



Practice Guidelines

For Family Physicians

Volume 6

Message from His Excellency

Prof. Dr. Hatem El Gabaly

Comprehensive development and modernization is one of Egypt's priorities and pursued objectives. Out of this rule, we are committed towards improving the quality of health care services available for all Egyptians; adults, children, the poor and the well-off.

The Ministry of Health and Population has adopted, as a top priority, developing current systems to provide and finance health services in guidance and vision of the political leadership to ensure high quality in service provision and meet needs and expectations of the population as well as keeping up with top-notch developments at all levels - primary, preventive, curative, diagnostic and rehabilitation.

This vision has been translated into a promising and ambitious Five Years Plan to institutionalize the Health Sector Reform Program on the national level. The plan is focusing on implementing the Family Health Model at all primary health care facilities in the 27 Governorates.

Our dream has been realized into a competent program of Health Sector Reform aiming to provide every person with high quality health services. These include physical, psychological and social welfare, which translate into high production and progress for our cherished Country, Egypt.

I am delighted to introduce to one of the important publications for the Sector of Technical Support and Projects, representing a great team effort "**The Practice Guidelines for Family Physicians**" for the family physician at all Family Health Unites of MOHP Distributed all over the Country .

Prof. Dr. Hatem El Gabaly

Minister of Health and Population

Preface

The Ministry of Health and population is working diligently to achieve equal and available quality health services for all citizens of Egypt. Our objective is to shape national policies for the goal of advancing health care delivery in all parts of the country.

Six years ago, the Ministry has adopted new policies and strategies in order to provide basic health services of high quality for all citizens in the framework of the Family Health Model. This has led to introducing new financing mechanisms that ensure the sustainability of finance and resources, and availability of affordable services along with effectiveness and efficiency of these services.

Having made situational analysis in details, highlighting points of weaknesses and strengths and defining actual needs, strategic plans were subsequently developed putting into practice the reforming infrastructure and human resources as well as partnerships between governmental, private and national sectors.

It gives me great pleasure to present this document. This system is in continuous reform, progressing incrementally, refining the knowledge base, and modifying concepts. This document is not the end product, but rather the first step of many others.

However, I hope it will help us towards our ultimate goal of a quality, effective, efficient, evidence based service to all Egyptians irrespective of geographical or social economic barriers.

The document is a collaborative work of the Ministry of Health and Population staff, and the Sector for Technical Support and Projects on both central and peripheral levels. Work in this document is subjected to continuous assessment, operation research, many of the issues presented in this document will be updated in further version.

Dr. Emam Mossa
Undersecretary of the Sector for
Technical Support and Projects

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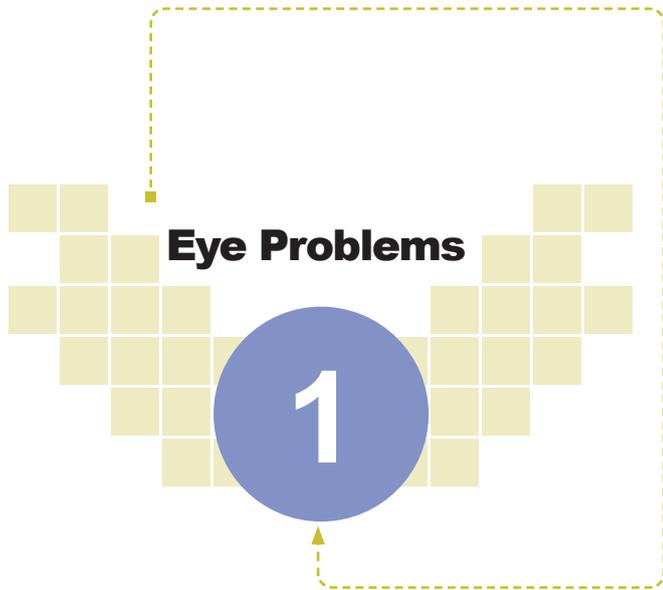
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Eye Problems

The Red Eye

Conjunctivitis: inflammation of the conjunctiva is the commonest eye problem seen in general practice:

- A. Infective Conjunctivitis (Bacterial or Viral)
- B. Gonorrhoeal in Ophthalmia Neonatorum
- C. Allergic Conjunctivitis

Treatment:

Treat with Topical Antibiotic Eye Drops and/or Anti-allergic Eye Drops.

Chloramphenicol “Antibiotic Preparation”:

Application:

- Eye drops (0.5%): Apply 1 drop at least every 2 hours and continue for 48 hours after healing.
- Eye ointment (1%): Apply either at night (if eye drops used during the day) or 3-4 times daily (if eye ointment used alone).
- Side-effects: Transient stinging

Corticosteroids or other anti-inflammatory preparations:

(e.g. Dexamethazone - Betamethasone eye drops and ointment)

Application: (For short term treatment of inflammation)

Frequent applications until condition is controlled then reduce frequency of application

Refer

- Refer all cases for ophthalmology opinion.

Signs of a Potentially Dangerous Red Eye:

- Decreased visual acuity
- Pain deep in the eye
- Absent or sluggish pupil response
- Corneal damage, fluorescein staining, history of trauma.

Refer patient to be seen by specialist the same day if in doubt.

Other Causes of Red Eye

- Orbital cellulites
- Episcleritis

- Scleritis
- Subconjunctival hemorrhage
- Iritis
- Blepharitis
- Acute glaucoma
- Foreign body
- Dry eye syndrome
- Corneal ulceration
- Corneal aberration
- Arc eye

Refer

Refer all Cases for Ophthalmology Opinion.

Saving Sight

Changing Lives

Trachoma is one of the most common causes of blindness in the developing world, and is most commonly associated with areas of extreme poverty. It is caused by bacteria called Chlamydia Trachomatis which is very similar to the one that causes the sexually transmitted disease Chlamydia.

Infection ---> repeated conjunctivitis

The infection spreads in a variety of ways:

The discharge, the flies & via fingers and clothes.

Beyond the irritation caused by conjunctivitis, there is more serious consequence: each infection leads to a small amount of scarring to the cornea & conjunctiva. This scarring builds up over years of repeated infection until trichiasis sets in (eyelashes turn inwards) ----> repeated trauma to cornea ---> it becomes opaque ---> causing vision to decline & irreversible blindness.

How can Trachoma be treated?

Antibiotics

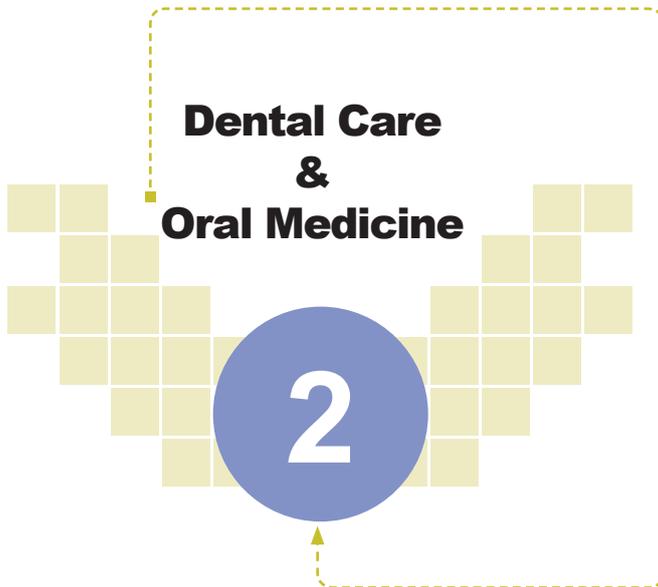
Facial cleanliness

Environmental change

Surgery for trichiasis

**Dental Care
&
Oral Medicine**

2



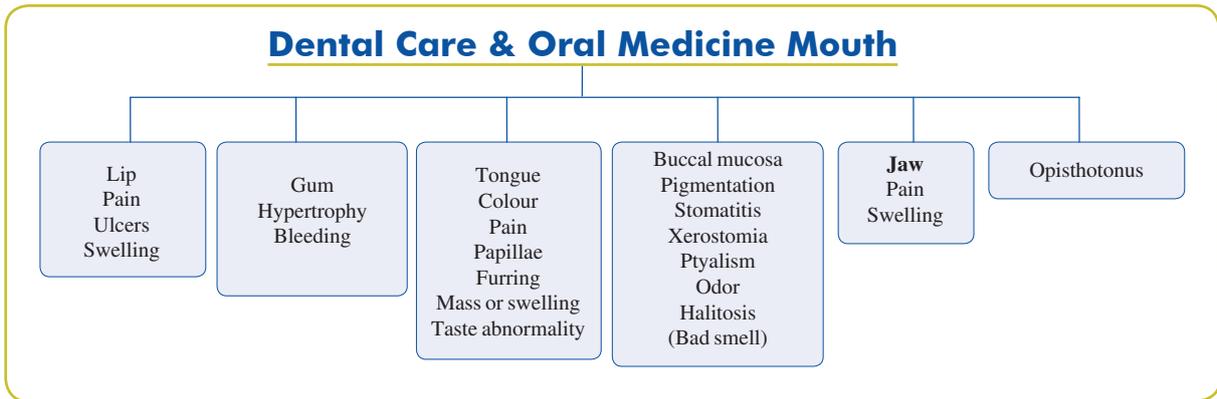


Figure "1": Flow-Chart Diagram for Symptoms of mouth disease

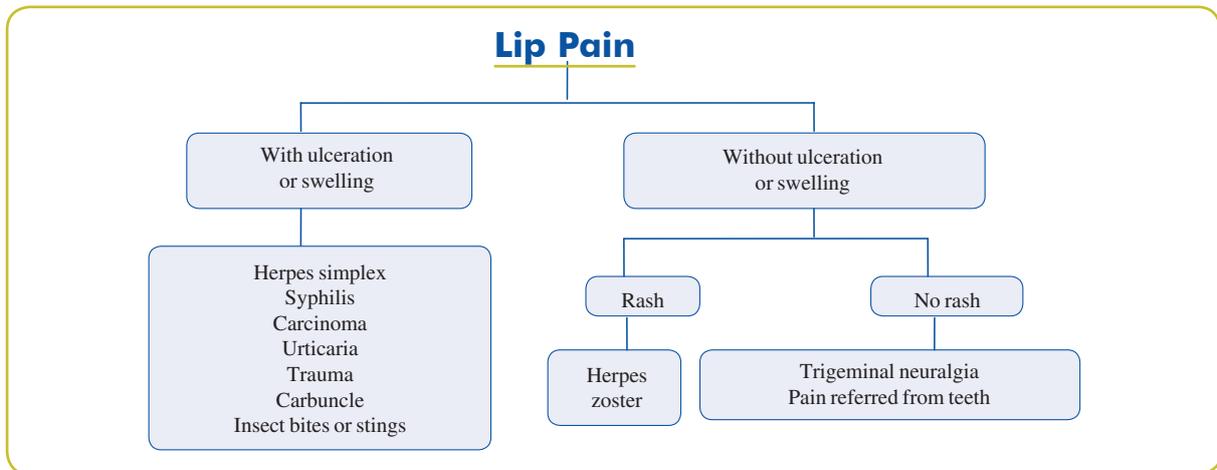


Figure "2": Flow-Chart Diagram for D.D. of Lip Pain

Trigeminal Neuralgia:

Paroxysmal attacks of severe unilateral lancinating pain along distribution of one of the branches of trigeminal nerve. Pain is precipitated by touching localized trigger zones. On examination, there are no motor or sensory changes.

