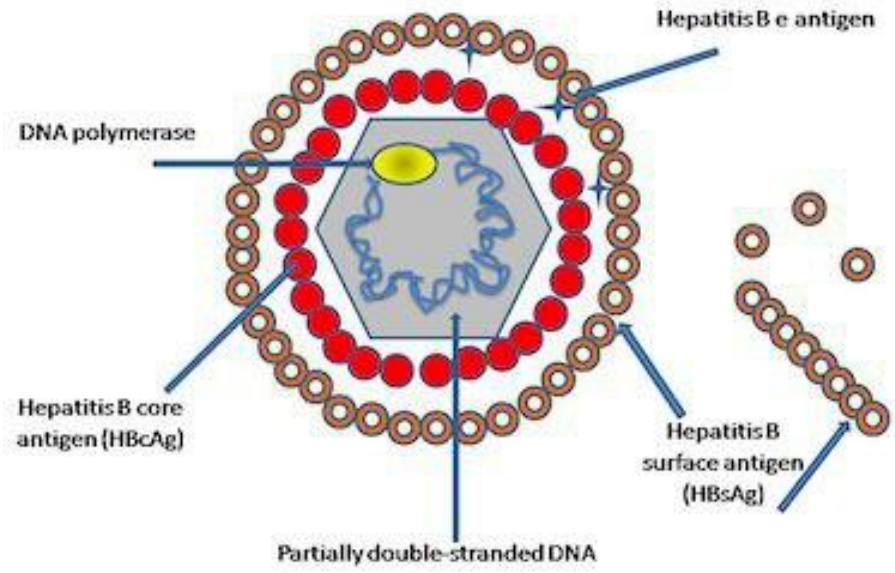
a. HAV marker [2]

Marker	Significance
Anti - HAV (IgM) Anti - HAV (IgG)	Recent HAV infection. Previous HAV infection or HAV vaccination; confers long-term protection

b. HBV marker [2]

Marker	Significance
HBs Ag	- Acute infection; its rise closely coincides with the onset of symptoms - If persist > 6 months indicate chronic hepatitis
Anti HBc Ag IgM	- Acute infection; Reliable single marker later in the acute phase as HBs Ag fall before the symptoms disappear
Hbe Ag	- Acute infection; a marker of active viral replication and usually correlates with HBV DNA levels - HBe Ag positive mothers put very high risk of perinatal transmission to their babies
Anti HBc Ag IgG	- Infection; recent or chronic
Anti HBs Ag	- If present alone, it indicates previous vaccination. - If present with anti-HBc Ag→ resolved infections.

Fig. 2- *Hepatitis B surface antigen* (HBsAg)



c. For HCV, HDV and HEV markers [1,2,3]

- Detect specific antibodies: Ac HCV, Ac HDV and Ac HEV
- Detect specific RNA by PCR (polymerase chain reaction).

2. Imagery: [3,6]

- Ultrasound, CT scan or MRI
- Liver biopsy
- Fibro-scan can also be performed to assess degree of liver fibrosis and scarring and monitor progression of liver disease.

3. **Differential diagnosis** [2,3,5]
   - Other virus may cause hepatitis as part of systemic infection: Epstein-Barr virus, cytomegalovirus, varicella zoster (chickenpox), herpes simplex virus and adenovirus.
   - Bacterial infections may cause hepatitis: Escherichia coli sepsis and leptospirosis.
   - Drugs: rifampicin, paracetamol overdose, isoniazid, phenytoin, valproic acid, carbamazepine, toxin (ethanol, poisonous mushroom).

V. Complications

- Acute liver failure (ALF) [2]
- Prolonged cholestatic syndrome: with problematic pruritus and fat malabsorption [2]
- HAV and HEV cause acute infection only. [2,3,5]
- HBV, HCV, and HDV may persist as chronic infection with chronic inflammation, fibrosis, and cirrhosis and the associated risk of hepatocellular carcinoma. [1,3,5,6]
- HIV infection and ethanol use increase the risk of HCV progression. [3]

VI. Treatment

- The treatment of acute hepatitis is largely supportive and involves rest, hydration, and adequate nutrition. Avoid hepatotoxic drugs: acetaminophen, paracetamol.
- Chronic hepatitis is an inflammatory process of the liver lasting longer than 6 months.
- Purpose of treatment of chronic hepatitis is to cure the illness, slow the advance of cirrhosis, reduce cases of liver cancer, improve long term survival.

1. **Acute hepatitis** [2,3,5]

Hospitalization is indicated for persons with severe vomiting and dehydration, signs of hepatic encephalopathy or signs of acute liver failure.

Acute liver failure management include:

- Referral to PICU in an expert center
- Monitor vitals, conscious state and hepatic / renal chemistry
- Fluid, glucose, ammonia and electrolytes monitoring
- Restrict or forbid proteins initially
  Gastroprotection: proton pump inhibitors
- Oral antibiotics (e.g. Neomycin) and Lactulose to sterilize the colon
- Correct coagulopathy by vit K, fresh frozen plasma
- In advanced cases with coma: Hepatic dialysis/transplantation.

2. **HBV: Chronic hepatitis B** [1,6,9]
   - The indications for antiviral therapy are generally based on serum HBV DNA, ALT levels, and the severity of the liver disease in combination with factors such as age, family history, and concomitant diseases. These factors are assessed comprehensively to determine the risk of disease progression.
   - Medication: Nucleoside analogs (Entecavir, Tenofovir) or Pegylated interferon alpha.
   - Antiviral therapy is the most important treatment for patients with chronic HBV infection. In addition, there are anti-inflammatory, anti-oxidation, liver protection, anti-fibrosis, and immune regulatory treatment options. *See Fig. 3*
3. **HCV: Chronic hepatitis C**
   - There is no vaccine for hepatitis C, but it can be treated with antiviral medications. [1]
   - Medications: Sofosbuvir (SOF), Daclatasvir (DCV), Ledipasvir (LED), Velpatasvir (VEL), Glecaprevir(G), Pibrentasvir (P) [3,5,8]
   - Direct-acting antiviral (DAA) treatment with an approved regimen is recommended for all children and adolescents with HCV infection aged ≥3 years as they will benefit from antiviral therapy, regardless of disease severity [8]
   - Treatment duration is short (usually 12 to 24 weeks) depending on the absence or presence of cirrhosis. *See Fig. 4*
   -

Fig 3- ***Algorithm for assessment, treatment and monitoring of people with chronic hepatitis B infection.*** [9]

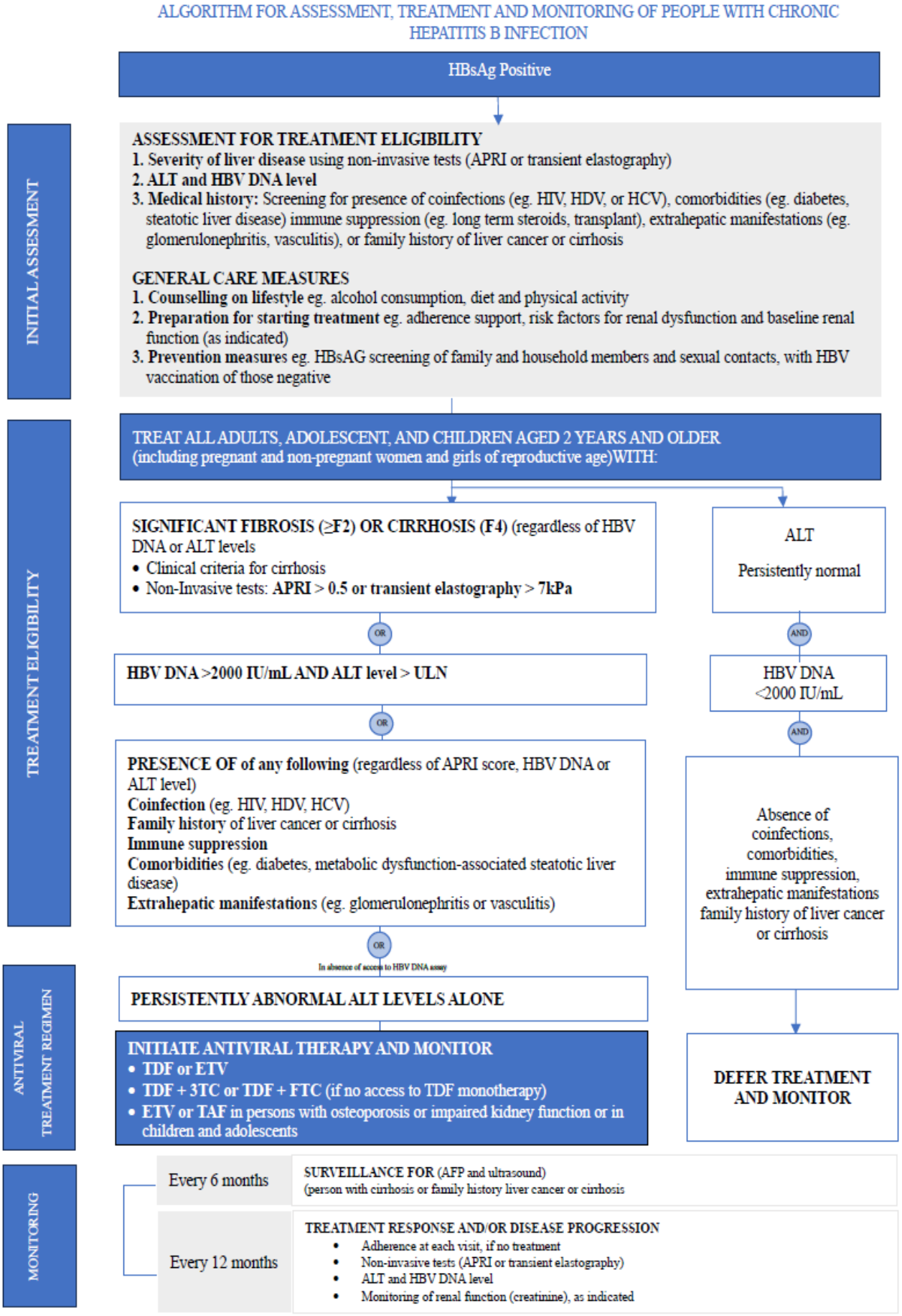


Table 1. ***Summary of Preferred and alternative first-line antiviral regimens*** [9]

Population	Preferred first-line regimen	Alternative first-line regimen	Special circumstances
Adults	TDF ETV	TDF + 3TC TDF + FTC (where TDF monotherapy is not available)	ETV TAF (for people with established osteoporosis and/or impaired kidney function)
Adolescents (12-17 years)	TDF ETV	TDF + 3TC TDF + FTC where TDF monotherapy is not available) TAF	
Children (2-11 years)	TDF* ETV		

TDF: tenofovir disoproxil fumarate; ETV: entecavir; 3TC: lamivudine; FTC: emtricitabine; TAF: tenofovir alafenamide fumarate.
*Low dose formulations of TDF may not be widely available

Table 2. ***Dosing in children and adolescent*** [9]

Drug	Patient group	Dose
ETV[a]	Weight <30 kg	0.015 mg/kg once daily (maximum 0.5 mg daily)
	Weight ≥30 kg	0.5 mg once daily
TDF[b]	Age ≥2 years	8 mg/kg once daily (maximum 300 mg daily)
	Age ≥12 years	300 mg daily
TAF[c]	Age ≥12 years	25 mg once daily

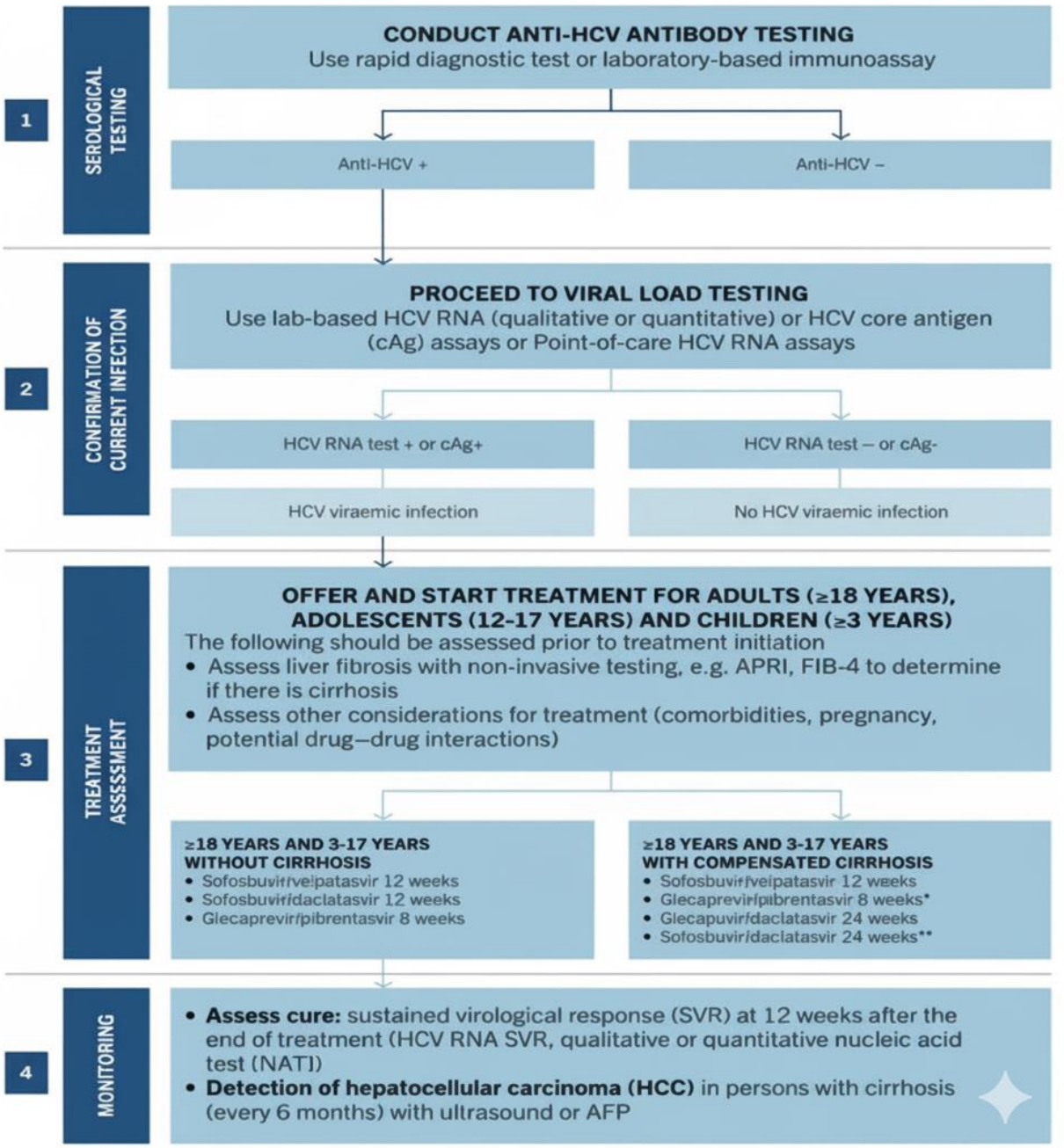
a ETV: approved for children aged two years or older.
b TDF: the EMA has approved TDF for children two years or older with CHB *(1)* and the FDA for children two years and older weighing at least 10 kg *(2)*.
c TAF: the EMA has approved TAF for children six years and older and weighing more than 25 kg *(3)* and the FDA for children 12 years and older with compensated liver disease *(4)*.

Table 3. ***Dosing of DAA regiments*** [8]

Recommended pan genotypic DAA regimens			Non-pangenotypic DAA regimen (in settings with minimal GT3 infection) [1]
SOF/DCV[2]	SOF/VEL	G/P[3]	SOF/LED
>26 kg 400/60 mg od (film-coated tablets)	>30 kg 400/100 mg od (FDC tablet)	>45 kg 300/120 mg od (FDC tablet or 6 packets of oral pellets)	≥35 kg 90/400 mg od (FDC tablet)
14-25 kg 200 mg/30 mg[2] (as single tablets, SOF preferred as smaller, 100 mg tablet)	17-29 kg 200/50 mg od (FDC tablet or granules)	-30-<45 kg 250/100 mg od (5 packets of oral pellets) -20-<30 kg 200/80 mg od (4 packets of oral pellets)	17-35 kg 45/200 mg (tablet)

	<17 kg 33.75/150 mg (FDC granules packets)	<20 kg 150/60mg od (3 packets of oral pellets)	<17 kg 33.75/150 mg (FDC granules packets)

Fig. 4- ***Summary algorithm for the diagnosis, treatment and monitoring of chronic HCV infection in adults, adolescents and children ≥ 3 years*** [8]



4. **HDV**: **Chronic hepatitis D**
   - This treatment is associated with significant side effects and should not be given to patients with decompensated cirrhosis, active psychiatric conditions and autoimmune diseases. [1]
   - Medications: Pegylated interferon alpha or Bulevirtide [1,9]
   - Treatment should last for at least 48 weeks irrespective of the patient's response.
   - Hepatitis D infection can be prevented by hepatitis B immunization, but treatment success rates are low. [1]

VII. Prevention and education

- Improved sanitation, food safety and immunization are the most effective ways to combat hepatitis A and E. [1,3,5]
- To reduce the risk of getting or spreading hepatitis B, C and D: [1,6,8]
  - Practice safe sex by using condoms and reducing the number of sexual partners
  - Avoid sharing needles or any equipment used for injecting drugs, piercing, or tattooing
  - Wash your hands thoroughly with soap and water after coming into contact with blood, body fluids, or contaminated surfaces
  - Testing of donated blood for the hepatitis and other viruses
  - Get a hepatitis vaccination
  - There is no effective vaccine against hepatitis C and D.

❖ **Vaccination** [2,7]

- **HAV vaccine** (e.g. Havrix®):
  - Inactivated vaccine, approved for children older than 12 months
  - Dose: 2 doses 6 months apart, IM.
- **HBV vaccine**

  Combined: Both vaccine and immunoglobulin

  A. *Post exposure prophylaxis for infant born to HBs Ag positive mothers*
  - HBV immunoglobulin 0.5 ml IM, within 12 hours after birth plus the first dose of HBV vaccine then at Week 6, Week 10 and Week 14 from Birth that it combined with others vaccines, see *National Immunization Program agenda*. [10]
  - Protective value of this regime is > 95%
  - Follow up: Post vaccination testing for HBsAg and anti-HBs should be done at 9, 18 months:
    - Positive for anti-HBs -> The child is immune
    - Positive for HBs Ag only -> The child is infected
    - Negative for both HBsAg and anti—HBs -> Repeat the vaccine B.

  B. *Post exposure in older child:*
  - HBV immunoglobulin: 0.06 ml/kg within 24 hours plus HBV vaccine which given at 0, 1, 6 months.

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Tetanus in children

KDAN Yuvathana, TE Haypheng, EANG Kim-Ean

I. Key Facts

- Tetanus is acquired through infection of a cut or wound with the spores of the bacterium Clostridium tetani, and most cases occur within 14 days of infection. Tetanus cannot be transmitted from person to person.
- Tetanus can be prevented through immunization with tetanus-toxoid-containing vaccines (TTCV). However, people who recover from tetanus do not have natural immunity and can be infected again.
- The majority of reported tetanus cases are birth-associated among newborn babies and mothers who have not been sufficiently vaccinated with TTCV.
- In 2018, about 25 000 newborns died from neonatal tetanus, a 97% reduction since 1988, largely due to scaled-up immunization with TTCV.
- In 2022, 84% of infants worldwide were vaccinated with 3 doses of diphtheria-tetanus-pertussis (DTP) containing vaccine. [1]

II. Overview

11. **Definition:** Tetanus is an acute infectious disease caused by spores of the bacterium *Clostridium tetani*. The spores are found everywhere in the environment, particularly in soil, ash, intestinal tracts/feces of animals and humans, and on the surfaces of skin and rusty tools like nails, needles, barbed wire, etc. Being very resistant to heat and most antiseptics, the spores can survive for years. [1]
12. **Causes/ transmission:**

    It's caused by the poison (toxin) of tetanus bacteria. Tetanus is not a contagious illness. The bacteria usually enter the body through a wound in the skin. Tetanus bacteria live in soil and animal manure. Tetanus occurs more often in warmer climates or during the warmer months. It can also be found in the umbilical stump of infants in developing countries. This occurs in places where the tetanus vaccine is not often used, and people may not know how to care for the stump after the baby is born. [2]
13. **Physiopathology:** Tetani spores usually enter through contaminated wounds. Manifestations of tetanus are caused by an exotoxin (tetanospasmin) produced when bacteria lyse. The toxin enters peripheral nerve endings, binds there irreversibly, then travels retrograde along the axons and synapses, and ultimately enters the central nervous system (CNS). As a result, release of inhibitory transmitters from nerve terminals is blocked, thereby causing unopposed muscle stimulation by acetylcholine and generalized tonic spasticity, usually with superimposed intermittent tonic seizures. [3]
14. **Risk factors**

For children:	**For newborn:**
- Unvaccinated: Children who haven't received the tetanus vaccine are at higher risk - Wounds: Deep or dirty wounds, especially those contaminated with soil or manure, can introduce tetanus spores - Injuries: Cuts, burns, or puncture wounds are common entry points for the bacteria - Warm Climates: The bacteria thrive in warmer conditions, increasing the risk in certain regions	- Unclean Birth Practices: Using non-sterile - instruments to cut the umbilical cord or applying contaminated materials to the umbilical stump - Unvaccinated Mothers: Newborns of mothers who haven't been vaccinated with tetanus-toxoid-containing vaccines are at higher risk - Unhygienic Delivery Conditions: Deliveries conducted in unclean environments or by individuals with unclean hands

III. Signs and Symptoms

After a child is exposed to tetanus bacteria, it may take from 3 to 21 days for symptoms to start. In babies, symptoms may take from 3 days to 2 weeks to start.

- The most common symptoms of tetanus include:
- Stiffness of the jaw (lockjaw or trismus)
- Stiffness of the abdominal and back muscles
- Contraction (tightening) of the facial muscles
- Convulsions
- Fast pulse
- Fever
- Sweating
- Painful muscle spasms near the wound area. If these spasms affect the larynx or chest, the child may not be able to breathe.
- Trouble swallowing.

❖ **Prognostic Scoring Systems in Tetanus Dakar Score**

Prognostic Factor	Score 1	Score 0
Incubation period	< 7 days	≥ 7 days or unknown
Period of onset	< 2 days	≥ 2 days
Entry site	Umbilicus, burn, uterine, open fracture, surgical wound, IM	All others plus unknown
Spasms	Present	Absent
Fever	> 38.4°C	< 38.4°C
Tachycardia	Children or Adult > 120 beats/min Neonate > 150 beats/min	Children or Adult < 120 /min Neonate < 150 /min
Total Score	Maximum = 6	Minimum = 0

(*Score maximum = 6, minimum = 0*)

Total Score	Disease severity	Mortality
0 – 1	No severe	< 10%
2 – 3	Mild	10-20%
4	Severe	20-40%
5 – 6	Very severe	> 50%

IV. Diagnosis

Tetanus is diagnosed on the basis of clinical features and does not require laboratory confirmation.