Treatment: Vitamin B12 1000µ IM/d for 1 wk
Carbamazepine 200mg tds.

If persistent refer to dentist

- **Lip pain with ulceration & herpes zoster**
→ see dermatology section

Refer undiagnosed cases

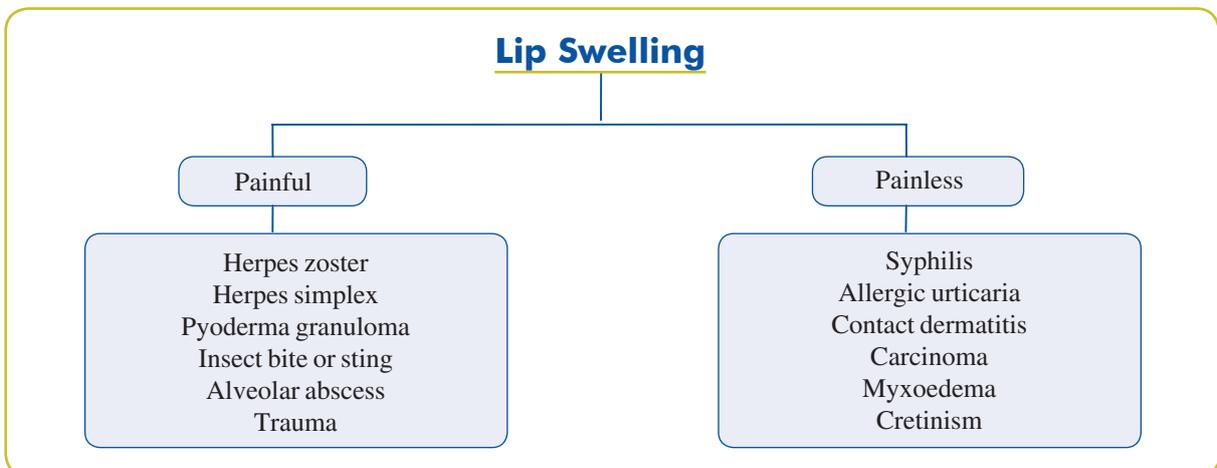


Figure "3": Flow-Chart Diagram for D.D. of Lip Swelling

Refer undiagnosed cases.

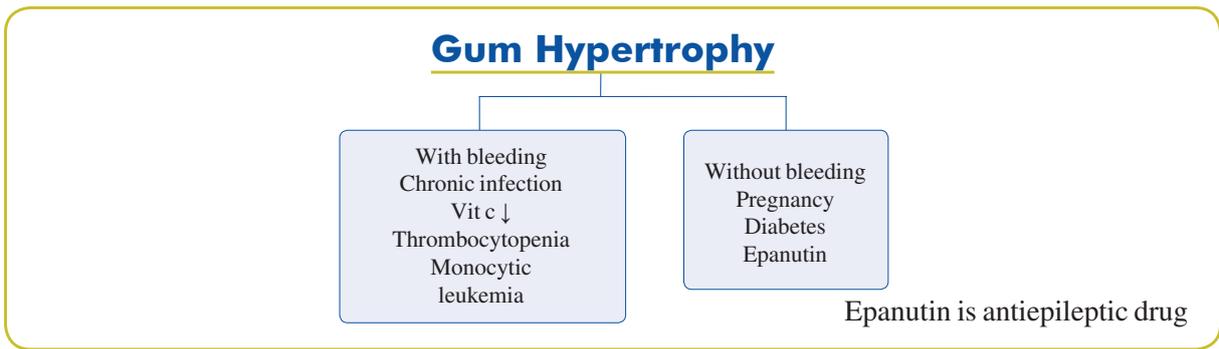


Figure "4": Flow-Chart Diagram for D.D. of Gum Hypertrophy

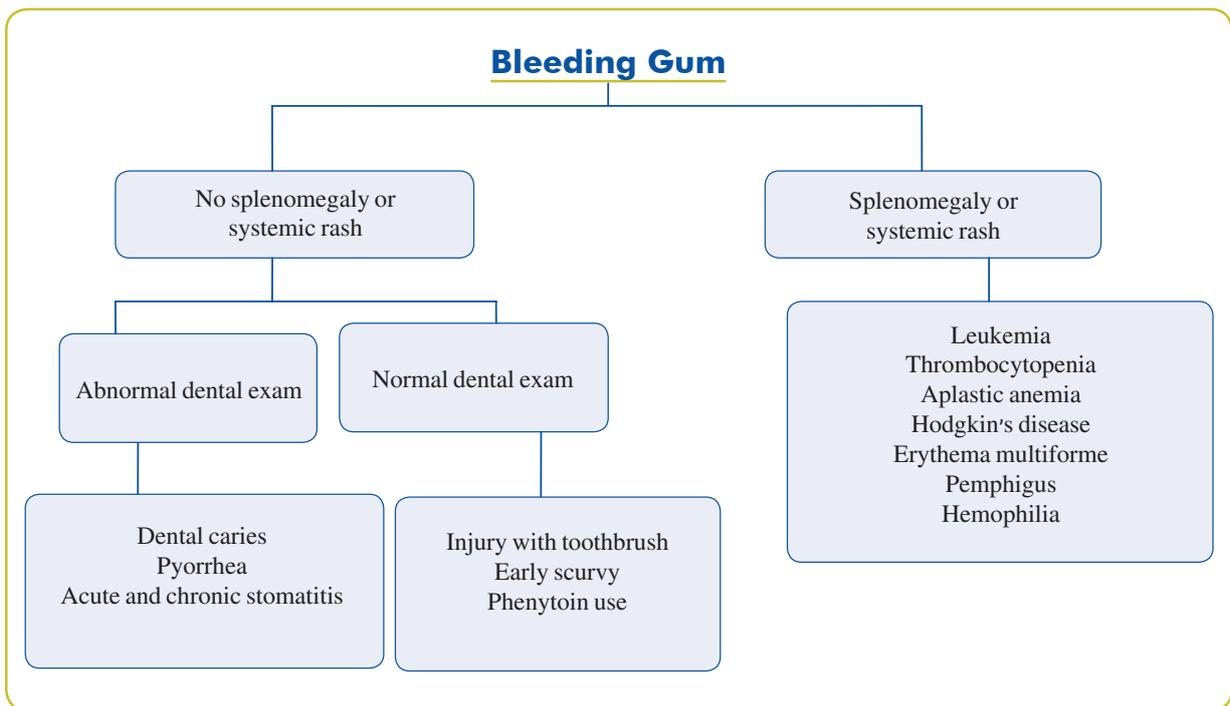


Figure "5": Flow-Chart Diagram for D.D. of Bleeding Gum

Bleeding Gum

• Bleeding Gums With No Splenomegaly or Rash:

- o Good oral hygiene is a must
- o Regular brushing
- o Regular visit to dentist

• Bleeding Gums With Splenomegaly or Rash:

- o It indicates serious disease; you have to refer for proper evaluation and diagnosis.
- o Also see skin section.
- o If bleeding gum is associated with other bleeding ---> **Refer**

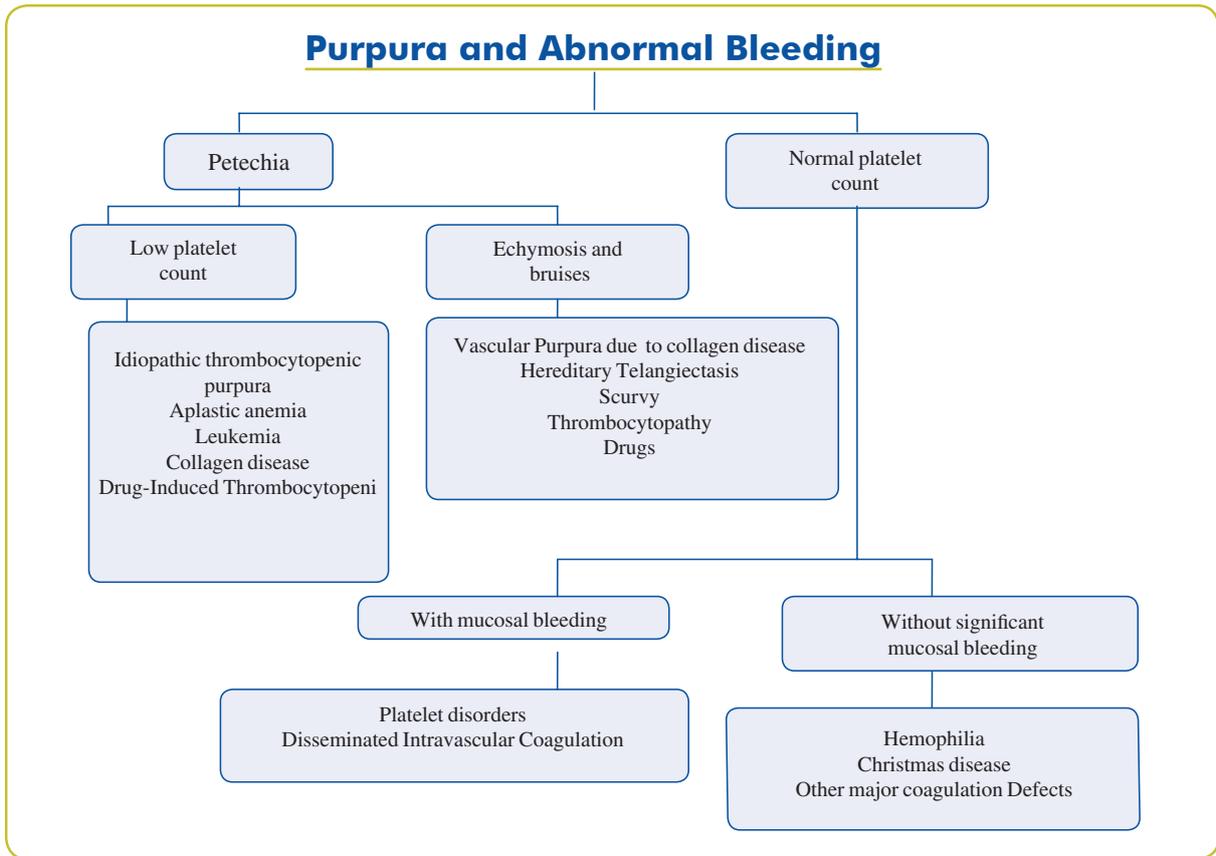
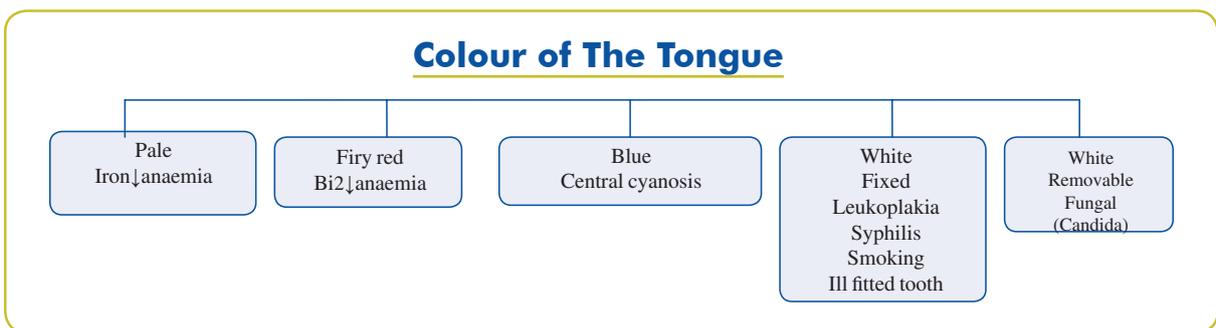