The WHO definition of a confirmed neonatal tetanus case is an illness occurring in an infant who has the normal ability to suck and cry in the first 2 days of life, but who loses this ability between days 3 and 28 of life and becomes rigid or has spasms.

1. **Laboratory finding:**
   - Blood counts and blood chemical findings are unremarkable.

- Wound cultures are only positive for C tetani in 30% of cases and therefore generally are not useful clinically. Moreover, cultures can be positive in patients without clinical tetanus symptoms.
- A lumbar puncture is not necessary for diagnosis. Cerebrospinal fluid (CSF) findings are normal, except for an increased opening pressure, especially during spasms. [4]

2. **Imagery finding:**
   - No systematic studies have found diagnostically-significant findings on imaging.
3. **Differential diagnosis**:
   - Hyper tonicity / hyper-excitability:
     - Neuroleptic intoxication (Haloperidol, chlorpromazine, metoclopramide)
     - Strychnine intoxication
   - Trismus can be observed in other ENT infections (maxillary arthritis, abscess...)
   - Dental infection (wisdom tooth)
   - Meningitis and encephalitis
   - Cerebral malaria (with convulsions). [5]

V. Complications:

- Vocal cord spasms
- Broken bones from severe muscle spasms
- Breathing problems
- Lung infection (pneumonia)
- High blood pressure
- Abnormal heart rhythms
- Blood clot in the lung (pulmonary embolism)

VI. Treatment

Hospitalization is necessary and requires 3 to 4 weeks on average. Correct management can reduce mortality by 50%, even in hospitals with limited resources.

- **General measures:**
  - The patient should be the sole occupant of a dark, quiet room: all stimulation (noise, light, touch) may trigger painful spasms that may cause critical respiratory distress.
  - Establish IV access: hydration, access for IV injections.
  - Insert a nasogastric tube: hydration and feeding, administration of oral medications.
  - Gentle aspiration of secretions (nose, oropharynx).
  - Provide hydration and nutrition in feeds divided over 24 hours.
  - In newborns, give expressed breast milk every hour (risk of hypoglycemia). All wounds should be cleaned and debrided as indicated.
  - Give oxygen if needed.

❖ Note: The total daily fluid requirement of a child is calculated with the following formula: *100ml/kg for the first 10 kg*, then *50ml/kg for the next 10 kg*, thereafter *25ml/kg for each subsequent kg*.

- **Tetanus Infant and Child**
  - Anticonvulsants:
    - *Diazepam* (PO, Rectal, IV):
      - 1 to 3mg/kg/dose, depending on the severity of contracture,
      - maintenance dose in 5 to 6mg/kg/day (maximum 10mg/kg/day) for 2 weeks and 1 week followed by gradual decrease.
    - *Phenobarbital*: 10mg/kg/ dose (PO) at first dose, then 5mg/kg/day in single dose for the following days.

- Antibiotics:
  - *Ceftriaxone* 200mg/kg/day (PIV) divided in 2 times at the first day, then 100mg/kg/day for 7 days
  - With *Metronidazole* 30mg/kg/day divided in 2-3 times for 7 days (PO, PIV)
- Vaccination and SAT
  - TIG (human immunoglobulin): 100 IU/kg, single dose IM (max 3,000 IU) Or SAT: 10,000UI in IVL
  - Completed by vaccination (National Immunization Program)
  - Cimetidine: 20mg/kg/day, divided in 2 times (PO, IVL, IM)
  - Antipyretic (if fever): Paracetamol 10-15mg/kg/dose, not to exceed 60mg/day
  - Adequate fluids and nutrition should be provided, as tetanus spasms result in high metabolic demands and a catabolic state. Nutritional support will enhance chances of survival.
  - Airway / respiratory control: drugs used to control spasm and provide sedation can result in respiratory depression. Patients must be carefully monitored and medication doses adjusted to provide maximal spasm and autonomic dysfunction control while avoiding respiratory failure. Nasotracheal intubation with assisted ventilation (if apnea). 10-15mg/kg/dose, not to exceed 60mg/day. [5]

VII. Prevention and Education

1. Prevention:

a. Post-exposure prophylaxis:

- In all cases:
  - Cleansing and disinfection of the wound, and elimination of foreign material.
  - Antibiotics are not prescribed routinely for prophylaxis. The decision to administer an antibiotic is made on a case-by-case basis, according to the patient's clinical status.
- Depending on pre-exposure vaccination status:
  - Tetanus vaccine (VAT) and immunoglobulin, (*see indications below*)

Risk	Complete vaccination (3 or more doses) Time since administration of latest dose:			Incomplete vaccination (less than 3 doses) or no vaccination or unknown status
	< 5 years	5-10 years	> 10 years	
Minor clean wound	None	None	VAT One booster dose	Initiate or complete VAT
All other wound	None	VAT One booster dose	VAT One booster dose	Initiate of complete VAT and Administer tetanus immunoglobulin

- Tetanus vaccine IM
  - Children and adults: 0.5 ml/injection
    - With no vaccination or unknown vaccination status: administer at least 2 doses at an interval of 4 weeks.
    - With incomplete vaccination: administer one dose. Then, to ensure long-lasting protection, administer additional doses as indicated in the table below.

b. Human anti-tetanus immunoglobulin IM

- Children and adults: 250 IU as a single dose; 500 IU for wounds more than 24 hours. Inject the vaccine and the immunoglobulin in 2 different sites, using a separate syringe for each. Or SAT: 1,500UI in IM

c. Routine vaccination (pre-exposure prophylaxis)

- Children: a first series of 3 doses of OPV + DTP + HepB + Hib + PCV before the age of 1 year, administered at an interval of 1 month (e.g. at the age of 6, 10 and 14 weeks), then a 4th dose between 12 and 15 years.
- Women of childbearing age: 5 doses during the reproductive years: a series of 3 doses (dT or TT) with an interval of at least one month between the 1st and 2nd dose and an interval of at least 6 months between the 2nd and 3rd dose, then two other doses, each at minimum interval of one year, e.g. during pregnancies.
- Pregnant women: if a woman has never been vaccinated or if her vaccination status is unknown: 2 doses of dT or TT during the pregnancy to reduce the risk of tetanus in at least 4 weeks later and at least 2 weeks before delivery. The vaccination regime protects more than 80% of newborns from neonatal tetanus. A single dose offers no protection. Continue vaccination after delivery to complete 5 doses, as for women of childbearing age. [5]

2. Education:

a. For Parents and Caregivers:

- Vaccination: Ensure that children receive the complete series of tetanus-toxoid-containing vaccines (TTCV) as part of their routine immunization schedule
- Clean Delivery Practices: Emphasize the importance of clean delivery practices, such as using sterile instruments to cut the umbilical cord and ensuring that the umbilical stump is kept clean and dry
- Wound Care: Teach proper wound care techniques, including cleaning all wounds thoroughly, removing dirt or foreign material, and seeking medical attention for deep or dirty wounds
- Hygiene: Promote good hygiene practices, such as washing hands regularly and keeping living environments clean to reduce the risk of tetanus spores entering the body
- Awareness: Raise awareness about the signs and symptoms of tetanus, such as muscle stiffness, spasms, and difficulty swallowing, so that early medical intervention can be sought if needed

b. For Healthcare Providers:

- Routine Immunization: Ensure that all children receive their tetanus vaccinations according to the recommended schedule
- Education During Prenatal Visits: Educate pregnant women about the importance of tetanus vaccination and clean delivery practices to protect both themselves and their newborns
- Postnatal Care: Provide guidance on proper umbilical cord care and wound management for newborns. [4]

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MEASLES

NY Theary, HU Sokheng, KHUN Leangchhun, YAY Chantana

I. Key Facts

Measles is a highly contagious, vaccine-preventable viral illness. Despite the existence of a safe and effective vaccine, measles remains a major cause of morbidity and mortality globally, especially in children. [1]

According to official data released by the Ministry of Health, measles outbreaks have occurred in Cambodia through last measles immunization campaign in 2007 to 2010 and 2010 was noted to have the largest number of measles cases in children. 575 cases (1.2%) of measles hospitalized were selected in clinical and epidemiological study among 48765 total pediatric admission in Jayavarman VII Hospital during 1 year's period in 2010 [2,4].

Accelerated immunization activities by countries, WHO, the Measles & Rubella Partnership and other international partners successfully prevented 56 million deaths between 2000-2021. Vaccination decreased measles deaths from 761 000 in 2000 to 128 000 in 2021. [3]

Through statistics of Jayavarman VII Hospital from 1st January 2021 to 31st December 2023, there were 44 suspected measles cases hospitalized (10 cases in 2021, 11 cases in 2022 and 23 cases in 2023).

II. Overview

1- Definition

Measles, also known as rubeola, is an acute febrile viral infection, characterized by fever, cough, coryza, conjunctivitis, and a specific enanthem (Koplik spots) followed by a generalized maculopapular eruption. [5]

2- Etiology and Transmission

Measles is caused by a paramyxovirus in the morbillivirus genus and family Paramyxoviridae. It is an enveloped, single-stranded, non-segmented, negative-sense RNA virus. It is genetically stable and it has only one serotype [5].

The measles virus has no animal reservoir and occurs only in humans. The virus is highly contagious, with each case capable of causing 14 to 18 secondary cases among susceptible populations. It is transmitted from person to person by respiratory droplets, small particles aerosols, and close contact from 4 days prior to the onset of rash to 4 days after the rash erupts. [6]

3- Physiopathology [7]

Measles is a systemic infection. In susceptible persons during incubation period, measles virus enters the lymphoid tissue of the pharynx and reproduces locally. After 2 to 3 days, a brief primary viremia occurs and disseminates the virus to reticuloendothelial system infecting mononuclear and macrophage cells.

After 5-7 days, a secondary viremia occurs, spreading the virus throughout the body and leading to the characteristic prodromal fever and cough. It is associated with epithelial necrosis and giant cell formation in body tissues. Cells are killed by cell-to-cell plasma membrane fusion associated with viral replication in many body tissues including central nervous system.

After additional 2 to 4 days, the characteristic rash occurs, marking the development of an effective immune response so that viral replication and symptoms begin to subside.

In severe measles, there is marked inflammation of the skin with hemorrhage into the dermis and dark staining of rash. The larynx is frequently oedematous, causing hoarse voice and some degree of respiratory obstruction.

4- Risk Factors for severity and death from measles [3]

- Malnutrition
- Vitamin A deficiency
- Immune deficiency.

III. Signs and symptoms [5,7]

1- **Incubation**: 8 to 12 days.

2- **Prodrome:** High fever, Koplik spots (pathognomonic sign of measles, appearing 1 to 4 days prior to the onset of the rash) and characteristic 3C's symptoms (cough, coryza and conjunctivitis).

3- **Rash:** It begins around the forehead (around the hairline), behind the ears, and on the upper neck as a red maculo-papular eruption. It then spreads downward to the torso and extremities, reaching the palms and soles in up to 50% of cases. The exanthem frequently becomes confluent on the face and upper trunk.

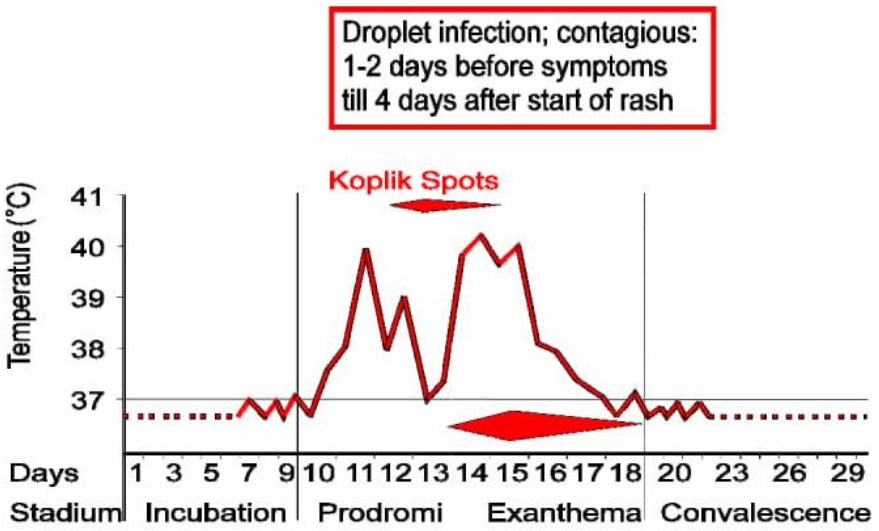
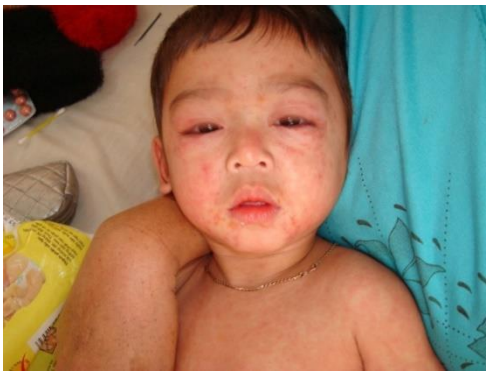
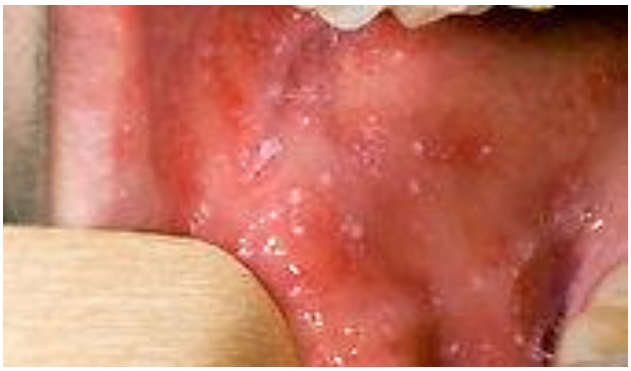


Figure 4. *Grades of fever in different clinical phases of measles (Ref. Prof. Yay Chantana, Measles, Clinical Practice Guidelines for Ped. 2013)* [5]



Facial Exanthem [Courtesy of JV7 H]



Koplik's Spots [Courtesy of JV7 Hospital]

IV. Diagnosis

The diagnosis of measles is almost always based on clinical and epidemiological findings.

1- **Laboratory** [5]

- Leucopenia
- Serology: IgM positive, IgG positive (a fourfold rise)
- In the current clinical practice, polymerase chain reaction (PCR) detection of viral ribonucleic acid from throat, nasal, nasopharyngeal, and urine sample is most often performed, with sensitivity approximately 100%.

2- **Differential diagnosis**

Measles is differentiated from those exanthematous diseases based on the past history of infectious disease and immunization's status, type of prodromal period, features of the rash, presence of pathognomonic or other diagnostic signs, and laboratory diagnostic tests.

- ***Rubella:*** The symptoms are often mild with low grade fever, arthralgia, occipital lymphadenopathy, upper respiratory symptoms preceding maculopapular rashes on the face, then progress from head to foot. The rash is fainter than measles' rash and does not coalesce. It lasts about 3 days. The diagnosis is confirmed by detection of rubella virus by PCR in nasal, throat, blood and CSF's samples or significant rise in rubella specific IgG or presence of IgM from paired acute and convalescent sera. [8]
- ***Parvovirus B19 infection*** (Erythema infectiosum or the fifth disease): The most common rash is red rash on the face, called "slapped cheek". It appears few days after initial symptoms such as fever, headache, cough, sore throat and joints pain. The patient may have second rash few days later on chest, back, buttock or arm or legs [9].
- ***Roseola Infantum:*** Abrupt onset of high fever lasting about 2 days in previously healthy infant, then defervesce with mild pink generalized and subtle maculo-papular rashes. It is caused by human herpes virus 6,7 (HHV 6,7) in genus of beta herpes virus hominis [10]
- ***Enterovirus infection***: Hand-foot-and-mouth disease with prodrome of fever, cough, sore throat, malaise lasting from 12-36 hours, then maculo-papular or vesicular eruption of hands, feet, and oral cavity develop. [11]
- ***Scarlet fever***: It is caused by group A beta-hemolytic streptococci. The syndrome characterized by sudden onset of fever, sore throat and bright-red exanthema edematous. The tonsils are exudative red associated with heavily coated tongue with a white membrane with edematous red papillae (classic appearance of white strawberry tongue). The characteristic rash appears 12-48 hours after the onset of fever, first on the neck and then extending to the trunk and extremities and last 4 to 5 days. [12]
- ***Kawasaki disease***: It is acute febrile vasculitis syndrome of early childhood. It is presented with prolonged fever (at least 5 days), rash, conjunctival injection, cervical lymphadenopathy, inflammation of lips and oral cavity, strawberry tongue and erythema and edema of hands and feet, desquamation of fingers and toes [13].

V. Complications [5]

- Pneumonia is the most common cause of death in measles. It may manifest as giant cell pneumonia caused directly by the viral infection or as superimposed bacterial infection. The most common bacterial pathogens are S. pneumoniae, H. influenzae, and S. aureus.
- Worsening of the nutritional state of the child because of anorexia, stomatitis, vomiting, diarrhea, fever and other complications.
- Obstructive laryngitis and laryngo-tracheitis
- Acute encephalomyelitis, subacute measles encephalitis and subacute sclerosing pan-encephalitis.
- Reactivation of tuberculosis
- Xerophthalmia and keratomalacia.

VI. Treatment

There is currently no specific antiviral therapy for measles infection.

1- Supportive Care [5]

- Nursing care of eyes and mouths
- Adequate fluid intake: oral rehydration solution, serum perfusion for diarrhea.
- Adequate nutrition, encourage the continuation of breast feeding if possible.
- Control of temperature: Paracetamol, Ibuprofen or tepid sponging for fever.
- Oxygen therapy, airway humidification in respiratory tract involvement and intubation with ventilation for respiratory failure.
- Antibiotic for bacterial complication (i.e. for pneumonia complication, please see clinical practice guideline of treatment of community acquired pneumonia).
- Advise the mother against harmful dietary practices such as fasting, drinking toad's blood.

2- Vitamin A supplementation [7]

The WHO recommends the administration of Vitamin A supplementation to all children with acute measles or within 3 months after measles infection:

- Infant < 6 months of age: Vitamin A 50 000 IU on 1st and 2nd days.
- Infant 6 – 11 months of age: Vitamin A 100 000 IU on 1st and 2nd days.
- Children over 12 months of age: Vitamin A 200 000 IU on 1st and 2nd days.
  If there are signs of xerophthalmia, another dose (3rd dose) of vitamin A is given on 14th day.

VII. Prevention and education [6,14]

According to National Immunization Program for Cambodia, MR (Measles and Rubella) vaccines in the current vaccination schedule recommended for children are the 1st dose on 9th month of age and the 2nd dose on 18th month of age. The vaccine is a live attenuated measles strain.

Measles is a vaccine-preventable infection. To eliminate measles, vaccination rates of the population must be in the 93% to 95% range. So, the people should be more educated about the importance of vaccination, should be informed that the adverse effects of the measles vaccination are rare and minor; without vaccination, there is a high risk of transmitting the infection to others and inducing serious complications.

Moreover, epidemiological surveillance for patients presenting with fever and rashes along with laboratory diagnosis, are crucial tools for early case identification to control transmission through isolation of susceptible contacts. Better treatment of measles cases to include vitamin A supplements, antibiotics if needed, and supportive care that prevent complications should be done.

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VARICELLA (CHICKENPOX)

SAR Bunthong, KHUN Leangchhun, YAY Chantana, HENG Sothy

I. Key Facts

- Varicella or Chickenpox is an acute infectious and contagious disease caused by the Varicella-Zoster Virus (VZV). [1]
- Primary varicella is endemic to all countries worldwide. [1]
- More than 90% of people become infected before adolescence. Its highest prevalence is in the 4 to 10-year-old age group. In tropical countries, varicella often occurs in older age group. [1,2]
- Most cases occur during the cool, dry season. [2]
- Varicella is considered a mild disease in general. In healthy children, the prognosis is excellent. However, immunocompromised or immunosuppressed individuals, the infection has high morbidity and mortality. [1]

II. Overview

1. Definition

Varicella is a highly contagious disease that spreads through coughing or sneezing of ill individuals or through direct contact with secretions from the rash. Varicella is an itchy, blister-like skin rash, caused by Varicella-zoster virus (VZV).

Varicella-zoster virus (VZV) is an alpha-herpes virus. Its infection causes 2 clinically distinct forms of disease:

- Primary VZV infection results in Varicella, or Chickenpox.
- Endogenous reactivation of latent VZV typically results in Herpes zoster, or Shingles. [3]

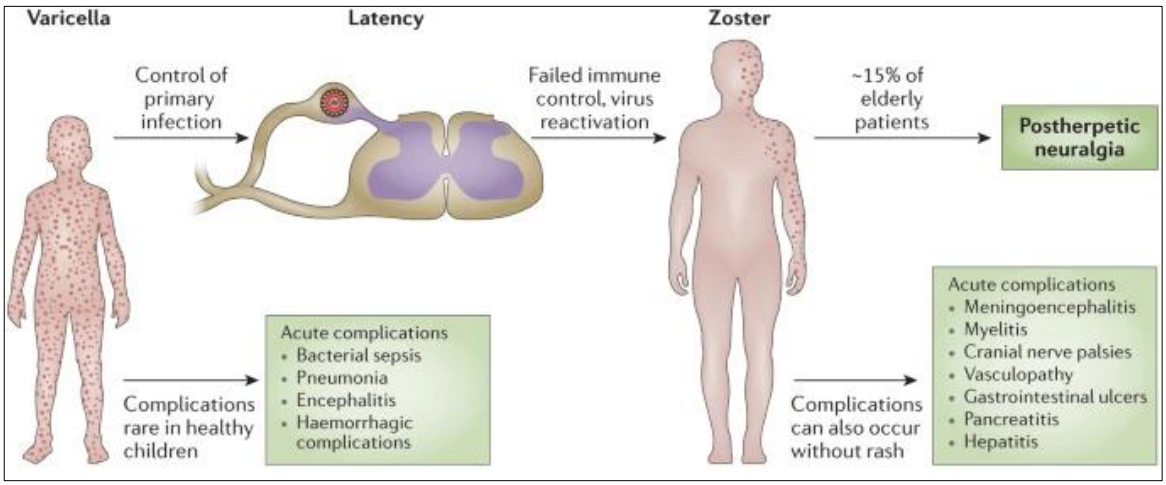


Figure 5. *Phases of VZV infection*

2. Transmission

Transmission occurs in susceptible hosts via contact with aerosolized droplets from nasopharyngeal secretions of an infected individual or by direct cutaneous contact with vesicle fluid from skin lesions.

The average incubation period for varicella infection is 14 to 16 days. [3]

III. Signs and symptoms

1. Prodrome

The early symptoms typically include fever (38 to 41°C), malaise, nausea, aching muscle, headache, or pharyngitis, loss of appetite. These early symptoms may occur 24 to 48h before the rash appears and persist during the first 2 to 4 days after the onset of the rash. [4]

2. Skin lesion:

The lesions begin as red macules on the face, scalp, torso, upper arms, and legs (also may occur on the palms, soles, and genital area). They rapidly become papules followed by characteristic **vesicles** and **pustules**. The vesicular rash of varicella, which is usually pruritic, appears in successive crops over several days.

The patient with varicella typically has lesions in different stages of development. New vesicle formation generally stops within 4 days, and most lesions have fully crusted by day 6 in normal hosts. **Crusts** tend to fall off within about 1 to 2 weeks and leave a temporary area of hypopigmentation on the skin from several days to several weeks. [4]

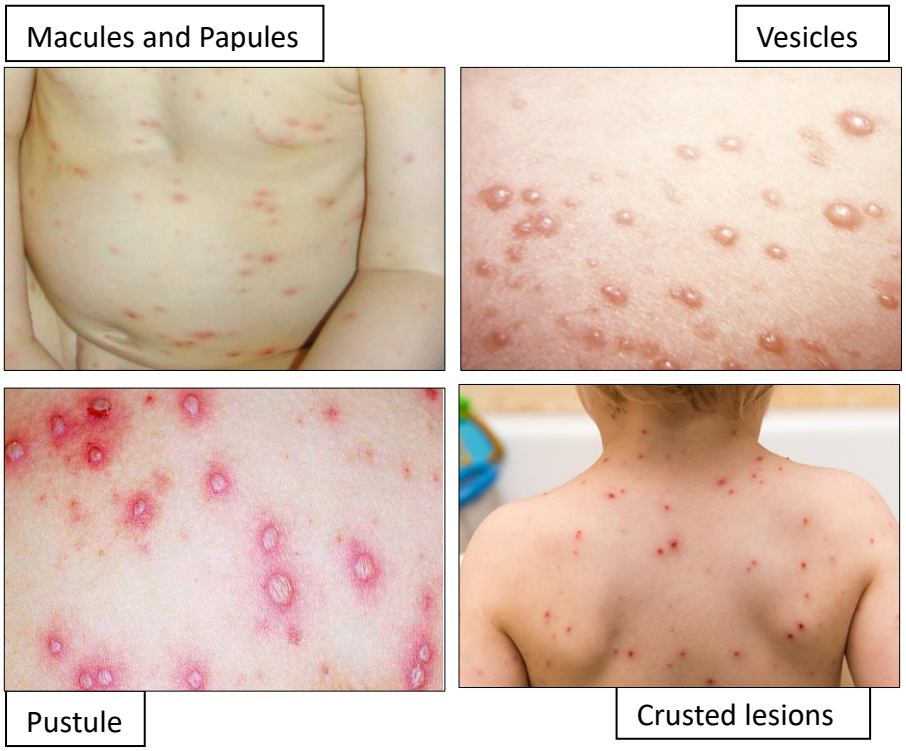


Figure 6. *Varicella lesion skin lesion in various stages*

IV. Diagnosis

1. The diagnosis of varicella is usually a **clinical diagnostic** based on the characteristic vesicular lesions. However, real-time PCR and ELISA methods of the fluids within the vesicles may be useful in the case of atypical rash [5].
2. **Other clinical forms**
   a. Immunocompromised or immunosuppressed hosts

      Disseminated varicella occurs in patients with a history of underlying malignancy, steroid use or immunosuppressive therapy, HIV infection, or solid organ

transplantation. Clinical manifestation includes ongoing development of crops of vesicles over weeks, large and hemorrhagic skin lesions, pneumonia, or widespread disease with disseminated intravascular coagulation.

b. Varicella in newborn baby

Congenital varicella syndrome is caused by vertical transmission from the mother during pregnancy. It occurs in infants whose mothers are infected between 8 weeks and 20 weeks of gestation. Clinical manifestations vary and include cicatricial skin lesions, red and inflamed skin, ocular defects (cataracts), low-birth-weight, microcephaly, abnormalities of the limb and central nervous system.

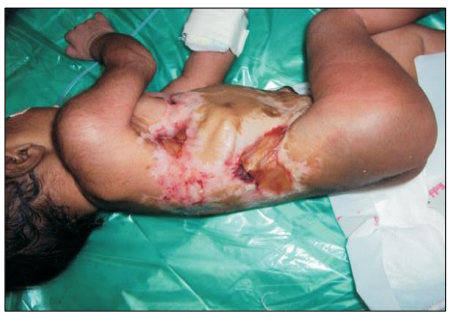
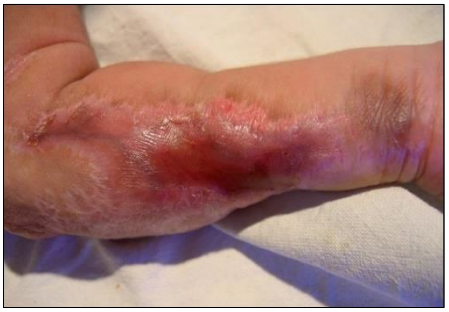


Figure 7. *Congenital varicella syndrome*



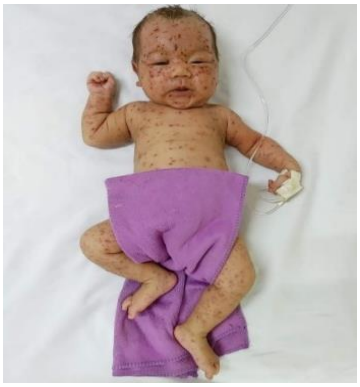


Figure 8. *Neonatal varicella*

c. Neonatal varicella is caused by transmission during delivery (trans-placentally as a result of maternal viremia) or after birth from the environment or infected care providers. [5, 9] Infants whose mothers demonstrate varicella in the period from 5 days prior to delivery to 2 days afterward are at high risk for severe varicella. [9]

Breastfeeding is not contraindicated in infants exposed to or infected with varicella. [10]

3. Differential diagnosis

- Coxsackievirus infection or hand-foot-mouth disease: fever, blisters on palm, sole and throat. [6]
- Mpox (Monkeypox): high grade fever, chills, muscle ache, sore throat, swollen lymph node. The mpox rash begins on the face and spreads over the body, extending to the palms of the hands and soles of the feet and evolves over 2 to 4 weeks in stages – macules, papules, vesicles, pustules then crusts. [7]
-

V. Complications

- Skin and soft tissue super-infections by group A streptococcus have included cellulitis, myositis, necrotizing fasciitis, and toxic shock syndrome.
- Neurologic complications can occur such as encephalitis which includes acute cerebellar ataxia or diffuse encephalitis.
- Reye syndrome caused by Aspirin (Salicylates) administration. It typically presents with nausea, vomiting, headache, excitability, delirium with frequent progression to coma.
- Pneumonia typically develops insidiously within 1 to 6 days after the rash [4].

- Complications are more common in premature neonates and neonates exposed before 7 days of age, unimmunized adolescents and immuno-compromised children. [8]

VI. Treatment

1. Supportive care

- Antihistamines are helpful for the symptomatic treatment of pruritus.
- Daily cleansing with warm water will help avoid secondary bacterial infection.
- Oral Paracetamol (40 to 60mg/kg/day divided in 4 doses) can be used to treat fever. [8, 11]

2. Antiviral therapy

Antiviral administration for 7 to 10 days is recommended in severe disseminated varicella, in immunocompromised host or in neonatal varicella.

- Oral Acyclovir: 20 mg/kg per dose (maximal dose 800 mg) four times daily.
- IV Acyclovir (Children ≥1 year and adolescents): 1500 mg/m^2 per day in three divided doses or 30mg/kg/day in three divided doses. [11]
- For newborns with severe disseminated VZV infection (e.g. pneumonia, encephalitis, thrombocytopenia, severe hepatitis), IV Acyclovir (30 to 60 mg/kg per day in three divided doses) is recommended [10].

VII. Prevention and education

1. Vaccination

- US CDC recommends 2 doses of varicella (chickenpox) vaccine for children, adolescents, and adults to protect against varicella. Children are routinely recommended to receive the first dose at age 12 through 15 months and the second dose at age 4 through 6 years old. [12, 13]
- Varicella vaccination is not included in the national immunization program in Cambodia.

2. Education

- As a protective measure, those infected are usually required to stay at home while they are infectious. [11]
- Children must be excluded from school/kindergarten/childcare until all lesions crusted over. [8]
- Keeping nails short and wearing gloves may prevent scratching and reduce the risk of secondary infections.
- Avoids using traditional medicine or treatment (bathing with tree leaves).
- Hospitalized patients with primary varicella should be isolated, placed on standard, contact, and airborne precautions to prevent the spread of infection to others.

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PERTUSSIS

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I. Key Facts

- Pertussis, commonly known as whooping cough, is a respiratory tract infection characterized by a paroxysmal cough. It first was identified in the 16th century.
- The incidence is greatest in infants younger than one year, who are at the greatest risk of morbidity and mortality. [1-6]
- The annual worldwide incidence of pertussis is estimated to be 48.5 million cases, with a mortality rate of nearly 295,000 deaths per year. [7]
- The case-fatality rate is high among infants in low-income countries. [8]
- Humans are the only hosts of B. pertussis; the risk of transmission is greatest during the catarrhal stage.
- The best way to prevent pertussis infection is to get the pertussis vaccine.
- The pertussis vaccine does not contain live bacteria and cannot give you the infection.

II. Overview

1. Definition

- Pertussis is a classic "whooping cough" syndrome of prolonged paroxysmal coughing.
- It is a serious respiratory tract infection caused by a bacterium gram-negative called Bordetella pertussis.

2. Etiology

Pertussis is caused by the gram-negative coccobacillus B. pertussis, a strict human pathogen with no known animal or environmental reservoir.

The organism can survive only a few hours in respiratory secretions.

3. Physiopathology

- Pertussis spreads quickly and easily through air droplets from coughing, sneezing, or speaking.
- After inhalation, the organism adheres to ciliated respiratory epithelial cells of the upper respiratory tract and nasopharynx.
- Once attached, they induce local tissue damage via tracheal cytotoxin, dermonecrotic toxin or pertussis toxin, this destructive process, with loss of the protective respiratory cells, is likely responsible for the cough.
- The long incubation period from 1 to 3 weeks but is most typically 7 to 10 days reflects the time necessary for B. pertussis to increase in numbers needed for progressive spread of infection in the respiratory tract and to produce enough toxin for eliciting damage and dysfunction of the respiratory epithelium.

4. Risk Factors

- Epidemic exposure
- Non vaccination in children
- Contact with an infected person
- Malnutrition or immune deficiency.

III. Signs and symptoms

- Classic pertussis: “The cough of 100 days” (up to date 2023)
- Symptomatic infection with B. pertussis is characterized by three phases:
- The catarrhal phase (1-2 weeks)
- The paroxysmal phase (2-4 weeks or longer) and
- The convalescent phase, as detailed below.
- 3 clinical phases:
    - Catarrhal phase:
        - is the earliest phase of illness and highly contagious.’

- it's nonspecific symptoms with URI (upper respiratory infection) including rhinorrhea, mild cough, nasal congestion and low grade fever.
- Paroxysmal phase:
  - characterized by paroxysmal cough with increased severity and frequency producing the characteristic whooping cough.
  - apnea, seizure, cyanosis, posttussive vomiting, or syncope can also occur.
- Convalescent phase:
  - is characterized by a gradual reduction in the frequency and severity of cough.
  - patients in the stage have chronic cough, which may last for weeks.

- Pertussis infection in infants maybe particularly severe, with increase rate of hospitalization.

IV. Diagnosis

- Pertussis is a clinical diagnosis.
- According to the Centers for Disease Control and Prevention (CDC) case definition, probable pertussis can be diagnosed without laboratory testing. [1]
  - an acute cough illness of ≥2 weeks and at least one of the following pertussis associated symptoms:
    - Paroxysms of coughing
    - Inspiratory whoop
    - Post tussive vomiting
    - Apnea, with or without cyanosis
  - an acute cough illness of any duration, with at least one of the above pertussis associated symptoms, and contact with a laboratory-confirmed.

1. Laboratory:

- Laboratory Findings

  CBC (completed blood count): The predominant nonspecific laboratory indication of B. Pertussis infection is a Leukocytosis resulting from lymphocytosis is commonly observed at the end of the catarrhal stage and throughout the paroxysmal stage of illness, although this phenomenon is more common in infants and children than adolescents. (Pertussis toxin stimulated T cell more increase production)
- Laboratory confirmation
  - When indicated, laboratory testing should be performed as soon as the diagnosis of pertussis is considered. B. pertussis is more difficult to grow/identify from specimens obtained during or after the paroxysmal stage and after antibiotic therapy has been initiated.
  - Microbiologic studies that can confirm the diagnosis of pertussis include bacterial culture, PCR, and serology.
- Culture of nasopharyngeal secretion:
  - Specificity 100%; sensitivity is 20 to 80%.
  - Traditional reference standard for diagnosis.
  - Sensitivity depends on duration of symptoms and decreases after two weeks of illness or antibiotics exposure.
  - Results available in 3 to 7days and not available in all laboratories.
- Polymerase chain reaction of nasopharyngeal secretions (PCR):
  - Specificity 88 to 98%; Sensitivity 61 to 94%.
  - More sensitive than culture and
  - Sensitivity decreases after three weeks of illness.
- Serology (ELISA) blood if possible: excellent sensitivity and specificity when the acute serum is collected early in the course of illness (2 weeks after cough onset).

2. **Chest radiography**

In uncomplicated pertussis, chest radiographs may be normal or demonstrate subtle abnormalities, such as perihilar infiltrates, or atelectasis, but these findings are nonspecific.

3. **Differential diagnosis**

- Bronchiolitis
- Bacterial pneumonia
- Other B. species such as B. para pertussis.
- Cystic fibrosis
- Tuberculosis
- Viral pathogens: RSV, adenovirus, Parainfluenza virus…

V. Complications

- The complications of pertussis are more likely to occur in infants <6 months of age.
- The most common complication of pertussis infection includes:
  - Apnea
  - Pneumonia or atelectasis
  - Weight loses secondary to feeding difficulties due to post tussive vomiting.
  - Seizures and encephalopathy
  - Death is rarely.

VI. Treatment

1. **General Measures:**

- Admission Criteria: [10, 11]
  - <Age 6months with concern for apnea
  - Apnea, cyanosis or seizures
  - Inability to feed due to prolonged cough.
  - Evidence of pneumonia.
  - Respiratory distress, manifested by tachypnea, retractions, nasal flaring, grunting, and the use of accessory muscles
- Discharge Criteria:
  - No evidence with cardio-respiratory failure or
  - Ability to tolerate coughing episodes without becoming hypoxic and/or bradycardic; most infants who are admitted to the hospital with pertussis continue to have coughing many weeks after discharge.
  - Ability to eat enough to gain weight
  - Reliable caretakers who are comfortable caring for the child at home.
- Supportive care:
  - Oxygen if necessary.
  - Paracetamol if fever >38 (10-15mg/kg/dose q6h)
  - Fluids and nutrition
  - Isolation: > 5days after use antibiotic
  - Anti-tussive: we do not suggest symptomatic therapies for pertussis-related cough. In small trials and a systematic review, symptomatic treatments, including bronchodilators, corticosteroids, antihistamines, and antitussive agents, have not been proven to be beneficial in patients with pertussis. (Known triggers for coughing paroxysms: exercise, cold temperatures, nasopharyngeal gastric tube should be avoided if possible.

2. **Antibiotics** (Term: ACE)

When administered early in the course (within seven days of symptom onset), antimicrobial therapy for pertussis may shorten the duration of symptoms and decrease transmission to susceptible contacts.

- Treatment is particularly important for infants <6 months because they are at increased risk for complications.
  - Azithromycin: (is the treatment of choice)
    - < 6 months of age: 10 mg/kg/day single dose for 5 days.
    - > 6 months of age: 10 mg/kg/day as a single dose on day 1 (maximum: 500 mg), then 5 mg/kg/day as a single dose on days 2–5 (maximum: 250 mg)
    - Adolescents and adults: 500 mg/day as a single dose on day 1, then 250 mg/day as a single dose on days 2–5.
  - Clarithromycin: 15 mg/kg/day twice per day for 7 days (maximum: 500mg twice daily).
  - Erythromycin: 40 mg/kg per day in 4 divided doses for 14 days (maximum: 2 g per day)
- In case allergic with macrolide: Bactrim (Trimethoprim/sulfamethoxazole)
  - Dose: TMP 8 mg/kg per day, SMX 40 mg/kg per day in 2 divided doses for 14 days.
  - Maximum dose: TMP 320 mg, SMX 1600 mg per day.
  - Contraindication: children aged <2 months. (The potential risk of kernicterus related to bilirubin displacement or bilirubin-induced neurological damage)

VII. Prevention and education

- Pertussis vaccines are given combined with diphtheria and tetanus DTP at ages 6, 10, and 14 weeks.
- Avoid close contact with sick people.
- Make sure to wash your hands frequently and practice good hygiene.
- Routine vaccination against pertussis following the national vaccination program is the best way.

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MUMPS

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I. Key Facts

- Mumps is a contagious viral illness attacked to parotid glands caused by a paramyxovirus.
- Humans are the only known host for the mumps virus.
- It occurs worldwide; the peak incidence is typically in the late winter to early spring. [(1)]
- Before the United States mumps vaccination program began in 1967, about 186,000 cases were reported each year.
- Since implementation of routine vaccination, there has been a more than 99 percent decrease; The number of cases reported in 2016 and 2017: 6369 and 5629.
- It most commonly affects young children. Orchitis is a potentially serious complication which may lead to infertility.
- Cases report at Jayavarman 7 hospital a fully year in 2023: 329 cases and 392 cases from 1/January until August/2024.

II. Overview

1. Definition

- Mumps is an acute viral disease characterized by painful enlargement of the parotid's glands.
- It's typically starts with a fever, headache, myalgia, fatigue, and anorexia, then leads to swelling of glands.

2. Etiology

- Mumps is caused by the RNA virus, Rubulavirus in the paramyxovirus family. This virus contains a single-stranded, negative-sense RNA surrounded by a glycoprotein envelope.
- Bacterial cases are usually secondary to staphylococcus aureus (suppurative parotitis).

3. Risk factors

- Epidemic exposure
- Contact with and infected person
- Individuals weakened immune systems or
- Unvaccinated.

4. Physiopathology

- The mumps virus replicates in the upper respiratory tract and is transmitted person to person through direct contact with saliva or respiratory droplets of a person infected with mumps from mouth, nose, or throat.
- Viral shedding in respiratory secretions precedes the onset of symptomatic illness. The incubation period is usually 16 to 18 days (range 12 to 25 days) from exposure to onset of symptoms. [4-5]
- Mumps enters the body and first infects the epithelial cells of the nasopharynx, where it starts replicating and causing local damage to the tissue.
- Then, the viremia spreads to many organs, including the salivary glands, gonads, pancreas, and meninges.

III. Clinical Features

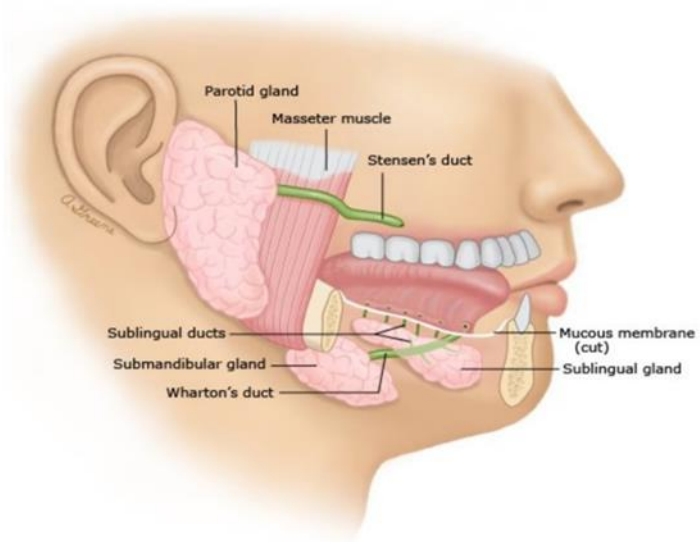
1. Signs and Symptoms

- Mumps typically begins with a few days of fever, headache, myalgia, fatigue, and anorexia; these manifestations are usually followed by development of salivary gland swelling within 48 hours.
- Parotitis occurs most commonly among children between two and nine years of age; Occasionally associated with earache, typically precedes parotid swelling. (6-7)
- Parotitis may be unilateral or bilateral. (3)
- Parotid swelling can last up to 10 days.
- Dysphagia and dysphonia are common.
- Testicular pain and swelling, usually begin 1 week after the parotid swelling of mumps.
- Behavior changes, seizures, and other neurologic abnormalities are rare.

2. Physical Exam

- Parotid glands rapidly progress to maximum swelling over several days.
- The ear is often displaced upward and outward.
- Submaxillary and sublingual glands also may be swollen.
- The opening submandibular duct (also known as Wharton duct) may be erythematous and edematous.
- Inflammation may be noted intraorally at the orifice of Stensen duct and can be enlarged, edematous, and swollen.
- Tender, edematous testicle in mumps orchitis. (usually unilateral)
- Some patients have nonspecific symptoms and may not present for clinical evaluation.
- Asymptomatic infection occurs in 15 to 20 percent of cases. (up-to-date).

Figure 1. Anatomy of the salivary glands and ducts



The three major salivary glands are the parotid, submandibular, and sublingual glands. Stensen's duct drains the parotid gland opposite the upper second molar. Wharton's duct drains the submandibular and some of the sublingual glands into the floor of the mouth near the frenulum of the tongue.

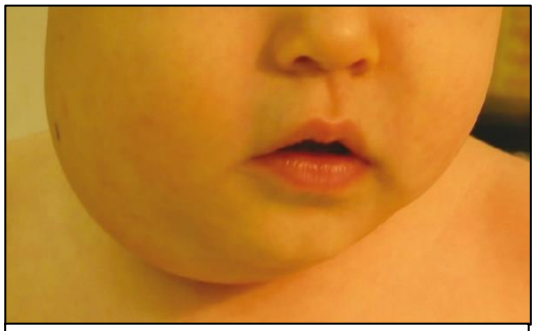


Figure 2. *Parotid gland swelling in a young child. There is swelling of the parotid anterior and inferior to the auricle, obscuring the angle of the mandible.*

3. **Laboratory:**

a. Laboratory finding

- Uncomplicated parotitis: Mild leukopenia with lymphocytosis
- Suppurative parotitis is commonly with leukocytosis secondary by staphylococcus aureus.
- Pancreatic involvement: Hyperamylasemia and elevated serum lipase.
- Lumbar puncture if meningitis is suspected: CSF pleocytosis (predominately mononuclear)

b. Laboratory confirmation

Two diagnostic specimens should be collected if possible.