Figure "6": Flow-Chart Diagram for D.D. of Purpura and abnormal Bleeding

Refer

Purpura & abnormal bleeding

It indicates serious disease; you have to refer for proper evaluation and diagnosis.



• **In Iron defficiency anaemia:** confirmed by complete blood picture (CBC)

- o ↓HB
- o ↓ MCV
- o ↓MCH
- o ↓MCHC

Treatment:

1. Treat the underlying cause

2. Give oral iron to correct anemia, 1 tablet tds. & check CBC after 2 wks →↑ in HB 1g/wk. If no response refer
3. Replace iron stores: continue oral Iron 6 months after correction of anemia.

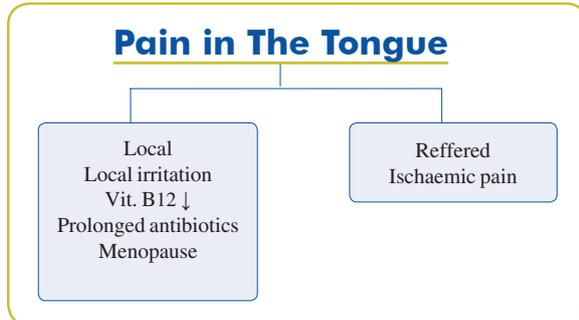
• **In Vitamin B₁₂ Deficiency Anemia:**

Treatment:

- Vit B12 1000µg IM twice for 3 wk, then every 3

months for the rest of the patients 'life.

- In case of central cyanosis, refer all cases for proper evaluation
- Leukoplakia is precancerous lesion, refer for excision
- Candida → see dermatology section



• In Vitamin B₁₂ Deficiency Anemia:

Treatment:

Vit B₁₂ 1000µg IM twice for 3 wk, then every 3 months for the rest of the patients 'life.

Prolonged antibiotics & menopause: give vit B complex

Referred pain: refer for further evaluation

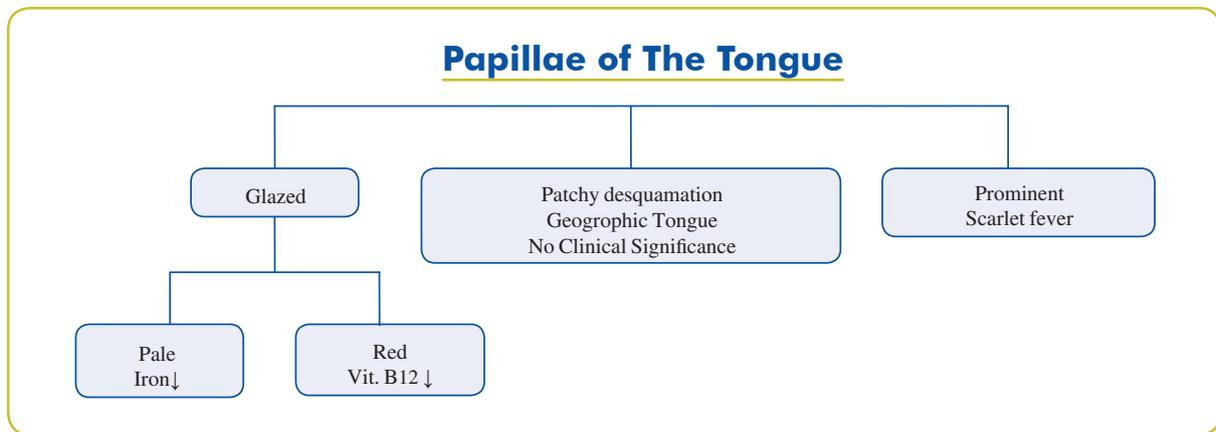


Figure :7": Flow-Chart Diagram for D.D. of Papillae of The Tongue

• In Iron Deficiency anaemia: Conffrm by Complete Blood Picture (CBC)

- o ↓HB
- o ↓MCV
- o ↓MCH
- o ↓MCHC

Treatment:

1. Treat the underlying cause
2. Give oral iron to correct anemia, 1 tablet t.d.s. & check CBC after 2 wks → ↑ in HB 1 g/wk → If no response refer for parenteral iron therapy.
3. Replace iron stores: continue oral Iron 6 months after correction of anemia.

• In Vitamin B₁₂ Deficiency Anemia:

Treatment:

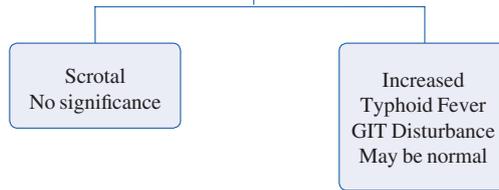
Vit B₁₂ 1000µg IM twice for 3 wk, then every 3 months for the rest of the patients 'life.

Patchy desquamation: no clinical significance, and needs no treatment.

• Prominent Papillae (Scarlet Fever):

- o Oral penicillin 500mg four times daily for 10 days
- o Individuals allergic to penicillin can be treated by erythromycin 250mg four times for 10 days.

Furring of The Tongue



Scrotal tongue needs no treatment as it has no clinical significance.

Increased furring in Typhoid fever: ciprofloxacin twice daily for 14 days.

Tongue Mass or Swelling

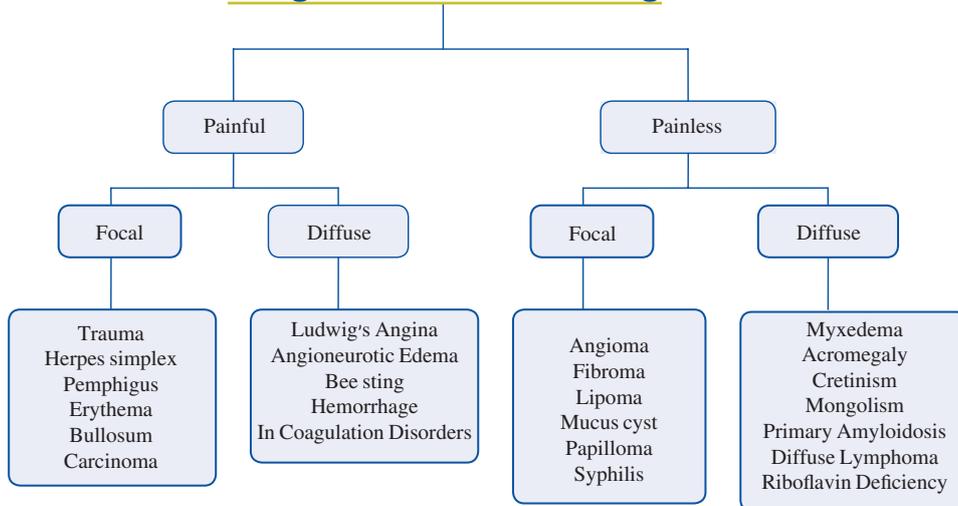


Figure "8": Flow-Chart Diagram for D.D. Tongue Mass or Swelling

Refer

Painful swelling must be referred to surgery for differential diagnosis
Painless swelling referred for further evaluation & proper diagnosis.