- Detection of mumps virus RNA by reverse-transcriptase polymerase chain reaction (RT-PCR; performed on serum or oral swab; the same specimen may also be used for virus culture). Oral swab specimen should be obtained as soon as possible after onset of parotitis. (ideally within three days and not more than eight days after parotitis onset).
- Positive serum mumps immunoglobulin IgM antibody (typically remains positive for up to four weeks. [8]
    - The IgM response may not be detectable until five days after symptom onset in some cases.
    - Serum mumps IgM testing should be collected 5 to 10 days after symptom onset.

4. **Imaging**

- Ultrasonography of the parotid glands showed: enlargement of the gland, multiples hypoechognic nodules, increased vascularity on power Doppler.
- Scrotal ultrasonography must be performed when orchitis is clinically suspected.
- If concern exists for meningitis or encephalitis, head MRI should be considered, prior to lumbar puncture procedure to obtain CSF. (cerebrospinal fluid).

IV. Diagnosis

1. **Patients with typical manifestations:**

The diagnosis of mumps should be suspected in patients with typical clinical manifestations and relevant epidemiologic exposure (respiratory or household contact with an individual with known or suspected mumps). (1)

2. **Patients with neurologic involvement:**

- Mumps meningitis or encephalitis should be suspected in patients with relevant clinical manifestations
- Fever, headache, and nuchal rigidity suggest meningitis.
- Fever and altered consciousness suggest encephalitis.

❖ **Differential diagnosis**

- Other viral causes of parotitis include influenza A virus, parainfluenza, adenovirus, coxsackievirus, Epstein-Barr virus (EBV), cytomegalovirus, herpes simplex virus, human immunodeficiency virus (HIV).
- Suppurative parotitis (bacterial, especially Staphylococcus aureus).
- Tumors, hemangiomas, lymphangiomas of the parotid gland.
- Adenitis (cervical lymphadenitis)

- Epididymoorchitis: other viral causes of orchitis include rubella, coxsacki.e. echovirus, parvovirus or sometimes due to bacteria sexually transmitted likes chlamydia and gonorrhea.
- Allergic reactions rare.

Complications and prognostic

1. **Possible complications (luckily very rare)**

- Orchitis (inflammation of testicles) or Oophoritis (swollen ovaries) and sterility.
- Meningitis: is the most common neurologic complication of mumps virus infection. (1%-10%).
- Encephalitis: rarely causes permanent sequelae.
- Facial nerve palsy
- Deafness
- Less common complications occasionally associated with mumps infection include thyroiditis, myocardial involvement, pancreatitis, interstitial nephritis, and arthritis.

2. **Prognosis**: mumps infection is usually good and recover fully within 2 weeks.

V. Treatment

- There is no specific antiviral therapy for treatment of mumps.
- Uncomplicated mumps usually complete recovery in 1 to 2 weeks is the rule.
- Management consists of supportive care: [9]
  - Use of an analgesic/antipyretic agent such as acetaminophen.
  - Parotid discomfort may be managed by application of warm or cold packs.
  - Orchitis may be managed with nonsteroidal anti-inflammatory agents, support of the inflamed testis, and cold packs.
  - Antibiotics against bacteria should be used in cases of suppurative parotitis.
  - Bed rest/Fluids.

VI. Prevention and education [10]

- Hospitalized patients with mumps should be isolated with droplet precautions until the parotid swelling has resolved.
- Outpatients with mumps should avoid contact with others from the time of diagnosis until at least five days after the onset of symptoms, by staying home from school or work and staying in a separate room.
- Wash hands regularly and encourage children cough or sneeze into their elbows.
- Vaccination:
  - A single 0.5-mL subcutaneous injection of live mumps vaccine (usually given together with measles and rubella, the MMR) at 12 to 15 months. A second vaccination is recommended between 4 and 6 years of age.
  - Vaccine should not be administered to children who are immunocompromised by disease or pharmacotherapy, or to pregnant women.
  - Children with HIV infection who are not severely immunocompromised should be immunized with the MMR vaccine.
  - But this mumps vaccine is not yet available in Cambodian National Immunization Program.

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RICKETTSIA DISEASES

TE Haypheng, KDAN Yuvathana, EANG Kim-Ean

I. Key Facts

- Rickettsial infection is a group of diseases and is caused by intracellular bacteria Rickettsiae of family Rickettsiaceae, and divided into the group typhus, Spotted Fever, and scrub typhus.
- The rickettsial disease is widespread worldwide, and different regions are having different Rickettsiae epidemics that are based on vector habitants.
- In Cambodia, the most common subgroup of Rickettsiae Family that caused disease were Scrub typhus and murine typhus.
- Rickettsia disease is commonly caused by undifferentiated febrile illness with a wide range of disease presentations.
- Eschar lesion should be not used only to determinate diagnosis and is usually not presented in lice or flea rickettsial born disease.
- Case mortality is certainly prevented by clinical suspect and empirical treatment.

II. Overview

1. Definition

Rickettsia disease is a zoonosis that is caused by the intracellular bacteria Rickettsiae. This organism is a gram-negative bacillus and is classified as an important arthropod disease which is carried and transmitted from the bite of ticks, mite, lice, or fleas. The rickettsia diseases could be from a species of a group of the family Rickettsiaceae. [1]

2. Epidemiology

The distributions of Rickettsiae species are worldwide, but different regions are differently species habitant. The disease is caused from the family Rickettsiaceae which can be divided into three groups: typhus group rickettsiae (TGR), spotted fever group rickettsiae (SFGR) and scrub typhus group orientiae (STGO). In South-East Asia, scrub typhus and murine typhus are the highest prevalence, but and the cases from SFGRs group were also scatter reported.[2]

In Cambodia children, Scrub typhus and murine typhus were significant note among rickettsia infection in the seroprevalence study. The Seropositivity of scrub typhus (ST) and murine typhus (MT) among undifferentiated febrile illness was estimated at 4.2% and 5.3% of total admission cases, and the peak age was 8–11 years and 12–15 years, respectively. Anyway, all age groups from 0-15 year in Cambodia were also used to exposure, and there was no gender difference. [3]

3. Causative agents

Generally, Rickettsia infection is a collective term that consists of many diseases from different species of family Rickettsiaceae. This bacterial is carried by vector (tick, mite, lice or flea) and transmit vie a bite wound or mucous membranes. The type of rickettsia infection relies on specific rickettsia that is inoculation. Spotted fever biogroups is a lice or tick-borne disease that cause Rocky Mountain spotted fever (RMSF) by Rickettsia rickettsia, Rickettsial-pox by Rickettsia akari etc. Typhus group is a lice or flea born disease and causative organisms is Rickettsia prowazekii or Rickettsia typhi which significant disease of murine typhus. Last but not least, Scrub typhus biogroup is mite born infection and is from a single taxonomic name: Orientia tsutsugamushi which are divided again into 3 major serotypes: Karp, Gilliam, and Kato. [1]

4. Risk factors and Mortality

The risk factors of rickettsial infection are also statistically related to residence, occupation, and yearly season. 1271/1832 (69.4%) confirmed case in Vietnam are people who are living in rural area, and farming is the occupation risk of Scrub Typhus (58.5%).

This could be related to living or working activity in the farm and vector habitant.

The mortality rate of rickettsial infection is 1.1%, but untreated scrub typhus is higher with 6% (range from 0-70%). [2]

III. Signs and symptoms

Many literatures support and suggest Rickettsial diseases are difficult to diagnose although expertise physician. These infections are defined as acute undifferentiable febrile illness sometimes, it needs physicians frequently to be aware of these illness as severe forms can lead to multiple organ failures and deaths if the treatment is delayed.

A part of the signs and symptoms of rickettsial infection could be variable based on rickettsial species, but generally the illnesses by these organisms may have similar manifestations and treatment. [1]

The common symptoms and signs of Rickettsial infection among 484 confirmed cases are: [2]

- Fever (100%)
- Headache (92.7%)
- Eschar (66.5%)
- Myalgia (54%)
- Cough (46.3%)
- Lymphadenopathy (44.7%)
- Conjunctivitis (36%)
- Nausea (31%)
- Sore throat (25.7%)
- Rash (25.7%)
- Retro-orbital pain (22.9%)
- Others: diarrhea, abdominal pain, Others: hepatosplenomegaly, subcutaneous Hemorrhage.

❖ **Note**: Eschar is a painless and bite lesion of tick or mite, so flea or lice rickettsial borne diseases usually doesn't have. Early eschar can look like vesicle or plaque, then developed into centra ulcer (0.5-3cm). The healing lesion are brown black crust, and usually it takes several weeks to completely healing. The eschar is frequently found at folding skin area (perineum, groin and axilla), but head or other sites should also be not missed [3]. Importantly, the prevalence of presented eschar is widely variable from 7 to 90% from observed cases. [2]

The severe form of rickettsial infection especially like scrub typhus is frequently caused child condition worsening and lead to multiple organ failures and death. According to the etiology cause of acute meningoencephalitis among children from 1 month to 15 years, Orientia Tsutsugamushi shared 55 cases amount total 513 case in Kantha Bopha hospitals. [4]

IV. Diagnosis

The definitive diagnosis of rickettsial infections are generally challenges, thus clinical diagnosis is often used to determine the case and treat to prevent serious complications. The difficulty of finding positive diagnosis is related unspecified signs and symptoms of Rickettsial, huge diversity of rickettsial species and rickettsial diseases, similar presentations with other illness, or lack of diagnostic methods in hospital practices. Anyway, the clues of suspect cases are (1) a history of vector exposure, (2) recent travel or living in endemic areas, and (3) similar illness in family members or coworkers. [1]

1. Investigation

a. Standard diagnostic:
Rickettsial infection could be laboratory diagnosis with serology test [IFA, fourfold increasing titer], molecular test by PCR, or biopsy on eschar lesion and the pathological hallmark is a lympho-histiocytic vasculitis.

b. Culture: as intracellular bacteria generally need tissue culture, thus is generally non-practical in hospital setting.

c. General Blood test:
Generally, most basic blood tests such as CBC count, CRP, or others are considered non-specific tests. Anyway, among observed case showed leukocyte count is usually normal,

low platelet count (51.3%), increasing ALT count >40IU/L (86.4%), slightly elevating bilirubin, and hypoalbuminemia.

2. **Differential diagnosis:**
   - Measles,
   - meningococcemia,
   - secondary syphilis,
   - viral infections
   - dengue infectious mononucleosis,
   - enteroviral infection etc. [1]

V. Complications

- Venous thrombosis
- Pneumonitis
- Pericarditis, myocarditis, heart failure
- Severe disease occurs more commonly in patients with G6PD deficiency, cardiac insufficiency, or immunocompromise. [1]

VI. Treatment

1. **Antibiotic therapy**

a. Any suspect case, Empirical treatment should be initiated:

- Drug of Choice: Doxycycline IV/PO 2.2 mg/kg/dose twice daily, maximum dose: 100mg/day, duration is minimum 5-7 days and is up to 14 days for severe cases.
- Alternative choice: Erythromycin (30-50 mg/kg/day PO divided t.i.d or q.i.d) trimethoprim-sulfamethoxazole (8-12 mg TMP/kg/day PO divided b.i.d. [1]
  - ❖ *Note:* Majority of case is afebrile less than 72 hours after treatment. [2]

b. Supportive therapies

- Airway, Breathing, and Circulation resuscitations in case of emergency condition
- Fluid resuscitation or Intravenous fluid supporting in case of severe cases
- Antipyretic in case of fever

VII. Prevention

- No vaccine currently is available
- Avoid going to endemic area or Clothing to cover the entire body should be worn in tick-infested areas or use insecticide spraying
- Control of rats, ticks, mites and fleas: individual and collective protection with insecticides.

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MELIOIDOSIS

TEN Raksmey, NY Theary, CHRUN chhunny, IV Malene, KHUN leangchhun, YAY chantana

I. Key Facts

- **Melioidosis** is an under-recognized fatal infectious disease in human caused by *Burkholderia pseudomallei*. This pathogen is inherently resistant to many first-line antibiotics and carries a high mortality rate up to 40% case fatality rate in untreated patients.
- Melioidosis is endemic in tropical countries such as Southeast Asia and Northern Australia, India, Taiwan, and China. The first few cases of melioidosis were reported from Myanmar in 1911. As of 19 July 2020, more than 35, 000 human cases in more than 50 countries were reported globally. The estimated incidence rate varies from country to country; 19.6 per 100, 000 person-years in Australia and 12.7 per 100, 000 person-years in Thailand.
- Retrospective data from 2018 Malaysian National Surveillance of Antimicrobial Resistance (NSAR) in 47 isolates of which 27 were pediatric patients less than 15 years old showed that 36 isolates or 76.6% were from blood, and 11 isolates or 23.4% from pus/wound. Upon antimicrobial susceptibility testing, all isolates were found to be sensitive to Amoxicillin/clavulanic acid, Ceftazidime, Imipenem and Trimethoprim/Sulfamethoxazole but none was sensitive to Gentamicin and Amikacin. The study showed that melioidosis in children often caused a septicemic form of infection
- In Cambodia, few microbiologically confirmed cases have been described based on first national Melioidosis in Cambodia at Pastor Institute, National Pediatric Hospital, Kantha Bopha Hospital, Jayavarman VII Children Hospital, Angkor Hospital for Children, Kg. Cham and Takeo Referral Hospitals.
- In Jayavarman VII Hospital from 1st January 2022 to 31st august 2023, there were 205 hospitalized children having confirmed with Melioidosis of which 48 or 23% were isolated from blood and 157 or 77% were isolated from pus (localized melioidosis). There were totally 12 deaths or 25% among bacteremia patients or 5.85% among total Melioidosis cases. Antibiogram from blood culture showed that the bacteria was sensible 100% to Augmentin, Ofloxacin and Chloramphenicol and 73% to Cefuroxime but only 10% to Bactrim, and antibiogram from pus culture showed that the germ was sensible 100% to Ceftriaxone, 99% to both Augmentin and Ofloxacin, 98% to Chloramphenicol, 65% to Cefuroxime but only 9% to Bactrim.

II. Overview

1. Etiology

Melioidosis is caused by a Gram -negative, facultative, intracellular bacterium *Burkholderia pseudomallei*, formerly known as *Pseudomonas pseudomallei,* in the family Burkholderiaceae, found in soil (natural reservoir) and water.

2. Transmission

- Animals and humans usually acquire melioidosis from organisms in the environment. B. Pseudomallei is saprophytic bacterium that is widespread in soil and muddy water in endemic areas. The majority of the human cases were identified during the rainy season.
- Infection can occur mainly by contact with contaminated soil and water through penetrating wounds or skin abrasions, and ulcers or burns, by ingestion, or by inhalation. All three routes are thought to occur in animals. Infected animals can shed the organisms in wound exudates and, depending on the site of the infection, from other sources including nasal secretions, breast milk, feces, and urine.
- Transplacental transmission has been reported in goats, a pig and a spider monkey.

- Nosocomial transmission was reported in four cats at a veterinary hospital, possibly via contamination of a multidose injectable solution.
- Vector-borne transmission by mosquitoes (Aedes aegypti) and rat fleas (Xenopsylla cheopsis) has been reported, but the role of insect bites remains uncertain.
- There have been a few reports of zoonotic transmission, often after contamination of the lesions by exposure to infected animals, tissues including meat, milk. However, most people become infected directly from the environment. Inoculation through skin is thought to be the major route of transmission to humans. Inhalation, which usually leads to pulmonary form of the disease, may be particularly important during periods of heavy rainfall and strong winds. The importance of ingestion is controversial.
- Person-to-person transmission has been described rarely, generally to family members in close contact. (e.g. family members who nursed patients).
- Sexual transmission has also been suggested in some cases. Vertical transmission has rarely been proven, but a few cases have been described in newborns. One infant may have been infected by nursing culture-positive breast milk.
- In non-endemic areas, contamination of the environment from infected animals or humans is a concern. Shed organisms can survive for months or years in soil and water. In one report, B. pseudomallei remained viable in triple distilled water for more than 3 years. This experiment is ongoing, and unpublished reports suggest that the organism is still present 14 years later.
- Other laboratories have reported that B. pseudomallei can survive in room temperature water for as long as 8 weeks, in muddy water for up to 7 months, and in soil for up to 30 months.
- This organism can also survive in some antiseptic and detergent solutions, and resists pH 4.5 for up to 70 days.

3. Risk Factors

The single most important risk factor for developing severe melioidosis is diabetes mellitus. The forest plot generated from six studies showed that patients with diabetes were 3 times more likely to develop melioidosis than patients with no diabetes. It could be associated with the defective innate immunity of diabetic patients and poor glycemic control. The other risk factors are hemoglobinopathies (e.g. Thalassemia), cancer, chronic renal diseases, chronic lungs diseases (e.g. Cystic Fibrosis), excessive alcohol ingestion, Occupation (rice paddy farmers) and patients with an immune deficiency of any kind.

4. Physiopathology

Melioidosis is an infectious disease caused by *B. pseudomallei* (formerly Pseudomonas pseudomallei). The organism is distributed widely in the soil and water of the tropics. It is spread to humans through direct contact with a contaminated source, especially during the rainy season. The disease usually occurs in the fourth and fifth decades of life, especially among those who have chronic comorbidities such as diabetes mellitus, alcoholism, immunosuppression, and renal failure. *B. pseudomallei* is considered a good candidate as a bioweapon because it is easily available in the tropics, fairly easy to cultivate, sturdy and it has a high potential to become bacteremic, thereby increasing morbidity and mortality. The incubation period in naturally acquired infections can vary from days to months to years. The incubation period after an aerosol attack is expected to be from 10-14 days.

a. Localized Form: Bacteria enter the skin through a laceration or abrasion, and a local infection with ulceration develops. The incubation period is 1-5 days. Swollen lymph glands may develop. Bacteria that enter the host through mucous membranes can cause increased mucus production in the affected areas.

b. **Pulmonary Form:** When bacteria are aerosolized and enter the respiratory tract via inhalation or hematogenous spread, pulmonary infections may develop. Pneumonia, pulmonary abscesses, and pleural effusions can occur. The incubation period is 10-14 days. With inhalational melioidosis, cutaneous abscesses may develop and take months to appear.

c. **Septicemia:** Bacteremia is observed with chronically ill patients (e.g., patients with HIV, patients with diabetes mellitus. They develop respiratory distress, headache, fever, diarrhea, pus-filled lesions on the skin, and abscesses throughout the body. Septicemia may be overwhelming, with a 90% fatality rate and death occurring within 24-48 hours.

d. **Chronic Form:** The chronic form involves multiple abscesses, which may affect the liver, spleen, skin, or muscles. It can become reactive many years after the primary infection.

III. Signs and symptoms

Most infections are asymptomatic. Acute infection, lasting less than 2 months, is the most common. Chronic infection has symptoms persisting longer than 2 months.

1. **Incubation period**

The incubation period for acute infection is 1 to 21 days (mean 9 days). However, the period can be very short (< 24 hours in near drowning) or up to many years (30 years) later (for latent reactivation).

2. **Acute Melioidosis** (85% of cases)

a. Acute Pulmonary Infection:

- It is the most affected organ (55%).
- It is presented with fever, headache, cough, dull aching chest pain, tachypnea, respiratory distress, crackle rales, purulent sputum, hemoptysis.
- With or without shock (fulminant septic shock with mortality rate of 84% in Darwin study).
- Pleural effusions have generally been uncommon in acute melioidosis but effusions and empyema can still occur, especially with lower lobe disease.
- There may also be multiples abscesses in abdominal organs.
- Chest radiography often has diffusely nodular infiltrates throughout both lungs, which coalesce, cavitate and progress rapidly, consistent with the caseous necrosis and multiple metastatic abscesses seen at autopsy.

b. Focal Infection:

- Hematogenous seeding and abscess formation can occur in any organ. Liver, spleen, skeletal muscle, prostate, and kidney are the most common abscess sites.
- Less common presentations of melioidosis include uncomplicated infections of the skin, subcutaneous tissues, or the eye. Corneal ulcerations resulting from trauma, which become secondarily infected with B. pseudomallei, are rapidly destructive.
- Septic arthritis and osteomyelitis have also been described, but cellulitis appears to be rare. In a prospective study of more than 2000 patients in Thailand, primary meningitis or endocarditis was not observed, but meningitis secondary to cerebral abscess rupture and mycotic aneurysms was seen.
- Other unusual melioidosis presentations include mediastinal masses, pericardial fluid collections and adrenal abscesses.
- In Thailand 30 % of the melioidosis cases in children present as acute suppurative parotitis.
- In Australia, approximately 4% of melioidosis cases in northern Australia present as brain stem encephalitis or encephalomyelitis with peripheral motor weakness or

flaccid paralysis or flaccid paraparesis. Features of the presentation include limb weakness, cerebellar signs, and cranial nerve palsies. Patients with this syndrome usually have an initial normal state of consciousness. Multiple focal B. pseudomallei micro-abscesses in the brain stem and spinal cord probably cause this syndrome.

c. Septicemia

- Patients with the acute septic form of melioidosis present characteristically with a short history of fever and no clinical evidence of focal infection. Most patients are profoundly ill with signs of sepsis. Septic shock may appear on presentation.
- Acute onset with high, tachypnea, myalgia, hepato-splenomegaly
- Markers of organ dysfunction, including leukopenia (particularly lymphopenia), hepatic dysfunction (raised aspartate aminotransferase, alanine aminotransferase, and bilirubin levels), renal dysfunction (raised urea and creatinine levels), and metabolic derangements (hyperglycemia and acidosis).
- Mortality: 90% without treatment and 50% with treatment

3. Chronic Melioidosis

- Chronic melioidosis is usually defined by symptoms lasting greater than 2 months and occurs in approximately 10% of patients.
- The clinical presentation of chronic melioidosis, presented as chronic skin infection, skin ulcers, and lungs nodules or chronic pneumonia, closely mimicking tuberculosis, sometimes being called “Vietnamese tuberculosis”.
- Chronic melioidosis can mimic tuberculous pericarditis.

IV. Diagnosis

1. Laboratory

Prompt diagnosis and treatment are critical. Guided by clinical syndrome, specimens from all relevant infection sites such as blood, cerebrospinal fluid, urine, sputum, throat or rectal swab, or skin lesions are collected for culture. The diagnosis is confirmed by growing *B. peusomallei* from the specimen. Detecting and measuring antibodies to the bacteria in the blood is another mean of diagnosis. There is also a serological test for melioidosis (indirect hemagglutination), but this is not commercially available in most countries.

2. Imaging: X-ray, Sonography, CT scan, MRI

Other diagnostic tools that may be useful in melioidosis are radiological tests such as **chest X-ray** for the diagnosis of pulmonary melioidosis, **computerized tomography (CT) scans** and **MRI** used to diagnose abscesses in the liver and spleen.

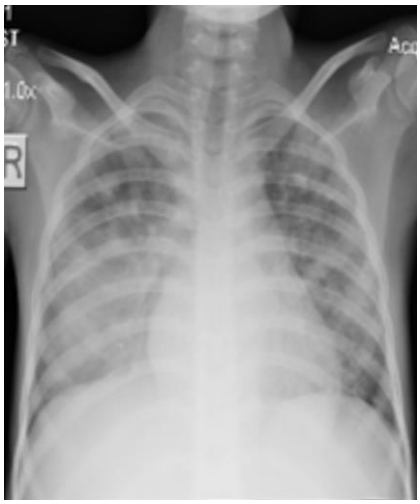

Figure 10. *Chest X-ray showed Severe Pneumonia in diabetes mellitus type1 patient having sepsis by P. pseudomallei*

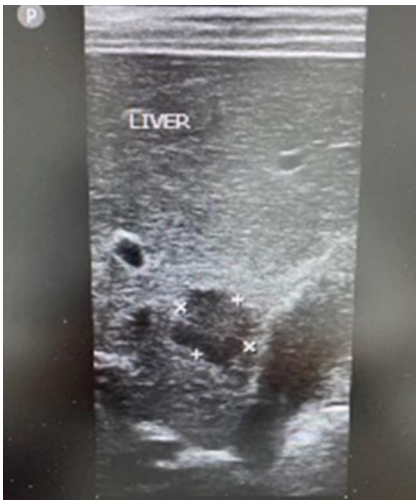

Figure 10. *Echography showed liver abscess in diabetes mellitus type1 patient having sepsis by P. pseudomallei*

3. Differential diagnosis

- Acute lungs symptoms - other causes of community acquired pneumonia such as E. Coli, Stahphylococcus Aureus, E. Coli, Klebsiella Pneumoniae.
- Chronic lung symptoms – TB (especially those with AFB smear negative sputum, those with previously treated TB), or other infections.
- Sepsis – other common causes of sepsis (E. coli, E. Coli, Stahphylococcus Aureus, Klebsiella Pneumonia, Salmonella Typhi/Paratyphi etc.)
- Deep abscesses – abscesses by Staphylococcus aureus, Klebsiella pneumoniae, TB, amoebic abscess,
- Lymphadenopathy – TB (especially those who may have previously been unsuccessfully treated with anti-tuberculous drugs)
- Skin abscesses – S. aureus, other infections
- Chronic skin ulcers/wounds unresponsive to commonly prescribed antibiotics
- Septic arthritis/osteomyelitis – S. aureus, TB.

V. Complications

Melioidosis can present in a variety of ways. Some of the more unusual types of infections are pericarditis, septic arthritis, necrotizing fasciitis, osteomyelitis, skin ulcers, body organs abscesses, bacterial pneumonia, septicemia, meningitis.

VI. Treatment

1. Current treatment

a. Initial intensive Phase

- Parenteral **Ceftazidime** and **Meropenem** are the choice of antibiotics to treat melioidosis. and the duration of treatment for intensive therapy was recommended to be at least 14 days. The minimum treatment durations for melioidosis with central nervous system infections, osteomyelitis, and deep-seated abscess were 8, 6, 4 weeks, respectively.
- Ceftazidime: 50mg/kg/dose IV every 6 - 8h for 2 – 4 weeks, max. 8g/d, or
- Meropenem: 25mg/kg, max. 1g IV every 8h for 2 – 4 weeks for septic shock, or for CNS infection, double dose is recommended (50 mg/kg/dose up to maximum of 2g IV q8) and de-escalate to Ceftazidime after improvement.
- Don't change treatment if the fever continues (median time for fever clearance is 9 days)
- Consider adding Co-trimoxazole (TMP-SMX) to intensive phase for deep tissue infection or patient's condition worsening despite drainage of pus (and isolate shows susceptibility to ceftazidime) or wanting to ensure no side effects to Co-trimoxazole prior to discharge on oral medications.

b. Eradication Phase

After at least 14 days IV therapy and clinical improvement, change to oral Cotrimoxazole or Co-amoxiclav for at least 3 months (12 weeks). Osteomyelitis and CNS infection require 6 months' treatment. Folic acid is also recommended when prescribing Co-trimoxazole.

- Trimethoprim-Sulfamethoxazole: 6/30 mg/kg/dose PO, max. TMP-SMX single strength 80mg/400mg 3t BID PO or double strength 160mg/800mg 1.5t BID PO + Folic acid 0.1mg/kg, max. 5mg PO for 12 – 20 weeks, or
- Augmentin (Amoxicillin/Clavulanic acid): 20mg/5mg/kg/dose, max. 2t for < 60kg and 3t for > 60kg every 8h PO for 12- 20 weeks.

c. Surgical treatment

Surgical drainage is usually indicated for prostatic abscesses and septic arthritis, may be indicated for parotid abscesses and not usually indicated for hepato-splenic abscesses. In bacteremia melioidosis unresponsive to intravenous antibiotic therapy, splenectomy has been attempted, but there is only anecdotal evidence to support this practice.

VII. Prevention and education

- B. Pseudomallei is widely distributed in soil and standing water in endemic regions.
- People with diabetes mellitus or other predisposing condition should take special precaution to avoid skin contact with these sources.
- Better glycemia control in diabetes mellitus patients might reduce the morbidity of melioidosis.
- In addition, gloves and rubber boots are recommended for anyone doing agricultural work.
- cleansed.
- A few outbreaks have been linked to contaminated drinking water supplies. Although small numbers of organisms may survive, chlorination of the water supply the risk of infection. Because B. Pseudomallei can be found in milk from infected ruminants, only pasteurized dairy products should be consumed.
- Veterinarians should take precautions to avoid exposure by using gloves and protective clothing when working with infected animals or collecting diagnostic samples. People who process meat should also wear gloves and disinfect knives regularly.
- In endemic areas, infected carcasses intended for human consumption are condemned and destroyed.
- Laboratory workers may be exposed in clinical samples from patients, even where melioidosis in not endemic.
- Practices such as sniffing opened culture plates should be discouraged. Post-exposure prophylaxis may be given after laboratory exposure to aerosols or contact with skin wounds or to people with risk factor for septicemia.
- In hospitals, ordinary precautions to prevent transmission in blood and body fluids should be taken. No vaccine is available.
- Early treatment with appropriate antibiotics after its detection is crucial in improving patient outcomes and minimizing the severity.
- More research works are needed to design and evaluate both pharmaceutical and behavior change interventions.

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SYSTEMIC FUNGAL INFECTION IN CHILDREN

SUY Keang, MILIYA Thyl, Ardura-Garcia CRISTINA, Turner PAUL

I. Key Facts

An increase in invasive fungal disease (IFD) in children has been observed over the last few decades owing to the growing number of immunocompromised children at risk for IFD. [1]

Incidence of IFD varies greatly between centres due to differences in geographic locations, number of risk factors and availability of care.[2]

Despite advance in diagnosis and treatment, invasive fungal infection remains a major cause of morbidity and mortality especially in patients with immunocompromised conditions such as preterm neonates, malignancy, HIV and immunosuppressive therapy.[2]

The overall in-hospital case fatality rate is 36% in low- and middle-income countries and 17% in high- income countries.[2,3]

Reversal of immune condition (i.e. stop immune suppressive therapy if possible), timely diagnosis and initiation of appropriate treatment are crucial to reduce mortality.

II. Overview

There are a large number of fungi capable of infecting humans. This guideline will focus only on the most common causes of invasive fungal infection in children and/or those with a high case fatality rate with geographic relatedness.

All patients with suspected or confirmed invasive fungal diseases should be discussed with infectious disease/clinical microbiologist as soon as possible.

1. Definition

IFD are defined as systemic infections resulting from the establishment of yeasts or moulds in blood or deep-seated tissues.[4]

In contrast to superficial fungal infections, IFDs are severe conditions with high rates of morbidity and mortality.

2. Causes

a. IFD can be caused by a multitude of fungi. The most common causes include:[1,3,4]

- Candida species, Aspergillus species, Cryptococcus species, Pneumocystis species
- Other mounds of clinically relevant include: Mucorales species

b. Invasive Candidiasis

- Beyond neonatal period, immunosuppressed and critically ill patients are at risk for invasive candidiasis with incidence rates varying from 0.261 to 14.1 episodes per 1000 PICU admissions.2,9
- Causes by Several Candida species have been found to cause infection in humans: Albicans: most common *C. parapsilosis, C. tropicalis, C. glabrata, C. auris:* an emerging multidrug resistant Candida species with potential to cause outbreaks. [6]

III. Sign and symptoms

- Clinical presentation of invasive candidiasis is often nonspecific.
- Invasive candidiasis should be suspected in patients with risk factors and unexplained fever or signs of sepsis despite adequate antibiotics.
- Investigations
  - Blood culture
  - Fungal culture and microscopic examination of appropriate liquid and solid specimens as mandated by clinical findings.[10]
  - Ophthalmological examination, cardiac and abdominal ultrasound or CT scan to look for deep seated infections.[10, 13]

IV. Treatment [10]

Antifungal therapy should be tailored according to susceptibility result when available and clinical status of the patients.

If present, central line or urinary catheter should be removed as soon as possible.

1. **Empirical antifungal:**
   - First line: Echinocandin (caspofungin or micafungin)
   - Second line: Amphotericin B (Amphotericin B deoxycholate is the first line treatment for neonate group)

     ❖ **Note:**

     Fluconazole should be used for targeted treatment if sensitive or as empirical treatment in places where fluconazole resistant candida is low.

     For patients with confirmed fungemia, antifungal therapy should be continued for 2 weeks after the last negative blood culture and recovery of neutropenia.

2. **Invasive Aspergillosis**

Invasive Aspergillosis (IA) is the second most common IFD after *Candida species* but with higher mortality.[2]

a. Causes: Several *Aspergillus species* have been found to cause infection in humans: *A. fumigatus* is the most common cause, *A. flavus, A. terreus, A. nidulans, and A. niger.*

b. Risk factors

Patients at high risk of developing IA include:

- De novo or recurrent leukaemia (AML or ALL)
- Bone marrow failures with profound neutropenia (i.e. aplastic anaemia
- Allogeneic Haemato Stem Cell Transplant (HSCT)

c. Transmission

- Inhalation of the fungal spores from the environment.
- Direct inoculation, such as via intravenous catheter sites, can also occur but is less common.
- There is no human-to-human transmission.8

d. Signs and symptoms:

IA usually involves:

- Pulmonary,
- Sinus,
- Cerebral or
- Cutaneous sites
- Rarely, other sites can be involved resulting in endocarditis, osteomyelitis, meningitis, or peritonitis.

  The hallmark of IA is angioinvasion with resulting thrombosis, dissemination to other organs and occasionally erosion of the blood vessel wall with catastrophic bleeding.8

e. Investigation: [10, 13]

- Galactomannan level in blood, BAL and CSF
- Fungal culture and microscopy of the deep-seated tissue including bronchoalveolar lavage (BAL)
- Blood culture rarely yields positive result in IA except in catheter-related infections.
- PCR-based diagnostic should not be used due to poor sensitivity and specificity profile.
- CT scan of the chest in children at high risk presenting with persistent fever and prolong neutropenia beyond 96 h or those with focal clinical findings.
- For patients with proven pulmonary Aspergillosis, a brain MRI should be done to look for CNS involvement regardless of neurological signs.

f. Treatment:[10, 13]

- Voriconazole: for children age 2 years and older. OR
- Amphotericin B: for children under 2 years or if voriconazole is unavailable.

Duration: minimum 6 weeks, longer for patients with prolonged and severe immunosuppression.

g. Prevention

- Reversal of underlying conditions
- Antifungal prophylaxis in recommended in high-risk populations:
  - Profound and prolonged neutropenia
  - Acute myeloid leurkemia
  - Recurrent acute lymphoblastic leukemia

3. Cryptococcosis

a. Causes: Cryptococcosis is usually caused by *Cryptococcus neoformans* and less commonly *C. gattii*.

b. Risk factors: [11]

- Untreated HIV,
- Hematologic malignancy,
- Immunosuppressive therapy,
- Solid organ or stem cell transplant recipient,
- Antibody deficiency,
- End stage liver or renal disease,
- Idiopathic CD4 lymphocytopenia.

c. Transmission

Inhalation of the spores or yeast into the lung is the reason for primary pulmonary infection while central nervous system infection occurs via hematogenous spread.[8]

d. Signs and symptoms

Depend on the organ affected including:

- Meningitis: suspected in children with untreated/noncompliant HIV presenting with meningeal signs,
- Isolated pulmonary disease or
- Disseminated disease.

e. Investigations:

- Lumbar puncture for CSF cell counts, culture and India ink or cryptococcal antigen for meningitis
- Cryptococcal antigen (CrAg) detection method or culture of body fluid or tissue specimens.
- BAL specimen culture to confirm pulmonary cryptococcal infection.

f. Treatment: [12]

Treatment consists of three stages: induction, consolidation, and maintenance.

- Induction**:**
  - First line: Single high dose (10mg/kg) of liposomal amphotericin B with 14 days of flucytosine and fluconazole (12mg/kg per day)
  - Second line: if first line not available: 14 days of amphotericin B deoxycholate (1mg/kg/day) and fluconazole (12mg/kg/day)
- Consolidation**:**
  Fluconazole 6-12mg/kg/day (max 800mg daily) for 8 weeks following induction phase.
- Maintenance**:**
  Fluconazole 6mg/kg/day until immune reconstitution (CD4 >200cell/mm^3).

g. Prevention:

- Early diagnosis and initiation of antiretroviral therapy
- Fluconazole for patients with advanced HIV disease

4. Pneumocystosis[11]

a. Causes: Pneumocystosis or pneumocystis pneumonia is caused by the fungus *Pneumocystis jirovecii.*

b. Risk factors:

- Low CD4 < 200 cells/mm3 for any reason
- Exposure to medication: chemotherapy, anti-inflammatory or immunosuppressive treatment associated with T-cell dysfunction
- Use of therapeutic dose of ≥ 0.3mg/kg prednisolone equivalent for ≥2 weeks in the past 60 days
- Solid organ transplant

c. Signs and symptoms

- Low grade fever
- Respiratory symptoms with cough, dyspnoea, and hypoxemia

d. Investigations:

- Chest radiographs often show bilateral diffuse interstitial or alveolar disease but can be normal in early disease.
- PCR on respiratory specimen (BAL, sputum or oral wash specimen)

e. Treatment:[14]

- Trimethoprim-sulfamethoxazole: 15mg/kg/day (trimethoprim component) in 3 or 4 divided doses for 21 days.
- Steroid for patient with hypoxemia (SpO2 <92% room air).

Table1. *Dose of oral prednisolone*

Age	Days 1-5	Days 6-10	Days 11-21
< 13 years	1mg/kg/dose, twice daily	0.5mg/kg/dose, twice daily	0.5mg/kg/dose daily
≥ 13 years	40mg, twice daily	40mg daily	20 mg daily

❖ Note: maximum doses should not exceed the dose for children older than 13 years

f. Prevention:

- Reversal of the underlying condition
- Cotrimoxazole is recommended in high-risk populations where underlying predisposing factors cannot be reversed.

5. Mucormycosis (previously called Zygomycosis)[16]

a. Causes: *Mucor species, Rhizopus species, Lichtheimia species, Cunninghamella species Apophysomyces elegans*, …

b. Risk factors

- Hematologic malignancy
- Haematopoietic stem cell or solid organ transplant
- Iron overload, deferoxamine therapy
- Burn or traumatic wounds
- Autoimmune disorders
- Prematurity

c. Sign and symptoms

Mucormycosis in children can be presented as

- Rhinoorbitalcerebral
- Pulmonary
- Cutaneous
- Gastrointestinal, or
- Disseminated disease

d. Investigations

- Histopathology of appropriate clinical samples
- Fungal culture of infected tissue

- Molecular testing such as nucleic acid amplifications may be used

e. Treatment:
Early and aggressive surgical debridement with antifungal therapy are the mainstays of treatment and Amphotericin B

f. Prevention:

- Prevention or reversal of the underlying conditions
- Antifungal prophylaxis is not recommended

Table2. *Antifungal drugs for systemic fungal infection*[10,15]

Drugs	Dose	Spectrum of activity
Fluconazole	12mg/kg once daily	Active against yeasts only
Voriconazole (Approved for children > 2 years)	For 2-14 y and < 50kg - 9mg/kg on day 1 then 8mg/kg twice daily For > 15 y or > 50kg - 6mg/kg on day 1 then 4mg/kg twice daily	Active against yeasts and moulds Therapeutic drug monitoring is recommended
Caspofungin (Approved for children > 3m)	70mg/m^2 BSA loading on day1 then 50mg/m^2 once daily thereafter Maximum 70 mg/dose	Active against *Candida and Aspergillus species*
Micafungin	- For children ≤30kg: 3mg/kg once daily, - For children ≥30kg: 2.5mg/kg once daily Maximum 150mg/day - For neonates: 10mg/kg once daily	Active against *Candida and Aspergillus species*
Amphotericin B (Liposomal) Preferred for all patients except neonate due to less toxicities.	3-5mg/kg once daily	Active against yeasts and moulds
Amphotericin B (deoxycholate)	1-1.5mg/kg once daily	**Note:** Amphotericin B deoxycholate is known for its high rate of toxicities including hypokalaemia, anemia, renal toxicities and anaphylaxis. - Premedication* and prolong infusion up to 4 hours are recommended to minimize adverse effects - Better penetration into the central nervous system, urinary tract and eye, thus recommended for infection involving these sites

**Pre-medications are given 30-60mn before amphotericin B deoxycholate infusion:*

- Paracetamol 15mg/kg 1 dose
- Chlorpheniramine 0.15mg/kg 1 dose
- Normal saline 10ml/kg infusion for 1 hour
- Hydrocortisone may be used if above medications do not control reaction
  Monitor kidney function and potassium level frequently and regularly while the patient is receiving amphotericin B deoxycholate.

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LIFE THREATENING SKIN AND SOFT TISSUE INFECTIONS IN CHILDREN

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I. Key Facts [1]

Skin and soft tissue infections (SSTIs) are prevalent in children.

The incidence of SSTIs is rising among children. Methicillin-resistant *Staphylococcus aureus* (MRSA) emerged in the 1990s and its prevalence is rising worldwide, becoming the leading cause of purulent SSTIs in certain locations, such as the US.

SSTIs can also present atypically and more severely in immunocompromised children.

II. Overview

SSTIs are typically easy to identify and manage with few complications. However, conditions like myositis, pyomyositis, and necrotizing fasciitis can be challenging to diagnose early, and even with appropriate antibiotics, may lead to significant morbidity and mortality. This guideline will focus on severe SSTIs requiring hospitalisation or extended management such as surgery. It will also include life-threatening conditions associated to frequent SSTIs pathogens, such as toxin-mediated manifestations.

A. Myositis

1. **Definition:** Inflammation of a muscle (usually voluntary one). It produces swelling, pain, tenderness on movement or palpation and weakness[1].
2. **Etiology[1]:** Infectious causes include bacteria, fungi, parasites and virus[2, 3] (see Table 1). Other causes include: drug-mediated, electrolyte imbalance, and autoimmune, genetic or endocrine disorders.

- Bacterial *myositis* is a diffuse infection of the muscle without an intramuscular abscess. It is rarer in children than adults. Usually causes focal muscle infection which may be acute, subacute or chronic. *S. aureus* is uncommon, though incidence is increasing. *S. pyogenes* (Gr. A *Streptococcus*, GAS) may evolve rapidly within hours, with the most severe presentation being necrotizing myositis. Myonecrosis (gas gangrene) may be caused by *Clostridium* spp. (*C. perfringens* the most common), and also by anaerobic streptococci, GAS and *S. aureus*. Polymicrobial (anaerobic and Gram-negative bacteria) myonecrosis may occur following extension of a subcutaneous tissue infection to the muscle, secondary to penetrating trauma. The most lethal pathogen is *Vibrio vulnificus* with a 10% mortality[4].
- Fungal myositis: Uncommon. Candida spp. as most common (especially C. tropicalis).
- Parasitic myositis: Not the focus of this guideline.
- Viral myositis: Multiple viruses may cause diffuse myositis, more common in children <14 years old. Most common are Influenza A and B.

3. **Risk factors[1-3]**

- Bacterial myositis: Muscular injury, surgery, ischaemia or foreign body.
  - GAS: Mostly spontaneous with no previous injury, may occur after GAS pharyngitis.
  - Clostridium spp.: Traumatic wounds with soil contamination, bowel or biliary system surgery, unhygienic injections.
  - Aeromonas hydrophila and Vibrio vulnificus: Traumatic wounds in freshwater environment or in contact with aquatic animals (salt water for V. vulnificus).
- Fungal myositis: Immunosuppression.

Table 1: *Common Infectious Causes Myositis*

Organism group	Organism
Gram-positive bacteria	Staphylococcus aureus
	Streptococcus pyogenes (group A Streptococcus)
	Streptococcus (groups B, C, and G; S. pneumoniae; S. anginosus)
Gram-negative bacteria	Aeromonas hydrophila
	Citrobacter freundii
	Enterobacter spp.
	Escherichia coli
	Proteus spp.
	Pseudomonas spp.
	Salmonella spp.
	Vibrio vulnificus
Anaerobic bacteria	Bacteroides spp.
	Clostridium spp.
	Streptococcus spp. (anaerobic, e.g., Peptostreptococcus)
Mycobacteria	Mycobacterium tuberculosis
Fungi	Candida spp.
Viruses	Enteroviruses (coxsackievirus B and echovirus)
	Human immunodeficiency virus (HIV)
	Human T-lymphotropic virus type 1(HTLV-1)
	Influenza A and B viruses

**Modified from Crum-Cianflone NF. Bacterial, fungal, parasitic, and viral myositis. Clin Microbiol Rev. 2008;21:473–94[2].*

B. <u>Pyomyositis</u>

1. **Definition:** Acute intramuscular infection of skeletal muscle through hematogenous spread of a microorganism. Affects mainly large-muscle groups and may result in localized abscess formation.
2. **Etiology[1]:** Most prevalent in tropical areas[5] and more common in children than adults and in males[1]. *S. aureus* is the causative bacteria in most cases (90%), with MRSA prevalence depending on location. GAS in 1-5% of cases, other bacteria include other streptococci, *E. coli, Citrobacter freundii, Serratia marcescens, Yersinia enterocolitica, Klebsiella* spp., and *Salmonella* spp.
3. **Risk factors:** Primary varicella rash or minor skin lesions for GAS pyomyositis[6].