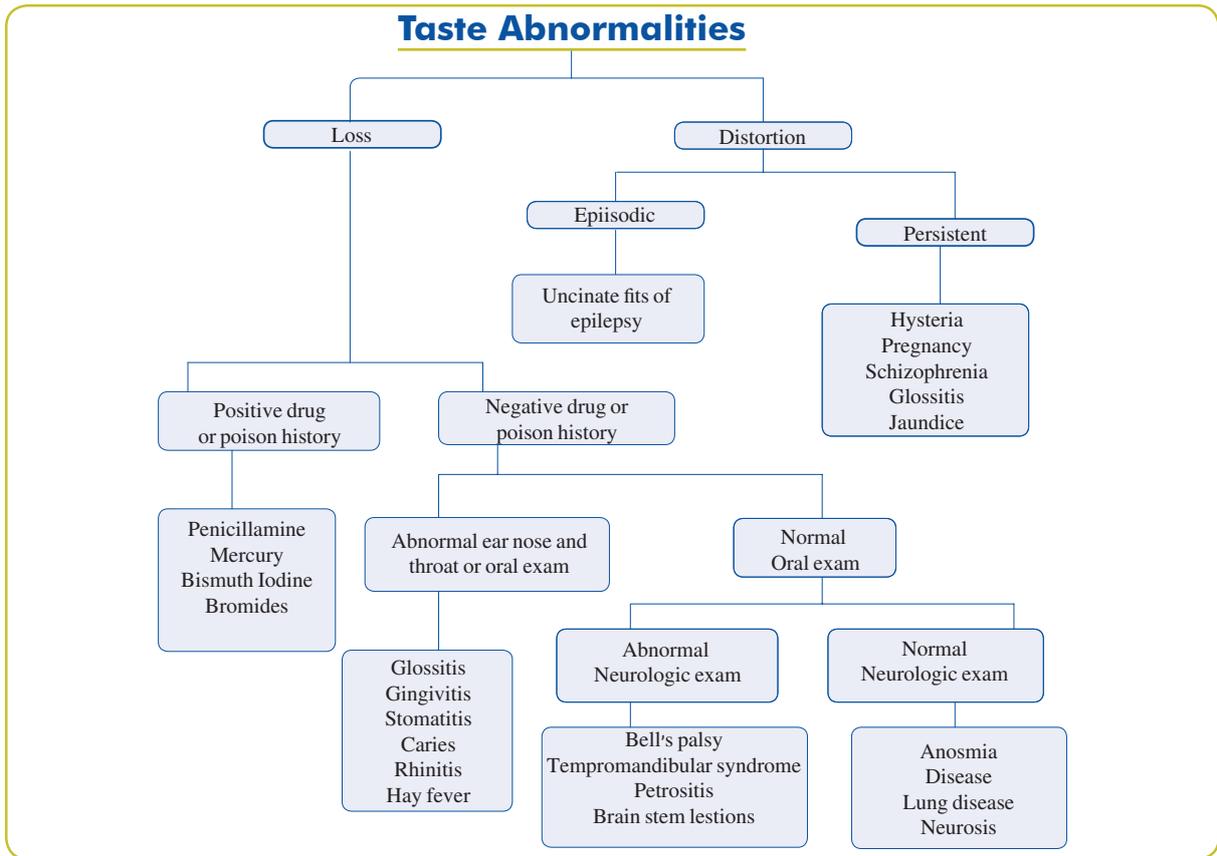


Figure "9": Flow-Chart Diagram for D.D. Taste Abnormalities

Revise drug treatment of the patient to exclude drug cause Then examine mouth locally to exclude local cause, if present refer to dentist

The remaining cases are referred for further evaluation & proper diagnosis

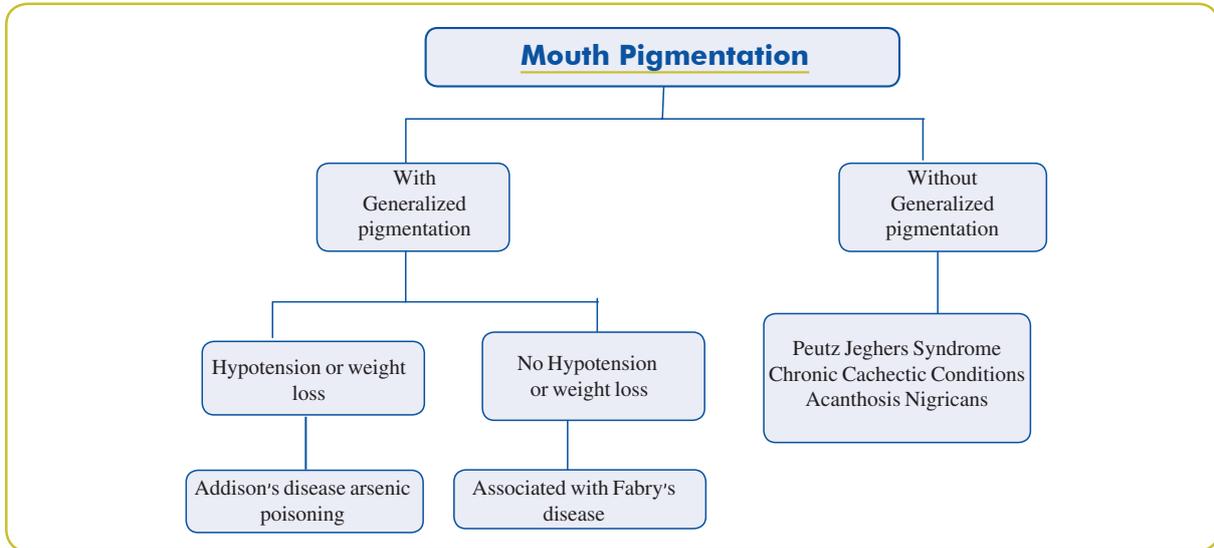


Figure "10": Flow-Chart Diagram for D.D. of Mouth Pigmentation

Fabry’s Disease:

X-linked recessive disease leading to accumulation of glycopospholipids in lysosomes of liver, kidney, blood vesels and nervous system.

Refer for genetic counselling and identification of carriers.

In Addison’s Disease:

Long term treatemnt with replacement glucocorticoids and mineralocorticoids.

Patient’s advice:

- o Carry a ‘steroid card’

- o Wear a Medic-Alert bracelet

- o Keep an (up to date) ampoule of hydrocortisone at home

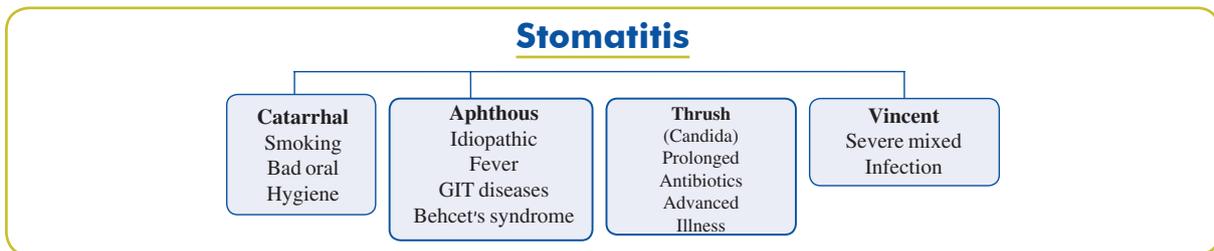
Peutz Jeghers:

Autosomal dominant disorder consists of mucocutaneous pigmentations and GI polyps.

Follow up every 2 years by x-ray & endoscopy

Acanthosis Nigricans:

Part of metabolic syndrome → see diabetic section



Stomatitis

• **Stomatitis:** inflammation of buckal mucosa.

• **Catarrhal in Flammation :**

Red, dry, swollen buccal mucosa, covered with brownish secretion and foul smelling.

It occurs with poor oral hygiene, and with excessive smoking. Treatment: stop smoking

and proper mouth hygiene

• **Aphthous :**

Painful Ulcer

Treatment: local anesthetic

• **Thrush :**

White removable membranes see dermatology section

Vincent :

Fever, ulcers and foul odor
broad spectrum antibiotic + flagyl

Then Refer All Cases.

Xerostomia

Mouth breather
Fear, anxiety
Fever
Dehydration
Drugs: atropin

Sjogren Syndrome:

keratoconjunctivitis sicca
• Idiopathic
• Associated with collagen disease.
• Associated with lympho proliferative disorders.

Treatment: treatment of the cause
chewing gums, pilocarpin

Refer undiagnosed cases

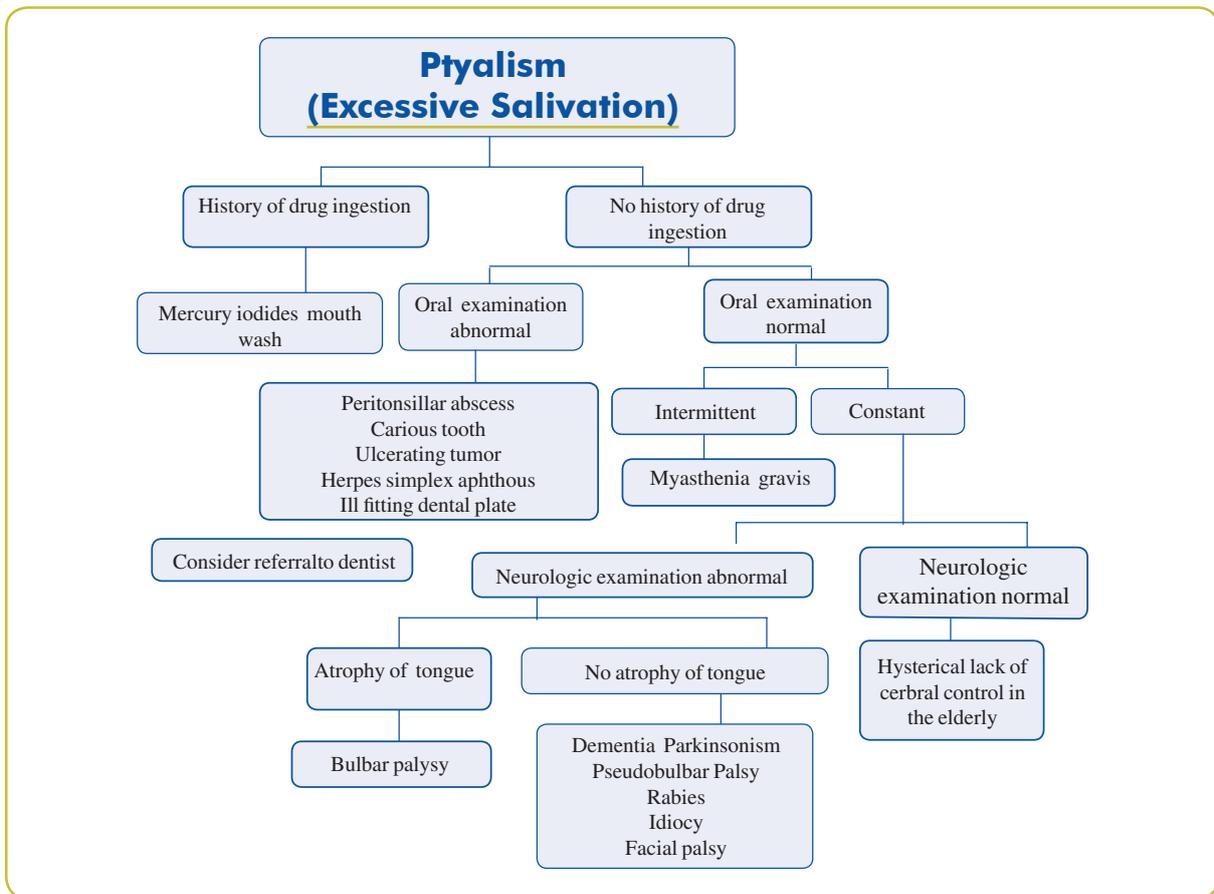


Figure "11": Flow-Chart Diagram for D.D. of Ptyalism (Excessive Salivation)

Ptyalism (Excessive Salivation)

Revise drugs of the patient

Then examine mouth cavity, if abnormalities → refer to dentist

Myasthenia Gravis:

Acquired condition is characterized by weakness and fatigability of proximal limb, ocular and bulbar muscles.