C. <u>Necrotizing fasciitis</u>

1. **Definition1:** A rapidly progressive bacterial infection of the subcutaneous soft tissue.
2. **Etiology** and **risk factors** and clinical manifestations: summarised in Table 2. In neonates**,** it may follow omphalitis or circumcision. The association between non-

steroidal anti-inflammatory use for primary varicella and necrotizing fasciitis has not been proven.[7, 8]

Table 2: *Aetiology, risk factors and clinical manifestations of different necrotizing fasciitis types*

Type	Bacteria	Risk factors	Clinical Manifestations
Meleney synergistic gangrene	*S. aureus,* micro-aerophilic streptococci	Surgery	Slowly expanding ulceration confined to superficial fascia
Clostridial cellulitis	*Clostridium perfringens*	Local trauma or surgery	Gas in skin, fascial sparing, little systemic toxicity
Nonclostridial anaerobic cellulitis	Mixed aerobes and anaerobes	Diabetes mellitus	Gas in tissues
Gas gangrene	Clostridial species (*C. perfringens, C. histolyticum,* or *C. septicum*)	Trauma, crush injuries, epinephrine injections; spontaneous cases related to cancer, neutropenia or chemotherapy	Myonecrosis, gas in tissues, systemic toxicity, shock
Necrotizing fasciitis type 1	Mixed anaerobes, gram-negative aerobic bacilli, enterococci	Surgery, diabetes mellitus, peripheral vascular disease	Destruction of fat and fascia; skin may be spared; involvement of perineal area in Fournier gangrene
Necrotizing fasciitis type 2 (most common)	GAS (Morerare: polymicrobial or isolated *S. aureus*)	Penetrating injuries, surgical procedures, varicella, burns, minor cuts, trauma	Systemic toxicity, severe local pain, rapidly extending necrosis of subcutaneous tissues and skin; gangrene, shock, multiorgan failure
Necrotizing fasciitis type 3 (very rare)	*Vibrio* spp. (marine)	Skin lesions exposed to sea water or marine animals	

*****Modified from Bisno AL, Stevens DL. Streptococcal infections of skin and soft tissues. N Engl J Med. 1996;334:240–245[9].*

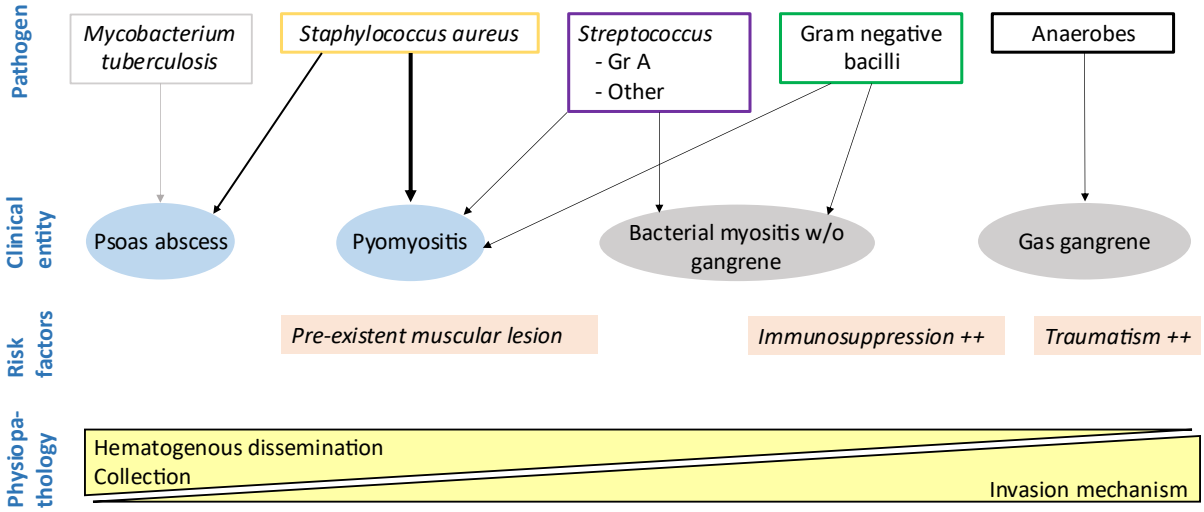
3. Physiopathology [1, 3]

- Bacterial soft tissue infections (Figure 1): *S. aureus* infections are most probably caused by transient bacteraemia together with predisposing muscular trauma or vigorous exercise, with no portal of entry, while GAS infections may also appear following a portal of entry[10, 11]. *S. aureus*, GAS, and *Clostridium* spp. express virulence factors that drive infection and tissue damage. *S. aureus* and GAS produce adhesins,

cytotoxins, superantigens, and immunomodulatory proteins; *C. perfringens* produces α-toxin and perfringolysin O; *C. septicum* produces cytolysin. Unlike *C. perfringens*, *C. septicum* is aerotolerant, enabling bloodstream spread and infection in healthy tissues.

- Viral myositis2, 3: Uncertain. Proposed mechanisms include viral invasion of muscle tissue and immune-mediated muscle damage triggered by the respiratory virus.

Figure 1: *Physiopathology of bacterial myositis and pyomyositis*



**Modified from: Molina B. Infectious myositis. Revue de médecine interne 2020;41:241–249[3].*

III. Signs and symptoms

1. Myositis [1-3]:

- Bacterial myositis:
  - Group A Streptococcus (GAS) infection: May present prodromal symptoms (rash, myalgia and flu-like symptoms) followed by severe local muscle pain (possible multiple sites), tense swelling and fever. [2]
  - Clostridium spp.: Severe muscle pain, sweet-smelling discharge, gas in affected tissues, no muscle contraction and lack of bleeding. Similar for polymicrobial no clostridial myositis.
- Viral myositis: Severe bilateral myalgia, mostly calf muscles and inability to walk[12], occurring once respiratory symptoms are declining. May manifest as pleurodynia if Coxsackie virus B, with chest pain and costochondral muscles tenderness.

2. Pyomyositis [1]:

- S. aureus: Mostly large leg muscles, but also other locations. Initial unspecific symptoms include low-grade fever, muscle aches, and cramping during several days, with firmness to touch. Multiple abscess in 25% of children. After days or weeks, erythema, swelling and warmth may develop. Pyogenic abscess of psoas muscle may present as lower abdominal or back pain radiating to hip, and limping13.
- GAS: May cause localized phlegmon, abscess or necrotizing fasciitis. Main symptom is intense pain with slight inflammation signs and muscle movement refusal. Will evolve to high fever, erythema and swelling.

3. Necrotizing fasciitis:

Soft tissue swelling and pain, 1-4 days after trauma or lesion, in a well-appearing child. Rapid progression of induration and oedema during 1st day, blistering and intense pain and tenderness which are out of proportion with cutaneous signs. Infection extends along the facial planes, causing necrosis of surrounding tissues.

IV. Diagnosis [1, 14]

1. **Imaging:** Magnetic Resonance Imaging (MRI) preferred modality over computed tomography (CT) or ultrasonography, as detects spread of inflammation along fascial planes and identifies specific compartments and structures affected. X-ray is not informative.
2. **Laboratory:**

- Serum creatinine kinase elevated in myositis and GAS pyomyositis [12, 15]
- Complete blood count with differential: Leukocytes are normal or high in GAS pyomyositis or necrotizing fasciitis, with shift to immature neutrophils15.
- Other: may include liver function tests, creatinine, electrolytes, coagulation, lactate, and inflammatory markers (C-reactive protein (CRP) or erythrocyte sedimentation rate).
- Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) Score: developed in adults for necrotizing fasciitis[16]. In children, the P-LRINEC only includes high serum CRP (>20 mg/L) and low serum sodium (<135mEq/L) as predictors, to identify children with suspected necrotizing fasciitis who need earlier surgical intervention, but evidence is weak. [17]

3. **Microbiology:** Recommendations include

- Blood cultures for severe SSTIs (if possible before antimicrobial therapy)14.
- Other cultures: cultures and gram stain of wound, debrided tissue and abscess material14.
- - Muscle biopsy: for fungal myositis diagnosis when risk factors, persistent symptoms and negative results from standard microbiological samples and imaging1-3.

V. Complications and prognosis

1. **Myositis:**

- Bacterial myositis: Compartment syndrome, bacteremia, toxic shock syndrome (TSS) (streptococcal or staphylococcal) and multiorgan failure.
- Viral myositis: May evolve to rhabdomyolysis with renal failure and compartment syndrome.

2. **Pyomyositis:** *S. aureus* pyomyositis may result in septicaemia or TSS in rare cases[18]. GAS may cause streptococcal TSS (shock signs and scarlatiniform rash).
3. **Necrotizing fasciitis:** Fulminant course often seen, 25-75% mortality rates, secondary to TSS and severe systemic toxicity or multiorgan failure and shock due to extensive necrosis and tissue damage[19, 20].

VI. Management[14]

1. **Bacterial soft tissue infections:** Comprises

- Supportive management: May need ICU care if multiorgan failure or shock.
- Surgical: Incision and drainage of fluid collections, debridement and compartment release. Amputation and skin grafting may be necessary in severe cases, especially for gas gangrene.
- Antimicrobial therapy: Intravenous empiric antibiotic treatment (see Table 3 for dosing):
  a. **Myositis**: Coverage depending on risk factors and suspected bacteria, if unclear, broad spectrum as recommended for necrotizing fasciitis.
  b. **Pyomyositis**: Coverage for S. aureus initially (cloxacillin or vancomycin if suspected MRSA)
  c. **Necrotizing** fasciitis and gas gangrene: Broad empiric antibiotic treatment to cover Gram-positive, Gram-negative and anaerobes (e.g. meropenem or combination treatment as mixed infections treatment in Table 3). Add vancomycin if risk of MRSA (high prevalence, hospital acquired infection or previously colonized).
  Targeted treatment once definitive etiologic diagnosis and antimicrobial sensitivities are available (Table 3). Switch to oral antibiotics is recommended if clinical

improvement, oral intake tolerance and source control (completed debridement and drainage). Total recommended antimicrobial treatment duration is 2-3 weeks.

- ❖ Adjuvant therapy: Clindamycin for its antitoxin effect, especially if associated streptococcal TSS[1, 21]. High dose immunoglobulin intravenous (IGIV) has been proposed for severe GAS infections, but evidence is weak (observational studies)[1]. Recommended for streptococcal TSS[21].

2. **Viral myositis:** Therapy is symptomatic, and the disease usually resolves in several days.[1-3]

Table 3: *Targeted treatment for life-threatening skin and soft tissue infections.*

Type of infection	Fist-line treatment	Paediatric Dosage	Comment
Mixed infections	Meropenem	20 mg/kg/dose every 8h IV	If penicillin allergy: Clindamycin or metronidazole plus aminoglycoside or fluoroquinolone (add *S. aureus* coverage if suspected)
	Piperacillin-tazobactam plus vancomycin	60–75 mg/kg/dose of the piperacillin component every 6 h IV 10–13 mg/kg/dose every 8h IV	
	Cefotaxime plus metronidazole or clindamycin	50 mg/kg/dose every 6 h IV 7.5 mg/kg/dose every 6 h IV 10–13 mg/kg/dose every 8h IV	
	+/- Vancomycin*	15 mg/kg/dose every 6 h IV	
Streptococcus	Penicillin plus clindamycin	60 000–100 000 units/kg/dose every 6 h IV 10–13 mg/kg/dose every 8 h IV	If penicillin allergy: Vancomycin
Staphylococcus aureus	Cloxacillin	50 mg/kg/dose every 6 h IV	If penicillin allergy: Vancomycin
	Cefazolin	33 mg/kg/dose every 8 h IV	
	Vancomycin*	15 mg/kg/dose every 6 h IV	
	Clindamycin	10–13 mg/kg/dose every 8 h IV	Inducible resistance in MRSA
Clostridium species	Clindamycin plus, penicillin	10–13 mg/kg/dose every 8 h IV 60,000–100,000 units/kg/dose every 6 h IV	5% of strains of C. perfringens are clindamycin resistant
Aeromonas hydrophila	Doxycycline plus ciprofloxacin or ceftriaxone	2 mg/kg/dose every 12 h IV (max 100 mg every 12 h) 15 mg/kg/dose every 12 h IV 50 mg/kg/dose every 12-24 h IV	Not recommended for age children. May need to use in life-threatening situations.
Vibrio vulnificus	Doxycycline plus ceftriaxone or cefotaxime	2 mg/kg/dose every 12 h IV (max 100 mg every 12 h) 50 mg/kg/dose every 12-24 h IV 50 mg/kg/dose every 6 h IV	Not recommended for age <8 y. May need to use in life-threatening situations.

Modified from Stevens DL. IDSA Practice Guidelines for SSTIs. CID 2014;59(2):147-59[14]

**: If suspected MRSA: high prevalence, hospital acquired infection or previously colonised.*

VII. Prevention

- Postexposure prophylaxis for invasive GAS may be indicated for high-risk close contacts (immunosuppressed, pregnant, have had recent surgery, or have any type of open wound): oral penicillin 25 mg/kg/dose (maximum 250 mg per dose) every 6 h, for 10 days22. Limited evidence.

- Infection control measures in hospitalised patients with life-threatening SSTIs depending on identified pathogen and source location (droplet and contact precautions).

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ANTIMICROBIAL EMPIRICAL THERAPY

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Principles of good antibiotic use

- Only prescribe antibiotics with a clear clinical justification where a bacterial infection is suspected or proven.
- Document in the chart because the antibiotic is being ordered
- An antibiotic is not an anti-pyretic – don't use antibiotics simply because a patient has fever
- Collect specimens for microbiology before giving antibiotics unless the situation is life-threatening
- Prescribe antibiotics according to the local guidelines and at the correct dose *(see Appendix A)*
- Surgical prophylaxis should be given for a maximum of 24 hours
- Choose the narrowest spectrum antibiotic possible for the required indication
- Narrow the antibiotic as soon as possible - e.g. when appropriate culture results are available
- Switch IV antibiotics to oral antibiotics as soon as possible and stop antibiotics as soon as possible– can do both these while patient is still admitted.

Follow the guidelines below to help choose empirical antibiotics

(i.e. causative organism NOT known) for the various clinical syndromes,

BUT remember to use frequent patient re-assessment and laboratory/culture results in order to adjust antibiotic treatment as appropriate.

SEPSIS SYNDROME						
Age	**Likely causative Organism**	**Choice of Antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice** (if no specific pathogen identified)	**Notes**
< 1 month	Early onset (< 48 hours): Group B streptococcus, *E. coli, Listeria monocytogenes, Haemophilus influenzae*	Ampicillin PLUS Gentamicin	IV	5-10 days	Co-amoxiclav for empiric step- down	This is choice of antibiotics for <u>empirical therapy</u> – i.e. causative organism not known. Should revise according to culture results.
	Late onset (> 48 hours old): Same as above, + *Staph aureus, S. pneumoniae, Klebsiella* spp., *Salmonella* spp, *Pseudomonas aeruginosa, Enterococcus* spp.					If not better and 48-hour culture is negative, consider Imipenem
≥1-month *Unknown source Communit y acquired*	*E. coli, H. influenzae, S. pneumoniae, Klebsiella* spp., *Salmonella* Typhi, *Salmonella* spp., *Staphylococcus aureus, N. meningitides*, Group A streptococcus, *Burkholderia pseudomallei*	Ceftriaxone	IV	5-10 days	Co-amoxiclav for empiric step- down	This is choice of antibiotics for <u>empirical therapy</u> – i.e. causative organism not known. Should revise according to culture results. If blood culture negative and no evidence of infection stop antibiotics at 48 hours If blood culture negative but clinical evidence of infection and improving treat for 5 days
≥1-month *Unknown source Hospital acquired*	*Klebsiella* spp., *E. coli*, *Staphylococcus aureus* (MRSA), *Acinetobacter*, *Pseudomonas aeruginosa*, other Gram-negative bacilli	-*If no shock*: Ceftriaxone (or consider diagnosis of viral illness and don't give any antibiotic) -*If shock or critically ill*: Imipenem	IV IV	5-10 days 5-10 days	Co-amoxiclav for empiric step- down	If blood culture positive treat specific pathogen If not better and 48 hours culture is negative, consider Imipenem If ICU patient and suspect staphylococcal sepsis, use Ceftriaxone + Cloxacillin until culture results

MENINGITIS (see also AHC Meningitis protocol)						
Age	**Likely causative Organism**	**Choice of Antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
<1 month	Group B streptococcus, *E. coli, L. monocytogenes, N. meningitidis, H. influenzae, S. pneumoniae, Salmonella* spp.	Ceftriaxone PLUS Ampicillin	IV	Minimum of 14 days	Whole course should be intravenous	Choice of antibiotics listed is for empirical therapy (i.e. causative organism not known). Ceftriaxone should be high dose given Q12hours Stop ampicillin if 48hour cultures negative for Listeria Can increase duration depending on clinical progress and repeat CSF results Monitor bilirubin for any neonate on Ceftriaxone
≥1 month	*N. meningitidis, H. influenzae, S. pneumoniae*	Ceftriaxone	IV	Minimum of 10 days	Whole course should be intravenous	Ceftriaxone should be high dose given Q12hours Can increase duration depending on clinical progress and repeat CSF results

ENDOCARDITIS						
Age	**Likely causative Organism**	**Choice of Antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
All ages	*S. aureus, S. viridans,* coagulase-negative staphylococci, Group A & Group B streptococcus, Enterococci, *S. pneumoniae, E. coli,* HACEK organisms *(Haemophilus, Actinobacillus, Cardiobacterium, Eikenella,* and *Kingella*)	Ceftriaxone	IV	Minimum of 4 weeks	Whole course should be IV	Ceftriaxone should be 100mg/kg divided Q12-24 hours Can add Gentamicin for up to 2 weeks if severe. If first culture is negative, should repeat 2-4 times 4 weeks is minimum empiric duration. Total duration and choice of antibiotics should be adjusted based on any specific organism isolated.

LOWER RESPIRATORY TRACT INFECTIONS, Severity definitions for pneumonia (WHO)

- MILD/MODERATE (OPD case) – Cough/difficulty breathing + fast breathing: ≥60/min if < 2 months; ≥50/min if 2-11 months; ≥40/min if aged 1-5 years
- SEVERE (IPD case) - Cough and difficulty breathing + one of: chest indrawing; nasal flaring; grunting (young infants)
- VERY SEVERE (ICU case) - Cough or difficulty breathing + one of: central cyanosis; severe respiratory distress; unable to drink or feed

Age	Likely causative Organism	Choice of Antibiotic	Route	Duration of therapy	Oral step-down choice	Notes
Pneumonia (neonatal community acquired)						
< 1 month	As with neonatal sepsis	Ampicillin PLUS Gentamicin	IV	5-10 days	Co-amoxiclav for empiric step-down	Revise treatment according to isolated organism
Pneumonia (community acquired) – standard in OPD: MILD/MODERATE						
≥1 month to <5 years	S. pneumoniae, H.influenzae	Amoxicillin	Oral	5-7 days		
≥5 years	M. pneumoniae, S. pneumoniae, C. pneumoniae, H. influenzae	Amoxicillin OR Macrolide	Oral	5 days		Acceptable macrolides: Clarithromycin or Azithromycin
Pneumonia (community acquired) – standard in IPD: SEVERE						
≥ 1 month	S. pneumoniae, H. influenzae (Also M. pneumoniae & C. pneumoniae in >5y)	Ceftriaxone (Q24) OR Co-amoxiclav	IV Oral	7-10 days	Amoxicillin OR Co-amoxiclav OR Cefixime OR Macrolide if >5y	If >5y, consider adding macrolide to initial treatment and also consider macrolide as oral step-down
Pneumonia (community acquired) – standard in ICU: VERY SEVERE						
≥ 1 month	S. pneumoniae, H. influenzae If considering *Staphylococcus aureus, Burkholderia pseudomallei*	Ceftriaxone Ceftazidime PLUS Cloxacillin	IV IV	7-10 days Minimum of 14 days	Co-amoxiclav OR Cefixime Co-amoxiclav	If not better and 48-hour culture is negative, consider Imipenem If suspect either Staph or Melioidosis, should treat both until culture results For melioidosis see organism-specific section below

Pneumonia (hospital acquired> 48 hours after admission to healthcare facility) – MILD (not VAP)						
All ages	*S. aureus*, Enterobacteriaceae, *P. aeruginosa, S. pneumoniae, H. influenzae*	Co-amoxiclav	Oral	7-10 days		
Pneumonia (hospital acquired> 48 hours after admission to healthcare facility) – MODERATE (not VAP)						
All ages	As with MILD Hospital-acquired pneumonia above	Ceftriaxone	IV	7-10 days	Co-amoxiclav /cefexime	
Pneumonia (hospital acquired> 48 hours after admission to healthcare facility) – SEVERE or VENTILATOR-ASSOCIATED (VAP)						
All ages	As above, plus ESBL gram-negatives	Imipenem	IV	7-10 days	Whole course should be IV	
Pertussis (whooping cough)						
All ages	*Bordetella pertussis*	Erythromycin OR Azithromycin OR Clarithromycin	Oral Oral Oral	14 days 5 days 7 days		
Melioidosis						
All ages	*B. pseudomallei*					See organism-specific section below
UPPER RESPIRATORY TRACT INFECTIONS						
Age	**Likely causative Organism**	**Choice of Antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
Tonsillopharyngitis						
All ages: *If well*	*Streptococcus pyogenes* (Group A strep), other Beta haemolytic streptococci	Penicillin V OR Amoxicillin 50mg/kg **QD** (Amox may be more palatable)	Oral Oral	10 days 10 days		- Most cases of pharyngitis in children are viral. To decide whether or not to treat with antibiotics, use the following scoring system: ○ temperature > 38° C : 1 point ○ no cough or no runny nose : 1 point ○ tender anterior cervical adenopathy : 1 point ○ tonsillar swelling or exudates : 1 point ○ age 3-14 years : 1 point

All ages: *Systemically unwell*	*Streptococcus pyogenes*, other Beta haemolytic streptococci	Penicillin G (Benzylpenicillin)	IV	10 days		- Score 0-1: no antibiotics, no further testing, symptomatic treatment - Score 2-3: do throat swab culture to confirm Group A streptococcal pharyngitis before giving antibiotics - Score 4-5: do throat swab AND give antibiotics
Sinusitis						
All ages: *Mild acute*	*S. pneumoniae, H. influenzae, Moraxella catarrhalis*	Amoxicillin	Oral	7-10 days		
Severe acute	Same as mild acute	Ceftriaxone	IV	10-14 days	Co-amoxiclav or cefixime	
Chronic	Same as acute + oral anaerobes	Co-amoxiclav	Oral	See note		Duration dependent on severity and clinical response
Otitis externa						
All ages	*Pseudomonas* spp. Enterobacteriaceae *S. aureus*	Ear drops – ciprofloxacin OR gentamicin Ear drops – ciprofloxacin OR gentamicin	Topical	5-7 days		If no improvement, send ear swab for culture and treat according to results Add Cloxacillin PO for severe & refractory cases
Otitis media (acute)						
Child > 2 years, non-recurrence	*S. pneumoniae, H. influenzae*	**Amoxicillin**	Oral	7 days		If no improvement, send ear swab for culture and treat according to results
Child <2 years or recurrent episode	*S. pneumoniae, H. influenzae*	**Amoxicillin**	Oral	10 days		If no improvement, send ear swab for culture and treat according to results