Refer for further evaluation

Cases of constant ptyalism refer for further evaluation

Pseudo Bulbar Palsy:

LMNL of 9th., 10th., 11th., 12th., cranial nerves

Facial Palsy

Parkinsonism

Dementia

Halitosis (Bad Odor)

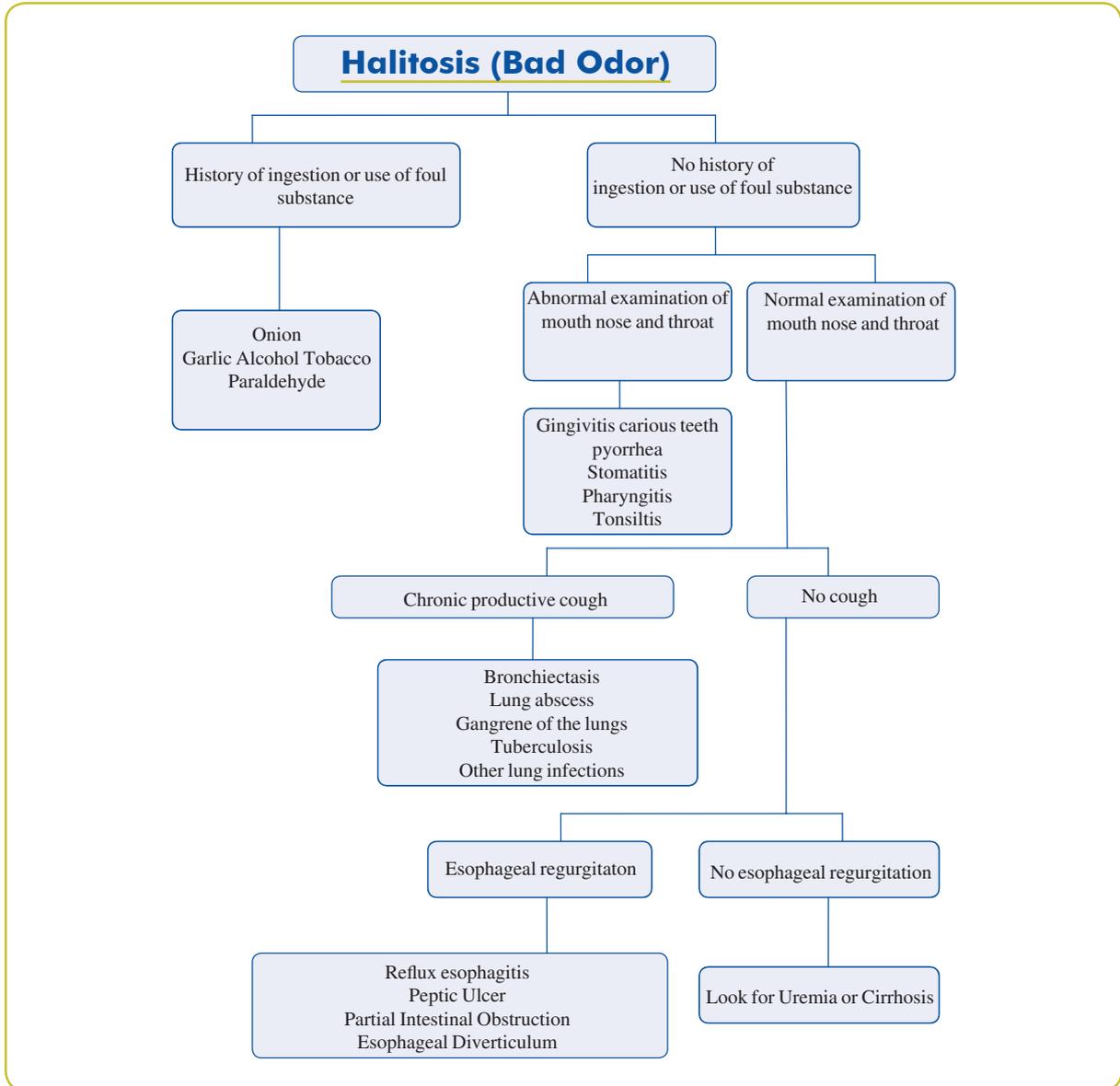


Figure "12": Flow-Chart Diagram for D.D. of Halitosis (Bad Odor)

Foul smelling → broad spectrum antibiotics and flagyl

Refer undiagnosed cases

Bronchiectasis

Lung abscess

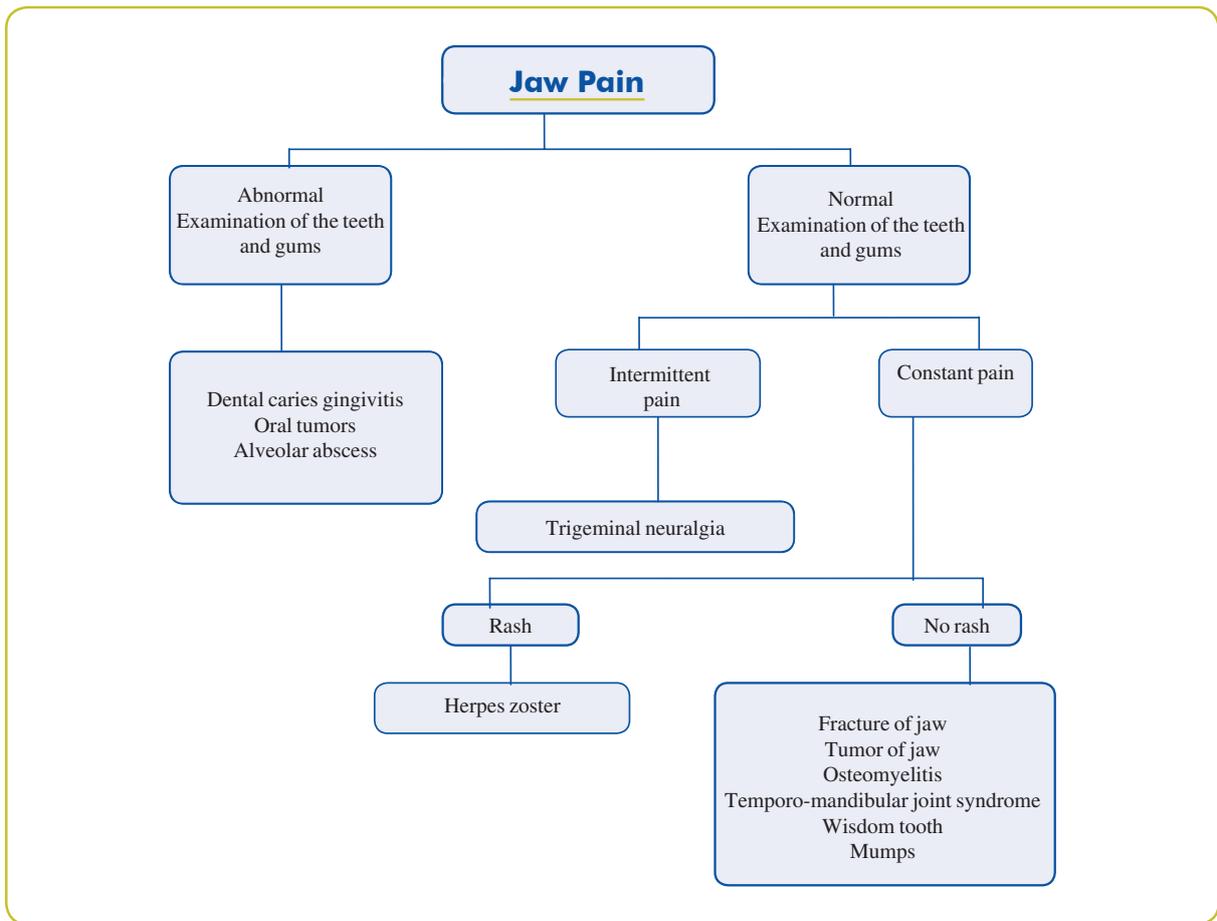


Figure "13": Flow-Chart Diagram for D.D. of Jaw pain

Jaw pain with abnormal mouth examination, refer to dentist

Trigeminal Neuralgia

Treatment: Vitamin B12 1000 µ IM / d for 1 wk
Carbamazepine 200mg t.ds.