All ages: *Treatment failure*		**Co-amoxiclav** OR Cefixime OR Ceftriaxone	Oral Or IV	10 days 10 days 3 days		Send ear swab for culture
Mastoiditis						
All ages: *Acute*	*S. pneumoniae*, Group A streptococci, *H. influenzae, M. catarrhalis, S.aureus*	Ceftriaxone	IV	2 weeks	Co-amoxiclav (should give IV antibiotics for at least 7-10 days)	Metronidazole should be included if acute mastoiditis is complication of a chronic infection
All ages: *Chronic*	*P. aeruginosa*, Enterobacteriaceae, *S. aureus* (including MRSA), anaerobic bacteria; consider MTB	Attempt to get appropriate specimens to guide choice before use of antibiotics				If no pathogen found, then give Co-amoxiclav empirically for 14 days and then reassess. If still not better, then strongly consider TB treatment or Melioidosis.
Epiglottitis						
All ages	*H. influenzae* (99%), *S. aureus*	Ceftriaxone	IV	7-10 days	Co-amoxiclav OR	
	aureus, *S. pneumoniae*				Cefixime	

SKIN AND SOFT TISSUE INFECTIONS, remember to consider tetanus boosters for certain scenarios e.g. bites, puncture wounds to feet						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
Puncture wounds						
All ages	Streptococci, *S. aureus*	Cloxacillin	Oral	5 days		Strongly consider tetanus booster
Folliculitis						
All ages	*S. aureus*	Cloxacillin	Oral	5 days		
Furuncles, carbuncles and abcesses						
All ages	*S. aureus*	Cloxacillin	Oral	5-7 days		Abscesses may require incision & drainage (I&D) in consultation with surgeon
Impetigo						

All ages	*S. aureus*	Cloxacillin	Oral	5 days		
Bites						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
All ages	ANIMAL BITES *Pasteurella canis,* *Pasteurella multocida,* *Staph aureus,* *Staphylococcus* spp., *Streptococcus* spp., Anaerobes HUMAN BITES *Staphylococcus* spp., *Streptococcus* spp., Anaerobes, *Eikenella corrodens*	Co-amoxiclav	Oral	5 days		Strongly consider tetanus booster For animal bites – see Rabies guideline

GASTROINTESTINAL						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
All ages	*S. pyogenes, S. aureus*, Group C or G beta- haemolytic strep *H. influenzae* also a cause in young infants	Cloxacillin OR Co-amoxiclav OR Ceftriaxone (if severe)	Oral IV	5-7 days 5-7 days 5-7 days	Co-amoxiclav/ Cefexime	
Gastroenteritis (acute watery diarrhea)						
All ages	Acute watery diarrhea is usually a viral infection and antibiotics are not necessary Cholera (*Vibrio cholerae*) is a possibility, especially if an outbreak is known to be occurring	Avoid antibiotic unless suspect cholera If suspect cholera: Erythromycin OR Azithromycin OR	Oral Oral	3 days single dose (20mg/kg)		Rehydration. Send stool for culture if bloody, mucoid positive for WBC, febrile, or severe disease. For antibiotic treatment of proven specific gastroenteritides – see "Dysentery" section

		Ciprofloxacin	Oral	3 days		
Dysentery						
All ages	*Shigella* spp., *Salmonella* spp.	Ceftriaxone OR	IV	5 days	Ciprofloxacin OR Azithromycin	Rehydration. Send stool for culture.
	Shigella spp. (if bloody), anaerobes	Ciprofloxacin	Oral/IV	5 days		
		OR				
		Azithromycin	Oral	5 days	3 days or single dose Single dose	
Intestinal parasites (this section is for all ages – 1st column is parasite-syndrome instead of age)						
Ascariasis	*Ascaris lumbricoides*	Mebendazole OR Albendazole	Oral Oral			
Hookworm	*Ancylostoma duodenale Necator americanus*	Mebendazole OR Albendazole	Oral Oral	3 days Single dose		
Trichuriasis	*Trichuris trichiura*	Mebendazole OR Albendazole	Oral Oral	3 days Single dose		400mg twice daily (BID); consider repeating after 3 weeks 200microg/kg per day
Strongyloi diasis	*Strongyloides stercoralis*	Children > 2 years: Albendazole Children > 5 years: Ivermectin	Oral Oral	7 days 2 days		
Threadwor m/pinwor m	*Enterobius vermicularis*	Mebendazole	Oral	Single dose		Suggest treatment of household at the same time to prevent re-infection; re-treat at 2 weeks
Tapeworm infection	*Taenia* spp. *Diphyllobothrium latum*	Praziquantel	Oral	Single dose		5-10mg/kg
Dwarf tapeworm infection	*Hymenolepis* spp.	Praziquantel	Oral	Single dose		15-25mg/kg

Giardiasis	*Giardia lamblia*	Metronidazole	Oral	5 days		15-30mg/kg/day divided TID
Amoebiasis	*Entamoeba histolytica*	Metronidazole	Oral	7-10 days		35-50mg/kg/day divided TID Following Metronidazole treatment course: should give diloxanide furoate or iodoquinol or paromomycin, if available, in order to eliminate the amoeba cysts.
Blastocystosis	*Blastocystis hominis*	Metronidazole	Oral	One day of treatment (3 doses)		Treat **ONLY** if symptomatic (e.g. abdominal pain, abnormal stool) **AND** if no other cause found.
Schistosomiasis	*Schistosoma japonicum* *Schistosoma mekongi*	Praziquantel	Oral			20mg/kg/dose three times daily
		Praziquantel	Oral	2 days of treatment (6 doses)		25mg/kg/dose three times daily
Clonorchiasis /Opisth orchiasis	*Clonorchis sinensis Opisthorchis viverrini*	Praziquantel	Oral			25mg/kg/dose three times daily
Necrotizing enterocolitis						
< 1 mo**nth**	Gastrointestinal bacteria	Ampicillin PLUS Gentamicin PLUS Metronidazole	IV	10-14 days		

RENAL AND GENITOURINARY						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
Urinary tract infections (Utis) - Simple utis						
All ages	*E. coli* (90%), *Enterococcus* spp ***Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., *Klebsiella* spp.**	First line: Ciprofloxacin	Oral	7 days		Send urine for microscopy and culture (collect urine as described in the urine collection guidelines) Can give 5 days' duration if afebrile simple UTI

Urinary tract infections (utis) – pyelopnephritis						
All ages	***E. coli* (90%), *Enterococcus* spp., *Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas, Klebsiella* spp.**	Ceftriaxone	IV	7-14 days		Fever + back/flank/loin pain OR systemically unwell OR <12 months Send urine for microscopy and culture
Vaginal discharge						
All ages	***Candida* spp., *N. gonorrhoeae*, Group A streptococcus/*H. influenzae/Moraxella catarrhalis/S. pneumoniae*,**	Ciprofloxacin AND Azithromycin	Oral Oral	Single dose Single dose		Consider foreign bodies/possibility of sexual abuse. Culture for gonorrhoea needs to be requested specifically (request this for all vaginal DC)

OPHTHALMIC INFECTIONS						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
Conjunctivitis						
All ages	*H. influenzae, S. pneumoniae, Staphylococcus* spp., *M. catarrhalis*	Chloramphenicol OR Gentamicin	Topical Topical	5 days 5 days		Irrigate gently with sterile 0.9% saline.
Conjunctivitis of the newborn (Ophthalmia neonatorum)	*Neisseria gonorrhoeae* *Chlamydia trachomatis*	Ceftriaxone 25-50mg/kg PLUS Erythromycin 12.5mg/kg four times a day	IV Oral	Single dose 14 days		If chlamydia or gonococcal infection is suspected, then request gonococcal culture and start empiric treatment Consider advising mother +/- sexual partners to get treated
Orbital cellulitis						
All ages	*S. pneumoniae, H. influenzae, S.aureus,* Group A streptococci	Ceftriaxone	IV	10-14 days	Co-amoxiclav	

Endophthalmitis						
All ages	Consult ophthalmologist					
SURGICAL INFECTIONS						
Age	**Likely causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
Septic arthritis						
Birth to < 3 months	*S. aureus*, Group B Streptococci, Enterobacteriaceae, *N. gonorrhoeae*	Ceftriaxone PLUS Cloxacillin	IV	21-42 days	Give whole course IV	Adjust choice according to isolated organism Change to monotherapy within 48-72 hours Remember adjacent bony involvement in 2/3 of cases
≥ 3 months	*S. aureus*, Group A streptococci, *S. pneumoniae*, Gram negative bacilli, *H. influenzae, N. meningitidis,* (*N. gonorrhoeae* if sexual exposure)	Ceftriaxone (add Cloxacillin if very severe illness or in ICU)	IV	21-42 days depending on clinical response and normalisation of CRP/ESR	Consider switch to oral antibiotics if CRP is normal at ≥ 7-10 days. Choice should be guided by culture.	Adjust choice according to isolated organism Change to monotherapy within 48-72 hours Maximum oral doses are required
Acute osteomyelitis						
Birth to < 3 months	*S. aureus*, Group B streptococci, Gram negative bacilli	Ceftriaxone PLUS Cloxacillin	IV	Minimum of 4 weeks		Adjust choice according to isolated organism Change to monotherapy within 48-72 hours

≥ 3 months	S.aureus, Group A streptococci, Gram negative bacilli (rare), Salmonella (rare)	Cloxacillin	IV	3-6 weeks depending on clinical response	Consider oral antibiotics if CRP is normal at ≥ 7- 10 days. Choice should be guided by culture.	Adjust choice according to isolated organism
Pyomyositis						
All ages	*S. aureus*	Cloxacillin	IV		Depends on culture results	Adjust choice according to isolated organism
Suppurative parotitis						
All ages	*S. aureus* and *B. pseudomallei*	Ceftazidime PLUS Cloxacillin	IV		Depends on culture results	Surgical drainage and samples for culture Narrow therapy when culture results available
Peritonitis						
≥ 1 month	Gastrointestinal bacteria	Ceftriaxone PLUS Metronidazole	IV	7-10 days	Co-amoxiclav OR Amoxicillin PLUS Metronidazole	For < 1 month: Ampicillin PLUS Gentamicin PLUS Metronidazole
Post-operative wound infection						
≥ 1 month	*S. aureus*, Beta hemolytic streptococci, anaerobes, Gram negative bacilli (depends on site of operation – latter mainly if urinary/gastrointestinal)	Ceftriaxone PLUS Metronidazole OR Co-amoxiclav OR clindamycin (if mild)	IV Oral	5-10 days depending on severity of infection; status of host	Co-amoxiclav OR Amoxicillin (if mild)	For < 1 month: Ampicillin PLUS Gentamicin PLUS Metronidazole
Open fractures						
All ages		Co-amoxiclav OR If severe or very contaminated: Ceftriaxone PLUS Metronidazole OR Cloxacillin PLUS Metronidazole	Oral IV	5 days 5-7 days		Consider tetanus booster

SPECIFIC INFECTIONS						
Age	**Causative Organism**	**Choice of antibiotic**	**Route**	**Duration of therapy**	**Oral step-down choice**	**Notes**
MELIOIDOSIS						
All ages	*Burkholderia pseudomallei*	Initial intensive therapy with maximum doses of: Ceftazidime OR Imipenem	IV	Minimum of two weeks	Follow-on oral eradication therapy: Co-amoxiclav (all ages) OR Co-trimoxazole PLUS doxycycline (only if child >8 years of age)	Oral follow-on to be given for a minimum of three months; 6 months if neurologic melioidosis or osteomyelitis. For co-amoxiclav use 20/5 mg/kg TID
ENTERIC FEVER/TYPHOID						
All ages	Salmonella Typhi/Paratyphi A	Ceftriaxone Azithromycin	IV Oral	Total duration should be 7 days for out-patient treatment OR 10-14 days if child admitted	Azithromycin	Step down to azithromycin when afebrile for 24hours Ciprofloxacin may be used ONLY if isolate is susceptible
LISTERIOSIS						
All ages	*Listeria monocytogenes*	Ampicillin +/- Gentamicin	IV	14 - 21 days	Whole course should be IV	If sepsis without CNS disease: 14 days If CNS disease: 21 days and add Gentamicin for 7 days
CULTURE-CONFIRMED MENINGITIS (see also AHC Meningitis protocol)						
All ages	Confirmed *N.meningitidis* meningitis	Benzylpenicillin (or narrowest susceptible	IV	7 days	Whole course should be IV	Consider single dose ciprofloxacin as prophylaxis for close contacts.

		antibiotic)				
	Confirmed *H. influenzae* or *S. pneumoniae* meningitis	Ceftriaxone OR Benzylpenicillin in penicillin-sensitive *S. pneumoniae*	IV	10-14 days	Whole course should be IV	If Haemophilus in CSF add Dexamethasone 0.8 mg/kg BID for 2 days For *H. influenzae*, consider prophylaxis for close contacts – CDC guidance suggests if 1 household contact <48 months or immunocompromised, all household should get prophylaxis – single dose ciprofloxacin
	Confirmed Group B streptococcus meningitis	Benzylpenicillin	IV	14 days	Whole course should be IV	
	Confirmed Gram negative bacillus (except *H. influenzae*) meningitis	Start with Imipenem	IV	21 days	Whole course should be IV	Change to Ceftazidime (melioid dosage) or Ceftriaxone (meningitis dose) if appropriate when culture result available
	Confirmed *Staphylococcus aureus* meningitis	Cloxacillin (if MSSA) Vancomycin (if MRSA)	IV	21 days 21 days	Whole course should be IV	
METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)						
All ages	*Staphylococcus aureus* Invasive disease (sepsis, meningitis, pneumonia, endocarditis, osteomyelitis, pyomyositis, septic arthritis) Non-invasive (skin, soft tissue)	Vancomycin Based on sensitivity	IV Oral	As per syndrome As per syndrome	As per syndrome	Duration of treatment should be according to the clinical syndrome, as detailed in these guidelines. If a range of duration is given, the higher end of the range is recommended for MRSA infections. If severe infection (e.g. sepsis, meningitis) then consider adding Gentamicin for 48-72 hours.

Appendix A - **ANTIBIOTICS**

Note: QD=Once daily BID=Twice daily TID=Three times daily QID=Four times daily IV=Intravenous CGA=Corrected gestational age

Antibiotic	Age	Route	Dose (mg/kg/dose)	Number of doses per day	Notes
Acyclovir IV	< 2 months (<30 weeks gestation)	IV	20	Q12 hours	Maximum: 3200mg per 24hours
	< 2 months (≥30 weeks gestation)	IV	20	Q8 hours	
	≥ 2 months	IV	10	Q8 hours	
Acyclovir Oral	≥ 2 months	Oral	10-20	QID	Neonatal oral dosing same as neonatal IV dosing Maximum: 3200mg per 24hours
Albendazole	≥ 2 months - <2 years	Oral	200	Single dose	
	≥ 2 years	Oral	400	Single dose	BID for 7 days for Strongyloidiasis
Amoxicillin	< 3 months ≥ 3 months	Oral Oral	10-20 10-20	BID TID	Double dose in severe infections (all ages) Maximum: 2000mg (2g) per 24hours
Ampicillin	< 7 days	IV	25-50	Q12 hours	Double dose in severe infections (all ages)
	≥ 7 days but < 2kg	IV	25-50	Q8 hours	Maximum: 12000mg (12g) per 24hours
	≥ 7 days (> 2kg)	IV	25-50	Q6 hours	
Co-amoxiclav (Augmentin®)	< 3 months ≥ 3 months	Oral Oral	15 10-15	BID TID	Maximum: 4000mg (4g) per 24hours
Azithromycin	≥ 2 months	Oral	10	Once daily (QD)	
Cefixime	≥ 1 month	Oral	4	Q12hours	Maximum: 400mg per 24hours

Ceftazidime	< 7 days	IV	50	Q12 hours	Maximum: 6000mg (6g) per 24hours
	≥ 7 days	IV	40-50	Q8 hours	
Ceftriaxone	*Non-meningitis* *Meningitis*	IV IV	50-80 50	Q24 hours Q12 hours	Maximum: 2000mg (2g) per dose Monitor bilirubin for any neonate on Ceftriaxone
Ciprofloxacin	< 28 days	IV	6-10	Q12 hours	Maximum: 800mg per 24hours
	≥ 28 days	IV	9-15	Q12 hours	For severe infection age >2m: give same daily dose per Q8 hrs.
	< 28 days	Oral	10-15	BID	Maximum: 1500mg per 24hours
	≥ 28 days	Oral	10-15	BID	
Clindamycin	< 7 days	Oral	5	BID	Maximum: 1800 mg per 24hours
	7-28 days	Oral	5	TID	
	≥ 28 days	Oral	5-10	TID	
Cloxacillin Cloxacillin	< 7days	IV	25	Q12 hours	Double the dose in osteomyelitis, cerebral abscess,
	7-28 days	IV	25	Q8 hours	meningitis
	≥ 28 days	IV	25	Q6 hours	Maximum: 6000mg (6g) per 24hours
	All	Oral	20-30	TID	Avoid if hepatic disease. Follow LFTs if long-term use. Maximum: 2000mg (2g) per 24 hours
Co-trimoxazole	≥ 6 weeks	IV	4-6 (trimethoprim) 20-30 (sulfameth)	Q12 hours	Increase to 5mg/kg/dose Q6 hours in Pneumocystis or other severe infection
Co-trimoxazole	≥ 6 weeks	Oral	4-6 (trimethoprim) 20-30 (sulfameth)	BID	Avoid under 6 weeks old

Doxycycline	Use ≥ 8 years old only *≤45 kg* *>45 kg*	Oral	 2 100 mg	 BID or QD BID or QD	Avoid under 8 years Maximum: 200 mg per 24 hours
Erythromycin	≥ 28 days	IV	5-12.5	Q6 hours	Maximum: 4000mg (4g) per 24hours
	< 7 days	Oral	10	BID	Maximum: 2000mg (2g) per 24hours
	7-28 days	Oral	10	TID	
	≥ 28 days	Oral	10-15	TID	
Gentamicin	< 28 days: *< 30 weeks CGA* *30-36 wks CGA* *≥ 37 weeks CGA* ≥ 28 days	IV			
			4	Q48 hours	
			4	Q36 hours	
			4-5	Q24 hours	
		IV	5-7.5	Q24 hours	
Imipenem	<7 days old	IV	20-25	Q12 hours	Maximum: 4000mg (4g) per 24hours
	7-28 days	IV	20-25	Q8 hours	
	28 days - 3 months	IV	25	Q6 hours	
	≥ 3 months	IV	15-25	Q6 hours	
Mebendazole	1-2 years				Safety and efficacy not established
	>2 years	Oral	100 mg OR 500mg	BID Single dose	3 consecutive days
Metronidazole	< 7 days 7-28 days ≥ 28 days	IV IV IV	7.5 7.5 (<2kg), 15 (>2kg) 10	Q24 hours (<2kg) Q12 hours (>2kg) Q12 hours	Maximum: 4000mg (4g) per 24 hours For all ages: consider first giving 15 mg/kg loading dose before starting the maintenance doses For amebiasis: Increase to 15-20mg/kg/dose Q8hr

Metronidazole	< 7 days 7-28 days ≥ 28 days	Oral Oral Oral	7.5 7.5 (<2kg), 15 (>2kg) 10	QD BID TID	Maximum: 4000mg (4g) per 24 hours For amebiasis: Increase to 15-20mg/kg/dose Q8hr
Penicillin G (Benzyl penicillin)	< 7days	IV	25,000 - 50,000 IU	Q12 hours	Double dose in severe infection for age >28 days
	7- 28 days ≥ 28 days	IV IV	25,000 - 50,000 IU 25,000 - 50,000 IU	Q8 hours Q6 hours	Maximum: 24 million IU per 24hours
Penicillin V	≥ 28 days	Oral	10-15	TID	Maximum: 1500mg (1.5g) per 24hours
Vancomycin	< 7days 7- 28 days ≥ 28 days	IV IV IV	10-15 10-15 10-15	Q12 hours Q8 hours Q6 hours	Maximum: 4000mg (4g) per 24hours

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សមាសភាពក្រុមការងារបច្ចេកទេសមគ្គុទេសក៍ព្យាបាលគ្លីនិកខេត្តសាស្ត្រកុមារ