If persistent refer to dentist

Cases with constant pain, refer for further evaluation

Herpes Zoster

Mumps

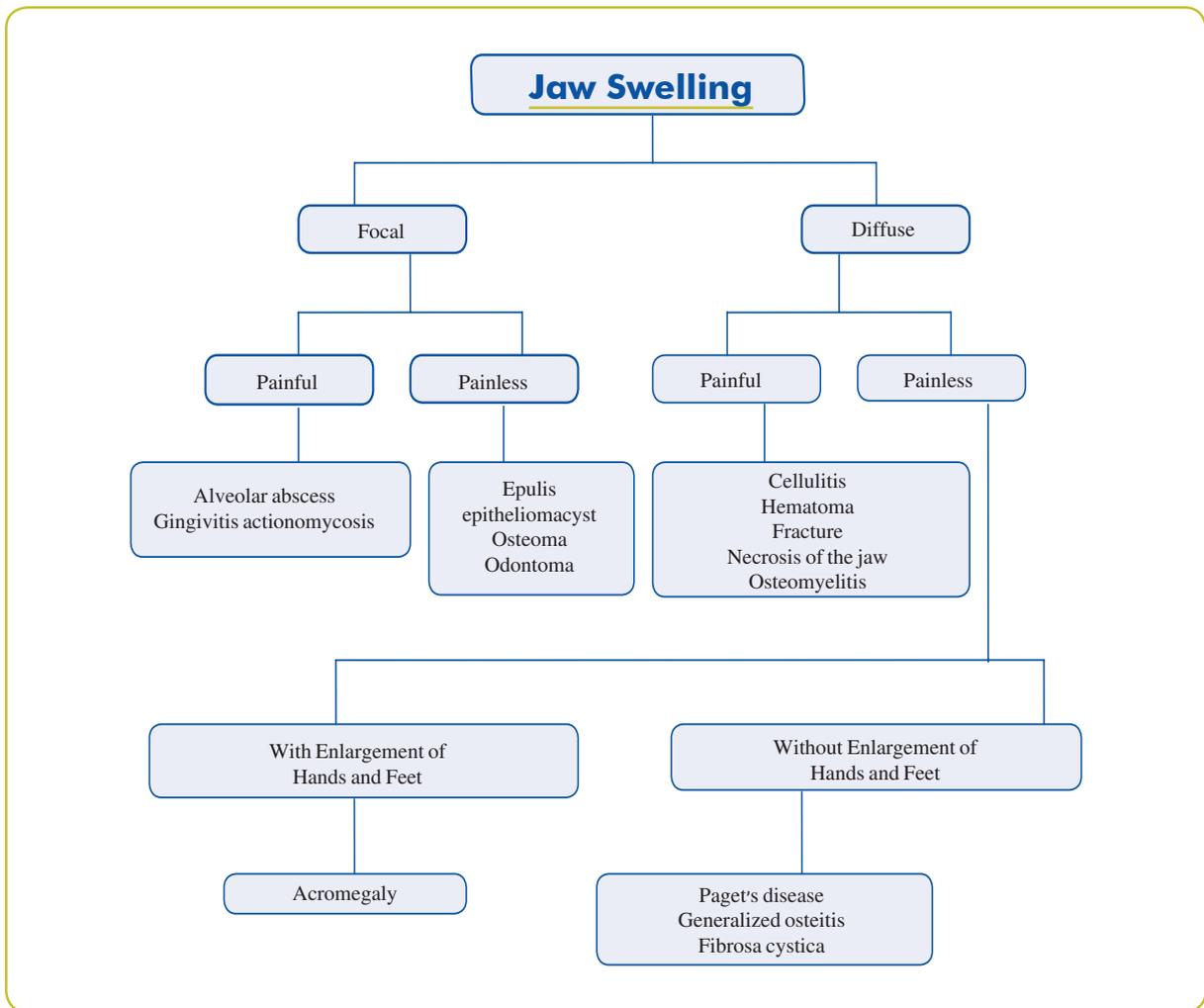


Figure "14": Flow-Chart Diagram for D.D. of Jaw Swelling

Paget's Disease

Osteitis Fibrosa Cystica

Acromegaly

Refer

Focal jaw swelling, refer to dentist

Diffuse jaw swelling, refer to surgeon

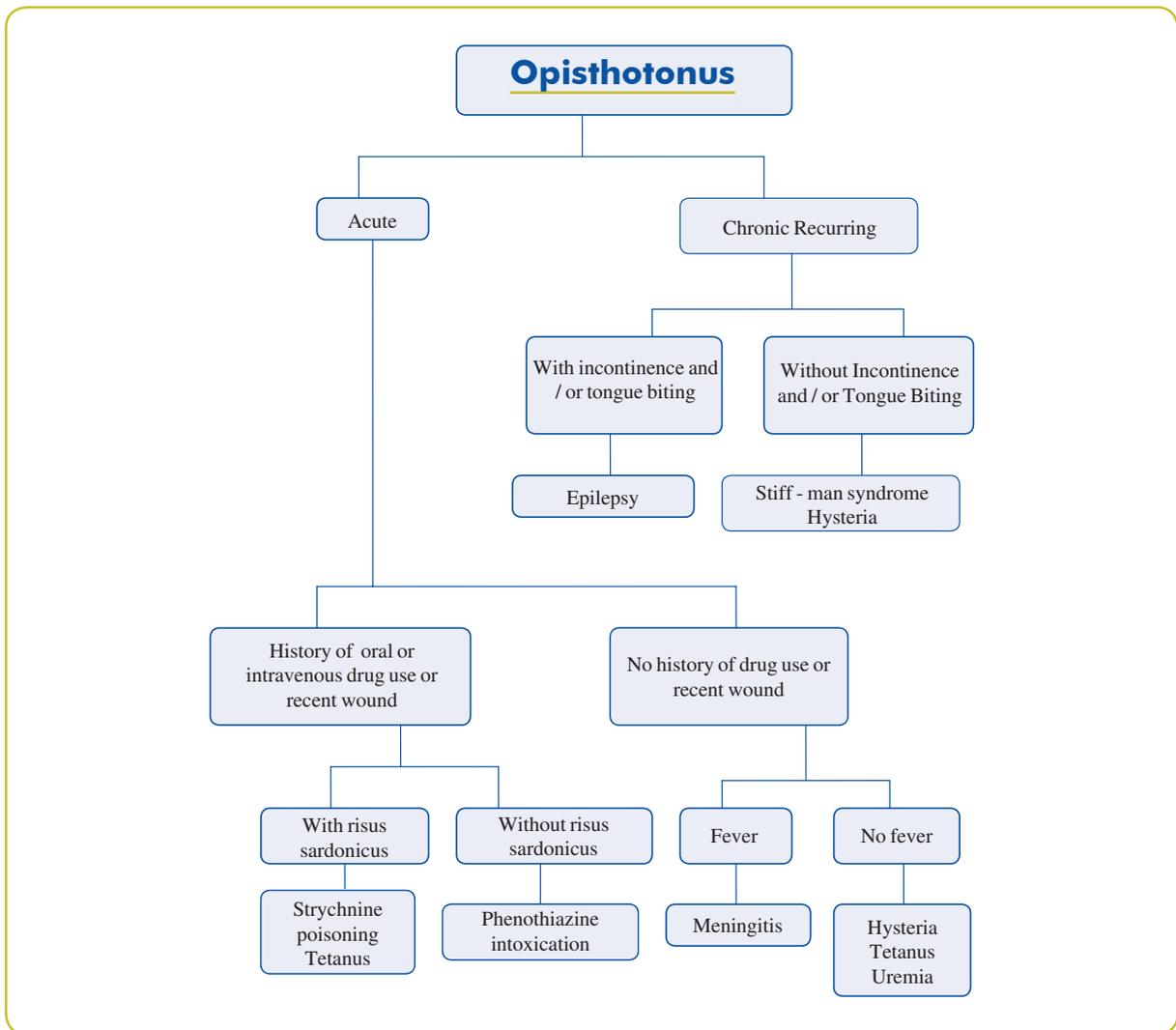


Figure "15": Flow-Chart Diagram for D.D. of Opisthotonus

Refer

Acute Opisthotonus: Refer to Emergency Unit

Chronic Recurrent Opisthotonus:

Epilepsy: In case of epilepsy:

- **Emergency Measures:**
 - o maintain airway patent
 - o Avoid tongue biting
 - o Exclude hypoglycemia
 - o If prolonged seizure >3 min give IV diazepam
- **Avoid Precipitating Factors:**
 - o Pyrexia: in children <5 yrs.

- o Sleep deprivation
- o Photosensitivity: flashing lights or flickering
- o Drugs: tricyclic antidepressants, phenothiazines
- o Withdrawal of anticonvulsant drugs
- o Metabolic abnormalities

Refer for EEG & CT

In case of hysterical seizures: Reassure and refer to a psychiatrist

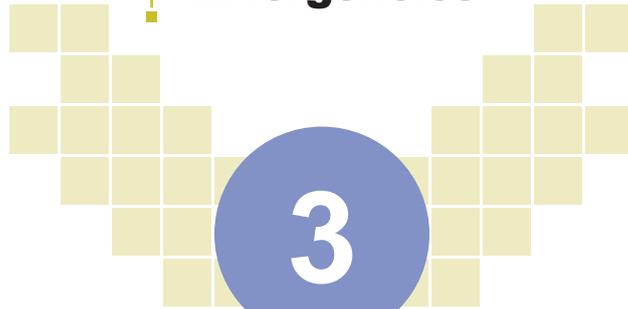
In the other cases refer for proper diagnosis.

Tetanus

Meningitis

Surgical Emergencies

3



Emergency Guidelines for Family Physicians

Topics:

- Basic life support
- Burns & scalds
- Shock
- Hemorrhage
- Fractures
- Domestic accidents
- Acute abdomen
- Intestinal obstruction
- Foreign body airway obstruction (choking)

Basic Life Support:

Definition:

It is the phase of emergency cardiac care that either prevents circulatory or respiratory arrest by prompt recognition and intervention, or externally support with cardiac pulmonary resuscitation (CPR) the circulation & respiration of a victim of cardiac and /or respiratory arrest.

The major objective of CPR is to provide oxygen to brain and other vital organs until appropriate, definitive medical treatment can restore normal heart & ventilation.

The victim whose heart & breathing have stopped for less than 4 minutes has an excellent chance for full recovery if CPR is administered immediately, after 4-6 minutes without circulation, brain damage may occur.

Sequence of Basic Life Support

1. The Assessment Phase (ABC Assessment)

- Airway: to determine unresponsiveness.
- Breathing: to determine breathlessness.
- Circulation: to determine pulselessness.

Assessment also involves observing and interacting with the victim. If unresponsiveness is established, activate the emergency medical system immediately.

2. Activate Emergency Medical System by Calling The Local Emergency Telephone Number.

3. Cardiopulmonary Resuscitation:

CPR includes the basic rescue skills, the victim must be supine and on a firm flat surface to help increase the blood flow to the brain. If the victim is lying face down, the rescuer must roll the victim as a unit "log roll" so that the head, shoulders & torso move simultaneously without twisting.