Technical Working Group of Clinical Practice Guidelines for Pediatrics

1.	ឯកឧត្តមសាស្ត្រាចារ្យ	**យឹត ស៊ុនណារ៉ា**	រដ្ឋលេខាធិការក្រសួងសុខាភិបាល	ប្រធាន
2.	លោកជំទាវសាស្ត្រា.	**អ៊ឹម សិទ្ធិការ្យ**	រដ្ឋលេខាធិការក្រសួងសុខាភិបាល	អនុប្រធាន
3.	លោកជំទាវសាស្ត្រា.	**អ៊ុំ សាម៉ុល**	អនុរដ្ឋលេខាធិការក្រសួងសុខាភិបាល	អនុប្រធាន
4.	ឯកឧត្តមសាស្ត្រា.រង	**ហេង សុទ្ធី**	អនុរដ្ឋលេខាធិការក្រសួងសុខាភិបាល	អនុប្រធាន
5.	លោកសាស្ត្រាចារ្យ	**គឹម អាង**	នាយករងមន្ទីរពេទ្យកុមារជាតិ	អនុប្រធាន
6.	លោកសាស្ត្រាចារ្យ	**ម៉ៃ ចន្ធនា**	ប្រធានមន្ទីរពេទ្យមន្ទីរពេទ្យជ័យវរ្ម័នទី៧	សមាជិក
7.	លោកសាស្ត្រា.រង	**ប៊ុនចាន់ យុត្តិរុទ**	ព្រឹទ្ធបុរសមហាវិទ្យាល័យវេជ្ជសាស្ត្រ ស.វ.ស	សមាជិក
8.	លោកស្រីសាស្ត្រា.ជំ.	**ហាវ រត្នាវី**	ព្រឹទ្ធបុរសរងមហាវិទ្យាល័យវេជ្ជសាស្ត្រ ស.វ.ស	សមាជិក
9.	លោកស្រីវេជ្ជបណ្ឌិត	**ក្រង ស៊ីដន**	អនុប្រធាននាយកដ្ឋានប្រយុទ្ធជំងឺឆ្លង	សមាជិក
10.	លោកសាស្ត្រា.ជំ.	**ឃុន លាងឈុន**	អនុប្រធានមន្ទីរពេទ្យមន្ទីរពេទ្យជ័យវរ្ម័នទី៧	សមាជិក
11.	លោកស្រីសាស្ត្រា.ជំ.	**អ៊ីវ ម៉ាឡែន**	អនុប្រធានមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
12.	លោកស្រីសាស្ត្រា.ជំ.	**ឡន យ៉ាណែត**	អនុប្រធានមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
13.	លោកសាស្ត្រា.ជំ.	**តឹក លីវណ្ណារ៉ា**	អនុប្រធានមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
14.	លោកសាស្ត្រាចារ្យ	**ស្រួ យីណា**	ប្រធានបណ្តុះបណ្តាលវិជ្ជាជីវៈបន្តនៃគណៈគ្រូពេទ្យជាតិ	សមាជិក
15.	លោកសាស្ត្រា.ជំ.	**សុខ សុទ្ធី**	ប្រធាន ការិ. បច្ចេកទេសមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
16.	លោកវេជ្ជបណ្ឌិត	**អ៊ាង តឹមអ៊ាន**	នាយករងមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
17.	លោកសាស្ត្រាចារ្យ	**អ៊ាប តឹកឆេង**	អនុប្រធាន ការិ. បច្ចេកទេសមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
18.	លោកវេជ្ជបណ្ឌិត	**តាត ឆុងឡឿន**	អនុប្រធាន ការិ. រដ្ឋបាលមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
19.	លោកសាស្ត្រាចារ្យ	**តែ ង៉ាន់ថា**	ប្រធានមន្ទីរពេទ្យបង្អែកខេត្តតាកែវ	សមាជិក
20.	លោកសាស្ត្រាចារ្យ	**លន ទ្រីយ៉ង់ប៉ារ៉ាទ្រីច**	អនុប្រធានមន្ទីរពេទ្យបង្អែកខេត្តកំពង់ចាម	សមាជិក
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22.	លោកស្រីវេជ្ជបណ្ឌិត	**សៀង សុឌី**	ប្រធានផ្នែកសង្គ្រោះទារកមជ្ឈជាតិគាំពារមាតានិងទារក	សមាជិក
23.	លោកសាស្ត្រា.ជំ.	**ឆាំ សារី**	ប្រធានផ្នែកសង្គ្រោះបន្ទាន់មន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
24.	លោកវេជ្ជបណ្ឌិត	**អៀ ឌីរៈ**	ប្រធានផ្នែកបេ១និងឆ្លុះក្រពះ ពោះវៀនមន្ទីរពេទ្យគន្ធបុប្ផា	សមាជិក
25.	លោកសាស្ត្រាចារ្យ	**ជាន សុផល**	ប្រធានផ្នែកលោហិតសាស្ត្រមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
26.	លោកសាស្ត្រាចារ្យ	**ជឹង ជា**	ប្រធានផ្នែកក្រពះពោះវៀនមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
27.	លោកវេជ្ជបណ្ឌិត	**ឆួន ច័ន្ទភក្ត្រា**	ប្រធានមន្ទីរពេទ្យកុមារអង្គរ	សមាជិក
28.	លោកវេជ្ជបណ្ឌិត	**ង៉ែត ពិសេស**	អនុប្រធានមន្ទីរពេទ្យកុមារអង្គរ	សមាជិក
29.	លោកវេជ្ជបណ្ឌិត	**មីលីយ៉ា ធីល**	ប្រធានផ្នែកមន្ទីរពិសោធន៍មន្ទីរពេទ្យកុមារអង្គរ	សមាជិក
30.	លោកសាស្ត្រាចារ្យ	**ថៃ ណារិទ្ធ**	អនុផ្នែកសង្គ្រោះបន្ទាន់និងពិគ្រោះជំងឺក្រៅមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
31.	លោកសាស្ត្រាចារ្យ	**ជា ពៅ**	ប្រធានផ្នែកជំងឺកុមារមន្ទីរពេទ្យបង្អែកខេត្តបាត់ដំបង	សមាជិក
32.	លោកវេជ្ជបណ្ឌិត	**ឆេង សំអាង**	ប្រធានផ្នែកជំងឺកុមារមន្ទីរពេទ្យមិត្តភាពកម្ពុជា-ជប៉ុនមង្គលបុរី	សមាជិក

33.	លោកស្រីវេជ្ជបណ្ឌិត	**តោក ឌី ឆិត**	វេជ្ជ.ឯកទេសផ្នែកមហារីកមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
34.	លោកវេជ្ជបណ្ឌិត	**កៅ សម្បត្តិ**	វេជ្ជ.ឯកទេសផ្នែកផ្លូវចិត្តកុមារមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
35.	លោកវេជ្ជបណ្ឌិត	**ឡាំ ពេជ្រកិត្យា**	វេជ្ជ.ឯកទេសផ្នែកលោហិតសាស្ត្រមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
36.	លោកស្រីវេជ្ជបណ្ឌិត	**គិត ជារ៉ូឆិក**	វេជ្ជ.ឯកទេសផ្នែកផ្លូវដង្ហើមមន្ទីរពេទ្យកុមារជាតិ	សមាជិក
37.	លោកវេជ្ជបណ្ឌិត	**ណាក់ ពន្លឺ**	វេជ្ជ.ឯកទេសជំងឺកុមារមន្ទីរពេទ្យមិត្តភាពខ្មែរ-សូវៀត	សមាជិក
38.	លោកវេជ្ជបណ្ឌិត	**ប៊ិន សង្កិនិសិទ្ធិ**	វេជ្ជបណ្ឌិតឯកទេសទារកមន្ទីរពេទ្យកាល់ម៉ែត	សមាជិក
39.	លោកវេជ្ជបណ្ឌិត	**សែម ច័ន្ទតារា**	វេជ្ជ.ឯកទេសជំងឺកុមារមន្ទីរពេទ្យបង្អែកខេត្តបាត់ដំប	សមាជិក
40.	អង្គការដៃគូអភិវឌ្ឍ	WHO, UNICEF, ACCESS, CHAI, RHAC-		សមាជិក

សមាសភាពអ្នករៀបរៀងមគ្គុទេសក៍ព្យាបាលគ្លីនិកវេជ្ជសាស្ត្រកុមារ

ល.រ.	នាម-គោត្តនាម		តួនាទី	ទីកន្លែងធ្វើការ	ឧច្ចលបន្ទុក
១	សាស្ត្រាចារ្យ	**យឹត ស៊ុនណារ៉ា**	រដ្ឋលេខាធិការ	ក្រសួងសុខាភិបាល	ប្រធាន
២	សាស្ត្រាចារ្យ	**អ៊ឹម សិទ្ធិការ្យ**	រដ្ឋលេខាធិការ	ក្រសួងសុខាភិបាល	អនុប្រធាន
៣	សាស្ត្រាចារ្យ	**អ៊ុំ សាម៉ុល**	អនុរដ្ឋលេខាធិការ	គណៈរដ្ឋមន្ត្រី	អនុប្រធាន
៤	សាស្ត្រាចារ្យ	**ឡាំ អេងហួរ**	អនុរដ្ឋលេខាធិការ	ក្រសួងសុខាភិបាល	អនុប្រធាន
៥	សាស្ត្រាចារ្យរង	**ហោ សុច្ឆី**	អនុរដ្ឋលេខាធិការ	ក្រសួងសុខាភិបាល	អ្នកនិពន្ធ/កែសម្រួល
៦	សាស្ត្រាចារ្យ	**ម៉ៃ៉ ចន្ធនា**	ប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យជ័យវ៉ែនទី៧	អ្នកនិពន្ធ/សម្របសម្រួល
៧	សាស្ត្រាចារ្យ	**គីម អាង**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ/សម្របសម្រួល
៨	សាស្ត្រាចារ្យរង	**អ៊ុត ម៉ាឡែន**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ/សម្របសម្រួល
៩	សាស្ត្រាចារ្យជំ.	**ឃុន លាងឈុន**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យជ័យវ៉ែនទី៧	អ្នកនិពន្ធ/សម្របសម្រួល
១០	សាស្ត្រាចារ្យជំ.	**ឆួន យ៉ាណែត**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
១១	សាស្ត្រាចារ្យជំ.	**តឹក លីវណ្ណារ៉ា**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
១២	វេជ្ជ.ឯកទេស(6)	**កែវ វណ្ណា**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
១៣	វេជ្ជបណ្ឌិត	**អ៊ាង គីមអ៊ាន**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
១៤	វេជ្ជបណ្ឌិត	**ម៉ែង ឆាយ**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
១៥	សាស្ត្រាចារ្យជំ.	**ឆួន ច័ន្ទភក្ត្រា**	ប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១៦	សាស្ត្រាចារ្យជំ.	**ង៉ែត ពិសេស**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១៧	សាស្ត្រាចារ្យជំ.	**លន ទ្រីយ៍ ប៉ាទ្រីច**	អនុប្រធានមន្ទីរពេទ្យ	មន្ទីរពេទ្យខេត្តកំពង់ចាម	អ្នកនិពន្ធ
១៨	វេជ្ជបណ្ឌិត	**លាន គីមស្រេង**	ប្រធានការិ.បច្ចេកទេស	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
១៩	វេជ្ជ.ឯកទេស(1)	**តាត ភុចធឿន**	អនុ.ការិ.រដ្ឋបាល	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
២០	វេជ្ជបណ្ឌិត	**មីលីយ៉ា ធីល**	នាយផ្នែកមន្ទីរពិសោធន៍	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ/កែសម្រួល
២១	វេជ្ជ.ឯកទេស(1)	**កៅ សម្បត្តិ**	នាយផ្នែកប្រព័ន្ធប្រសាទ-ផ្លូវចិត្ត	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ/កែសម្រួល
២២	សាស្ត្រាចារ្យជំ.	**ឆាំ សារី**	នាយផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
២៣	សាស្ត្រាចារ្យ	**ជាន សុផល**	នាយផ្នែកលោហិតសាស្ត្រ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
២៤	សាស្ត្រាចារ្យ	**ជឹង ជា**	នាយផ្នែកក្រពះពោះវៀន	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
២៥	វេជ្ជ.ឯកទេស(3)	**គោត ជីនិត**	នាយផ្នែកមហារីក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
២៦	វេជ្ជ.ឯកទេស(1)	**អៀ ធីរៈ**	នាយផ្នែកឆ្អុះក្រពះ ពោះវៀន	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
២៧	សាស្ត្រាចារ្យ	**ស្រួ យីណា**	គណៈគ្រូពេទ្យជាតិ	គណៈគ្រូពេទ្យជាតិ	អ្នកនិពន្ធ
២៨	សាស្ត្រាចារ្យជំ.	**ហាវ រ័ត្នារី**	ព្រឹទ្ធបុរសវេជ្ជ ស.វ.ស	សាកលវិទ្យាល័យ វ.ស	អ្នកនិពន្ធ
២៩	សាស្ត្រាចារ្យជំ.	**អ៊ូ ចេងឆៀម**	ទីប្រឹក្សាផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣០	វេជ្ជ. ឯកទេស(5)	**ឌី ហ**	នាយផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣១	វេជ្ជបណ្ឌិត	**ភ្ការ៉ន់ យុវឌ្ឍនា**	នាយផ្នែកជំងឺគ្រុនឈាម	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣២	វេជ្ជ. ឯកទេស(1)	**អាំង ខេមរិទ្ធ**	នាយផ្នែកទារក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៣	សាស្ត្រាចារ្យជំ.	**ង៉ែ ណារិទ្ធ**	នាយរងផ្នែកពិនិត្យរោគក្រៅ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៤	វេជ្ជ. ឯកទេស(2)	**តឺ សំណាង**	នាយរងផ្នែកជំងឺធ្ងន់កុមារ &ទារក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៥	វេជ្ជ. ឯកទេស(1)	**គិត ជារ៉ូនិច**	នាយរងផ្នែកជំងឺផ្លូវដង្ហើម	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ

៣៦	វេជ្ជ. ឯកទេស(1)	**តែ**	**ហៅថេង**	នាយរងផ្នែកជំងឺទូទៅកុមារ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៧	វេជ្ជ. ឯកទេស(1)	**លី**	**ឥវរៈ**	នាយរងផ្នែកត្រចៀកច្រមុះបំពង់ក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៨	វេជ្ជ. ឯកទេស(1)	**ឱច**	**រ៉ាឥន**	នាយរងផ្នែកជំងឺធ្ងន់កុមារ&ទារក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៣៩	វេជ្ជ. ឯកទេស(2)	**ចាប**	**ចរិយា**	នាយរងផ្នែកទារក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤០	វេជ្ជ. ឯកទេស(5)	**ចេង**	**សំរេច**	នាយរងផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤១	វេជ្ជ. ឯកទេស(1)	**ឡាំ**	**ពេជ្រកិត្យា**	នាយរងផ្នែកលោហិតសាស្ត្រ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤២	វេជ្ជ. ឯកទេស(1)	**ម៉ៀង**	**សុវណ្ណដុះ**	នាយរងផ្នែកលោហិតសាស្ត្រ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៣	វេជ្ជ. ឯកទេស(1)	**ឆាង សិរី**	**ឥរលក្ខណ៍**	នាយរងផ្នែកជំងឺមហារីក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៤	វេជ្ជ. ឯកទេស(1)	**សិង**	**សុពុទ្ធិឫទ្ធិ**	នាយរងផ្នែកជំងឺផ្លូវដង្ហើម	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៥	វេជ្ជ. ឯកទេស(1)	**ស៊ុន**	**សុឥត្ថា**	នាយរងផ្នែកត្រចៀកច្រមុះបំពង់ក	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៦	វេជ្ជបណ្ឌិត	**រស់**	**រិទ្ធីឥន្ត**	វេជ្ជបណ្ឌិតផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៧	វេជ្ជ. ឯកទេស(5)	**ញឹក**	**រតនាឥទ្ធ**	វេជ្ជ.ឯកទេសផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៨	វេជ្ជ. ឯកទេស(1)	**ឌិន**	**សឺយ**	វេជ្ជ.ឯកទេសផ្នែកលោហិតសាស្ត្រ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៤៩	វេជ្ជ. ឯកទេស(1)	**ច្រឺ**	**លីឆាង**	វេជ្ជ.ឯកទេសផ្នែកលោហិតសាស្ត្រ	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៥០	វេជ្ជ. ឯកទេស(1)	**ឡឹក**	**យ៉ាត់**	វេជ្ជ.ឯកទេសផ្នែកជំងឺផ្លូវដង្ហើម	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៥១	វេជ្ជ. ឯកទេស(6)	**ស្រឿង**	**សំរេច**	វេជ្ជ.ឯកទេស ផ្នែកសុខភាពផ្លូវចិត្ត	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៥២	វេជ្ជ. ឯកទេស(6)	**ខេង**	**ម៉ាយ៉ាឆុត**	វេជ្ជ.ឯកទេស ផ្នែកសុខភាពផ្លូវចិត្ត	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៥៣	វេជ្ជ. ឯកទេស(1)	**ព្រាប**	**ម៉េងម៉ាន់ឌី**	វេជ្ជ.ឯកទេស ផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យកុមារជាតិ	អ្នកនិពន្ធ
៥៤	វេជ្ជបណ្ឌិត	**ឫ**	**រ៉ានី**	នាយផ្នែកសុខភាពផ្លូវចិត្តកុមារ	មន្ទីរ.ជំងឺជំនះកណ្តាល	អ្នកនិពន្ធ
៥៥	វេជ្ជ.ឯកទេស(4)	**អ៊ុង**	**សាឥលី**	នាយផ្នែកសង្គ្រោះបន្ទាន់ដំងឺបេះដូង	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៥៦	វេជ្ជ.ឯកទេស(1)	**ចាន់**	**ម៉ារឌី**	នាយផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៥៧	វេជ្ជបណ្ឌិត	**ត្រួច**	**ឌីឡា**	នាយផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៥៨	វេជ្ជបណ្ឌិត	**ឆួន**	**ឆតឥមុល**	នាយផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៥៩	វេជ្ជ.ឯកទេស(1)	**សួន**	**ពិសី**	នាយផ្នែកសង្គ្រោះបន្ទាន់	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦០	វេជ្ជ.ឯកទេស(1)	**ឃុំង**	**សុជាតា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦១	វេជ្ជ.ឯកទេស(1)	**ម៉េង**	**លុន**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦២	វេជ្ជ.ឯកទេស(1)	**ឃៀន**	**គឹមឡេង**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៣	វេជ្ជ.ឯកទេស(1)	**ង៉ា**	**ស្រីល័ក្ខណ៍**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៤	វេជ្ជ.ឯកទេស(1)	**ហ៊ឹម**	**សុធារ៉ា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៥	វេជ្ជ.ឯកទេស(1)	**ស្រ៊ុន**	**ឥមុល**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៦	វេជ្ជ.ឯកទេស(1)	**ព្រំ**	**ជំនាញ**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៧	វេជ្ជ.ឯកទេស(1)	**ឆួន**	**ណារីម៉ា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៨	វេជ្ជ.ឯកទេស(1)	**អាន**	**មុនីច័ន្ទប្បរ**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៦៩	វេជ្ជ.ឯកទេស(1)	**សំអាន**	**កំញ្ញាណរ័ត្ន**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៧០	វេជ្ជ.ឯកទេស(1)	**គឹម**	**ជារ៉ា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៧១	វេជ្ជ.ឯកទេស(1)	**ចាន**	**ម៉ារណែត**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យគន្ធបុប្ផា	អ្នកនិពន្ធ
៧២	វេជ្ជ.ឯកទេស(1)	**អ៊ុន**	**ង៉ាល់ឡឺរី**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្ម័នទី៧	អ្នកនិពន្ធ
៧៣	វេជ្ជ.ឯកទេស(1)	**ជ្រុន**	**ឈុនឌី**	ប្រធានការិ.បច្ចេកទេស	មន្ទីរពេទ្យជ័យវរ្ម័នទី៧	អ្នកនិពន្ធ
៧៤	សាស្ត្រាចារ្យជំ.	**ឌី**	**ឆារី**	អនុ.ការិ.បច្ចេកទេស	មន្ទីរពេទ្យជ័យវរ្ម័នទី៧	អ្នកនិពន្ធ

៧៥	វេជ្ជ.ឯកទេស(1)	**ជា**	**ស៊ីដែន**	អនុ.ការិ.បច្ចេកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៧៦	វេជ្ជ.ឯកទេស(1)	**ស្រេង**	**លឹមហេង**	នាយផ្នែកសង្គ្រោះបន្ទាន់ជំងឺបេះដូង	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៧៧	វេជ្ជ.ឯកទេស(1)	**សរ**	**ប៊ុនថុច**	នាយផ្នែកសង្គ្រោះបន្ទាន់ទារក	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៧៨	សាស្ត្រាចារ្យជំ.	**ហ៊ឺ**	**សុខហេង**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៧៩	វេជ្ជ.ឯកទេស(1)	**សុខ**	**ឆ្លា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨០	វេជ្ជ.ឯកទេស(1)	**ឆែន**	**រស្មី**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨១	វេជ្ជ.ឯកទេស(1)	**តាំង**	**ឡេងហាក់**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨២	វេជ្ជ.ឯកទេស(1)	**ណាង**	**ស្រីណែត**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨៣	វេជ្ជ.ឯកទេស(1)	**ហេង**	**ឆ្កាំងហួយ**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨៤	វេជ្ជ.ឯកទេស(1)	**ម៉ុំ**	**សត្យា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨៥	វេជ្ជ.ឯកទេស(1)	**ជ្រា**	**មករា**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យជ័យវរ្មែនទី៧	អ្នកនិពន្ធ
៨៦	សាស្ត្រាចារ្យជំ.	**ជួប**	**ឫទ្ធ**	នាយផ្នែកបណ្តុះបណ្តាល-តម្រងនោម	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៨៧	វេជ្ជបណ្ឌិត	**អៀង**	**ហាប់ស្រេង**	នាយផ្នែកសង្គ្រោះបន្ទាន់និងជំងឺធ្ងន់	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៨៨	វេជ្ជបណ្ឌិត	**ឡូវ**	**កែ**	នាយផ្នែកពិគ្រោះជំងឺក្រៅ	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៨៩	វេជ្ជបណ្ឌិត	**ឡុច**	**ឫតុ័ក្រ**	នាយផ្នែកជំងឺទារក	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩០	វេជ្ជបណ្ឌិត	**ស៊ឹង**	**ហេង**	នាយផ្នែកជំងឺសម្រាកពេទ្យ	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩១	វេជ្ជបណ្ឌិត	**សរ**	**ឆុង្គី**	នាយផ្នែកវះកាត់	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩២	វេជ្ជបណ្ឌិត	**អ៊ុំ**	**ខែមួយ**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៣	វេជ្ជបណ្ឌិត	**គង់**	**សុចិន្តា**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៤	វេជ្ជបណ្ឌិត	**ស៊ុយ**	**ឆៀង**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៥	វេជ្ជបណ្ឌិត	**ប៉ែន**	**សុធាវី**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៦	វេជ្ជបណ្ឌិត	**ឡេង**	**ណារ៉ា**	វេជ្ជបណ្ឌិតវះកាត់	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៧	វេជ្ជបណ្ឌិត	**វណ្ណា**	**ធី**	វេជ្ជបណ្ឌិតវះកាត់	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៨	វេជ្ជបណ្ឌិត	**ប្រាក់**	**ម្ងៀរឡេង**	វេជ្ជបណ្ឌិតវះកាត់	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
៩៩	វេជ្ជបណ្ឌិត	**ឆ្លាង**	**ប៊ុនឆ្លាយ**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០០	វេជ្ជបណ្ឌិត	**យក់**	**ចន្ល័លក្ឃ្យឹ**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០១	វេជ្ជបណ្ឌិត	**ហ៊ីញ**	**សាលី**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០២	វេជ្ជបណ្ឌិត	**ឌុច**	**ផារ៉ា**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៣	វេជ្ជបណ្ឌិត	**សំ**	**លីវណ្ណៈ**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៤	វេជ្ជបណ្ឌិត	**ប៊ុន**	**សិរីលក្ខណ៍**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៥	វេជ្ជបណ្ឌិត	**ធី**	**ប៊ុនប៉ាច**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៦	វេជ្ជបណ្ឌិត	**ហាស់**	**សុធារក្ស**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៧	វេជ្ជបណ្ឌិត	**ស៊ូ**	**ធីរ៉ារ័ត្ន**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៨	វេជ្ជបណ្ឌិត	**ញ៉ាណា**	**ឆ្លាឌីន**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១០៩	សាស្ត្រាចារ្យជំ.	**ឆៅ**	**លក្ខិណា**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១១០	វេជ្ជបណ្ឌិត	**ឃឹម**	**សមិទ្ធិផលុន**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១១១	វេជ្ជបណ្ឌិត	**អ៊ុក**	**ចំរុង**	វេជ្ជបណ្ឌិត	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ
១១២	វេជ្ជបណ្ឌិត	**យិន**	**សុភត្រ្តបុត្រ**	វេជ្ជបណ្ឌិតឯកទេស	មន្ទីរពេទ្យកុមារអង្គរ	អ្នកនិពន្ធ

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(1) *វេជ្ជបណ្ឌិតឯកទេសរោគកុមារ*

(2) *វេជ្ជបណ្ឌិតឯកទេសរោគកុមារនិងទារក*

(3) *វេជ្ជបណ្ឌិតឯកទេសរោគកុមារនិងមហារីកកុមារ*

(4) *វេជ្ជបណ្ឌិតឯកទេសកុមារនិងបេះដូងកុមារ*

(5) *វេជ្ជបណ្ឌិតឯកទេសវះកាត់កុមារ*

(6) *វេជ្ជបណ្ឌិតឯកទេសវិកលវិទ្យា*

(7) *វេជ្ជបណ្ឌិតឯកទេសត្រចៀក ច្រមុះ បំពង់ក និងប្រព័ន្ធការស្តាប់*