Figure "16": Position of the Victim

A. Airway

The first action for successful resuscitation is immediate opening of the airway, the tongue and epiglottis

are the most common cause of airway obstruction in the unconscious victim . Since the tongue is attached to the lower jaw , tilting the head back and moving the lower jaw forward to open the airway (head tilt / chin lift maneuver , figures 17&18)

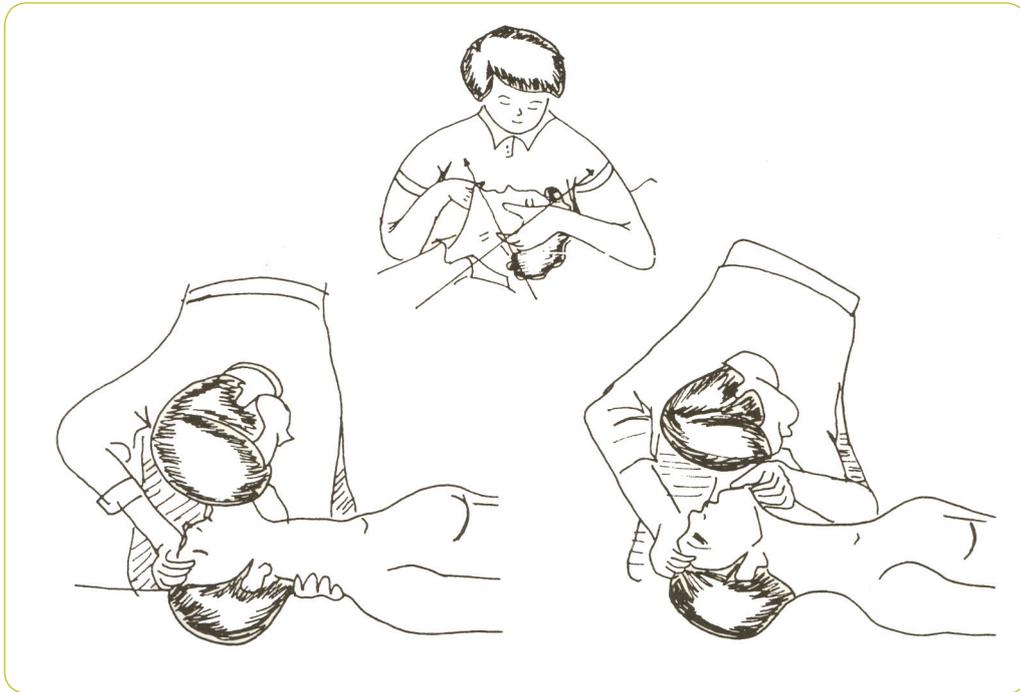


Figure "17": Head tilt and chin lift

Basic Life Support

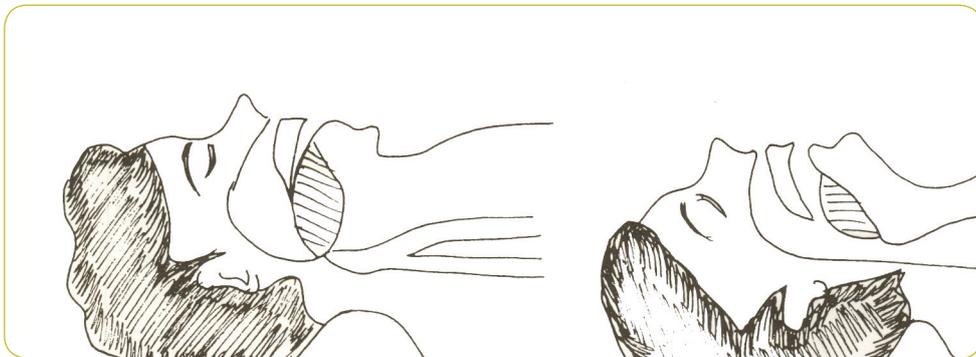


Figure "18": Tongue obstructing airway; opening the airway by head tilt

B. Breathing

When breathing stops , cardiac arrest and death quickly follow . Breathing is assessed by placing your ear over the victim's mouth and nose while maintaining an open airway .

While observing the victim's chest :

- Look ... for the chest to rise and fall
- Listen ... for the air escape during inhalation
- Feel ... for the flow of air

Mouth to mouth breathing is the quickest way to get oxygen into the victim's lung Or mouth to nose breathing , this technique is more effective in some cases than mouth to mouth technique especially when

the mouth can not be opened (trismus) or seriously injured (figures 19 & 20)

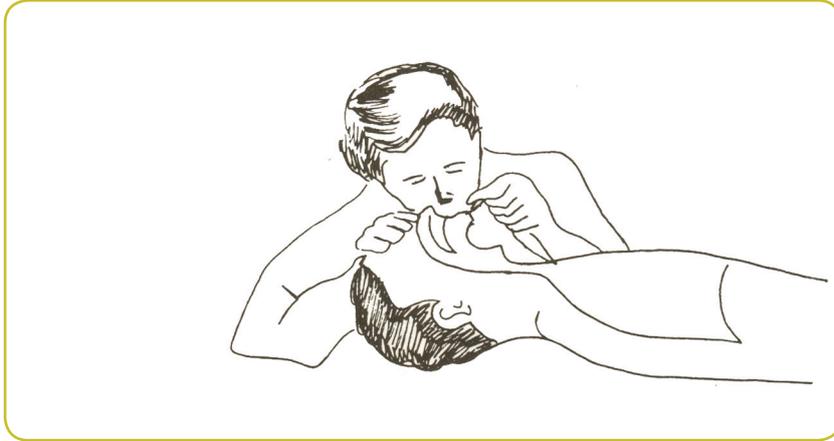


Figure "19": Mouth to Mouth Breathing

Basic Life Support

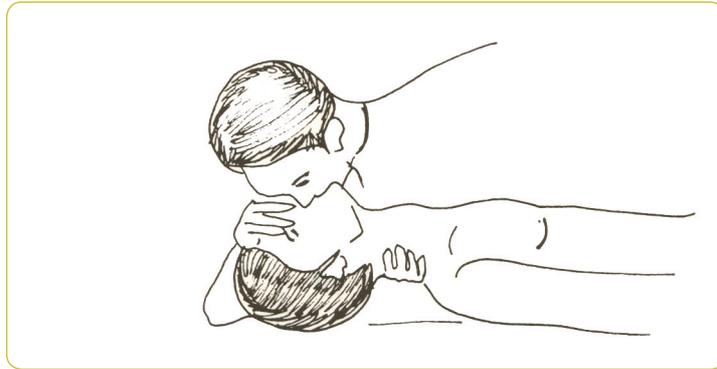


Figure "20": Mouth to nose breathing

C. Circulation

Assessment of circulation to determine pulselessness .

Cardiac arrest is recognized by pulselessness in the large arteries of the unconscious victim (Carotid artery - figure 6).

This assessment should not take more than 5-10 seconds .

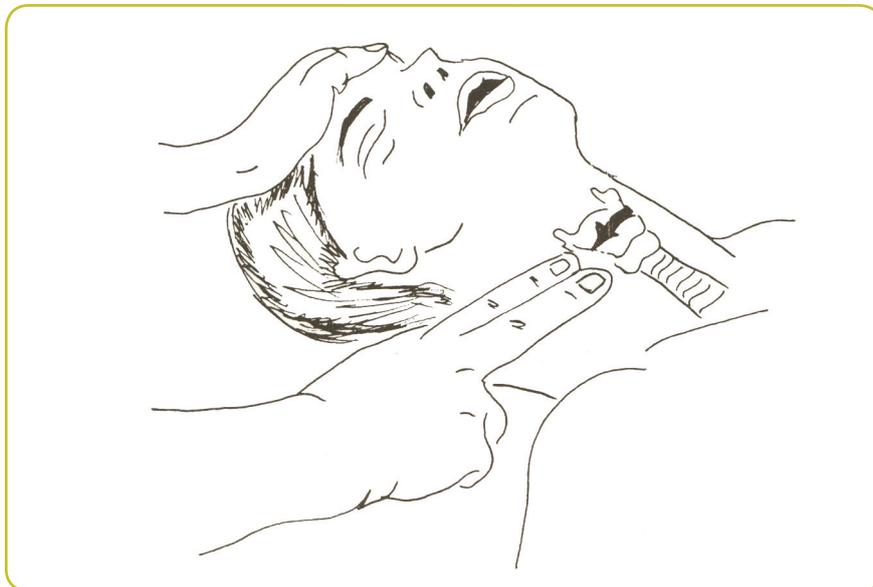


Figure "21": Locating the carotid pulse

The third skill of CPR is chest compression, which replaces the heart beat of the victim. They thus maintain some blood flow to the lung, brain, coronary artery and other major organs. chest compression technique is to compress the heart between the spine and the sternum, which creates pressure in the thoracic cavity as well as direct compression of the heart generating about 20% to 30% of the normal cardiac output (Figure 22, 23, 24 & 25).

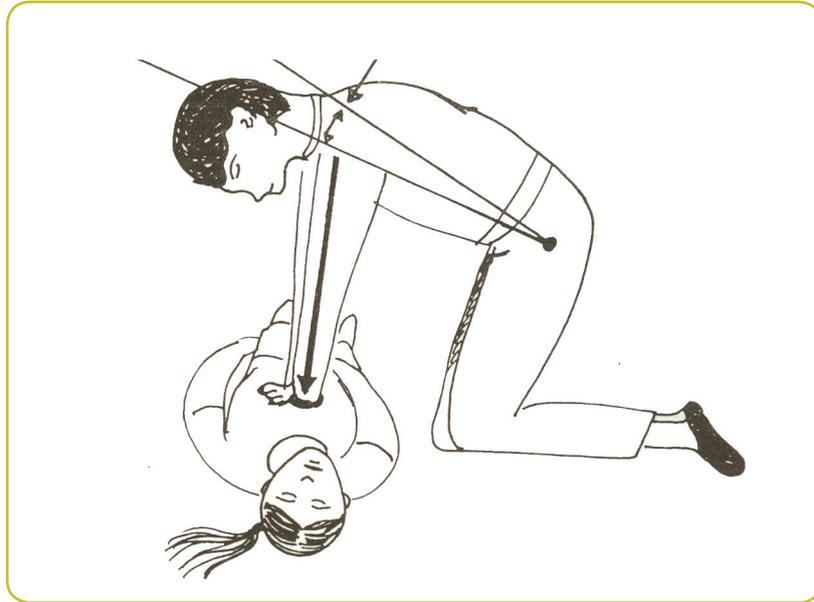


Figure "22" : proper position of rescuer

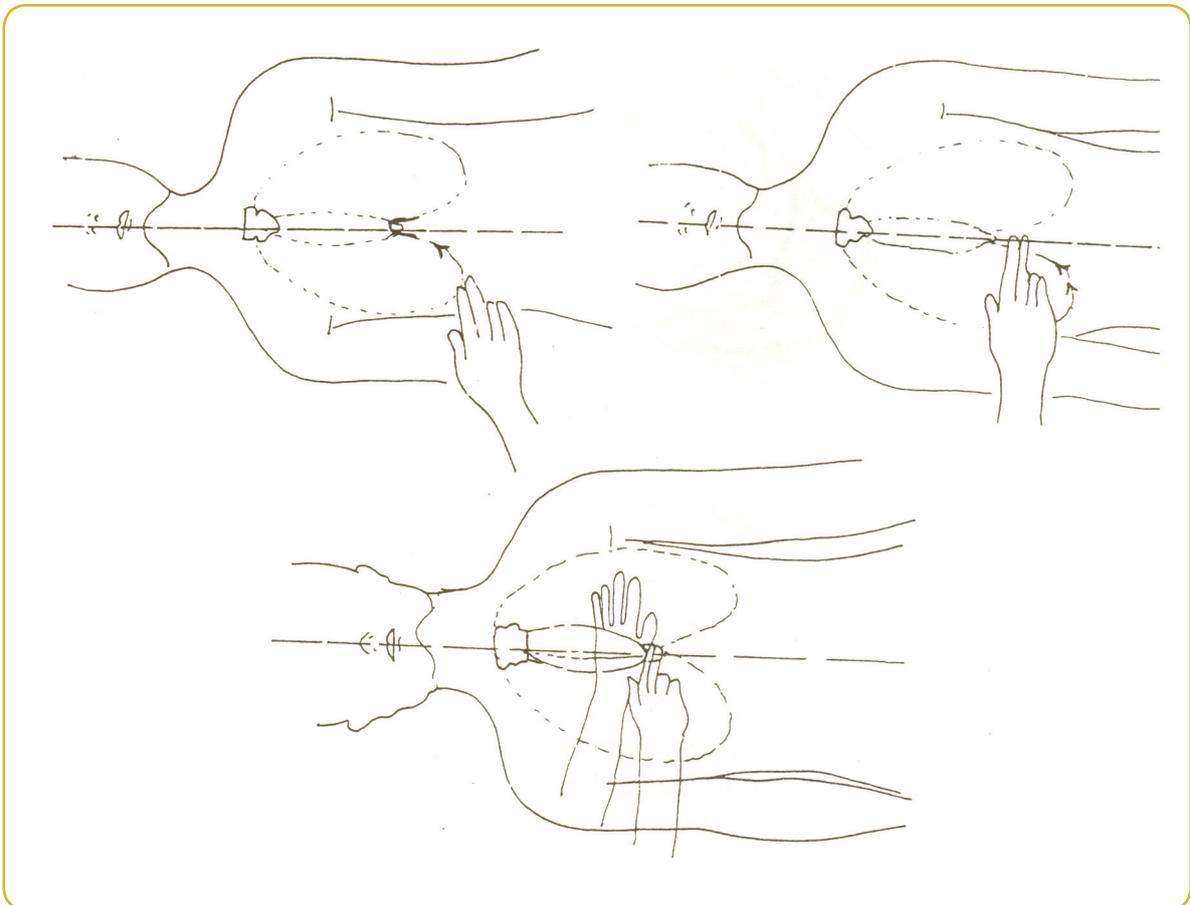


Figure "23": Finding proper hand position

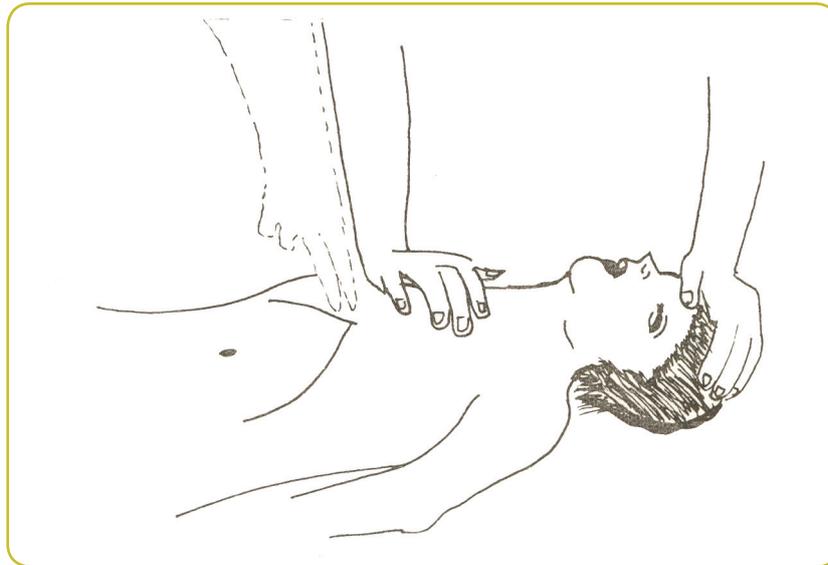


Figure "24": Hand position for external chest compressions

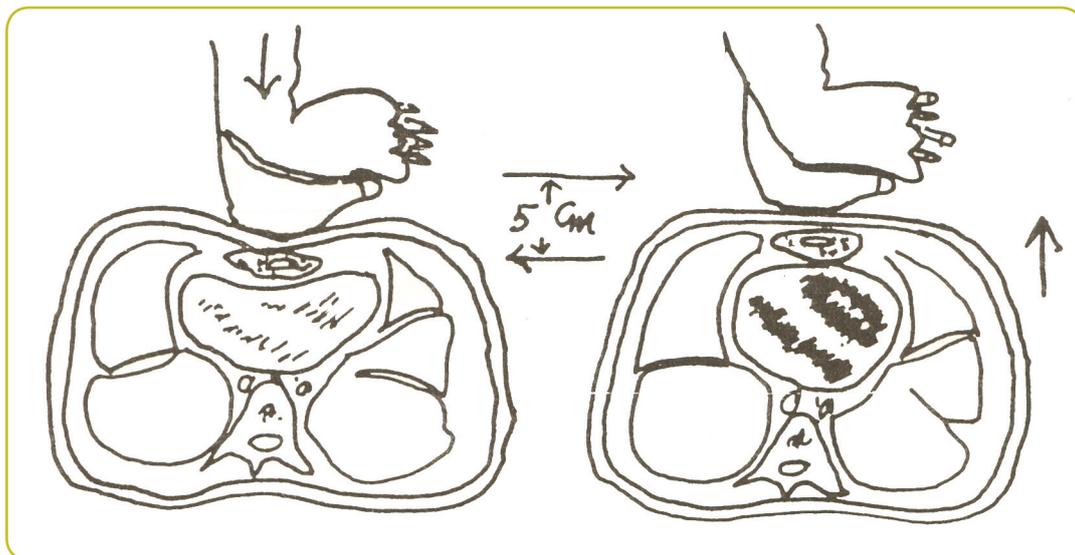


Figure "25": Chest compressions

Two – Rescuer CPR :

One rescuer moves to head, opens the airway and checks the pulse, while the other rescuer locates the area of chest compression and finds the proper hand position, this should take 5 seconds only. If there is no pulse, the ventilator person gives 2 breaths and compression counting 5 times (2 Breaths-5 Compressions).

CPR in Infants and Children :

Cardiopulmonary resuscitation and air way obstruction management for children over 8 years old is the same for the adult. but for small children (from 1-8 years)and

infants (Less than 1 year) there are important differences in techniques as a result of small size and physical immaturity of the age group. These differ in giving breathing (1.0-1.5sec/infantandchild).Chestcompression depth (1.3 to 2.5 cm in infants and 2.5 to 3.8 cm in child). Chest compression in infants is performed with 2 fingers on the lower third of the sternum and in a child with the heel of one hand on the lower third of the sternum.

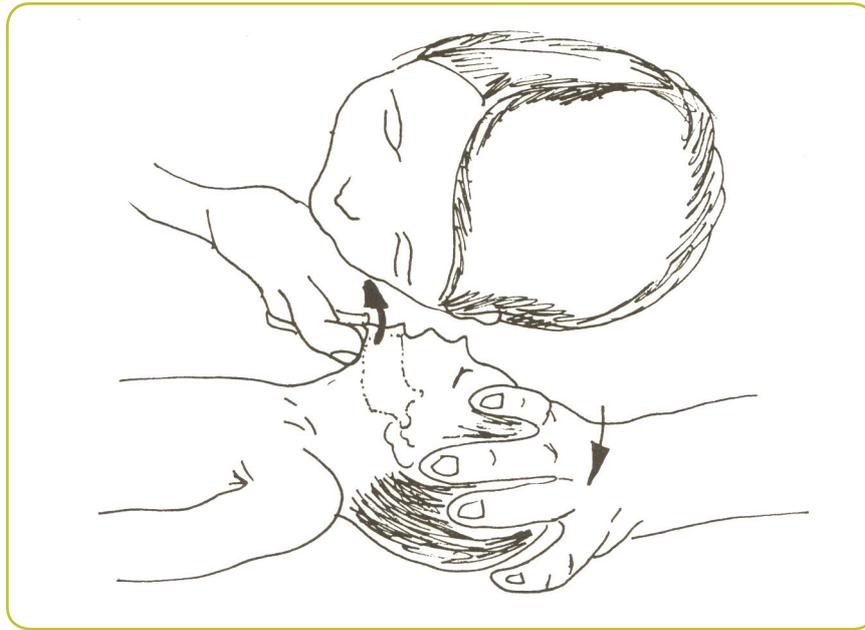


Figure "26": head tilt and chin lift for an infant

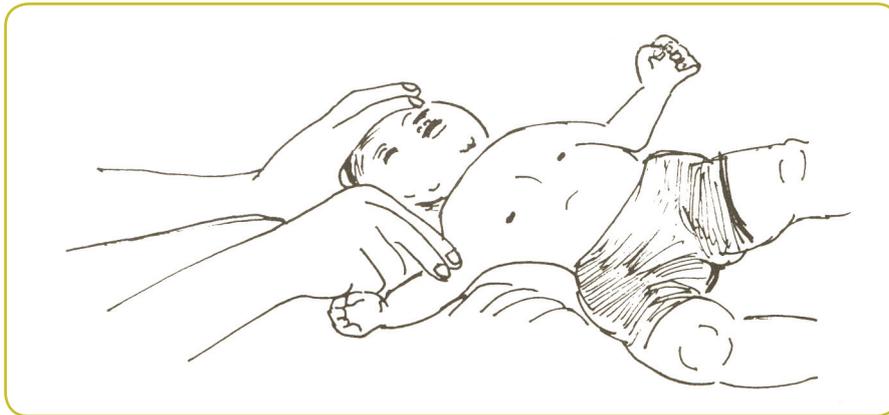


Figure "27": In an infant check for the brachial pulse

Basic Life Support

Respiratory Emergency:

Definition: Respiratory Emergency is that condition where normal breathing stops OR oxygen intake markedly falls that it becomes insufficient to support life.

Causes: Upper air way obstruction can cause unconsciousness and cardiopulmonary arrest. An unconscious victim can develop air way obstruction when the tongue falls backward into the pharynx, regurgitation of stomach contents into the pharynx, bleeding from head and facial injuries may also obstruct the upper airway, particularly if the victim is unconscious. Foreign body airway obstruction usually occurs during eating.

Management of Obstructed Airway :

The Heimlich maneuver (sub diaphragmatic abdominal thrusts) (Figures 11, 12) is recommended for relieving foreign body airway obstruction. By elevating the diaphragm the Heimlich maneuver can force air from the lungs to create an artificial cough intended to expel a foreign body obstructing the airway. Each individual thrust should be administered with the intent of relieving the obstruction. It may be necessary to repeat the thrust multiple times during each sequence to clear the airway.



Figure "28": Heimlich maneuver for conscious-

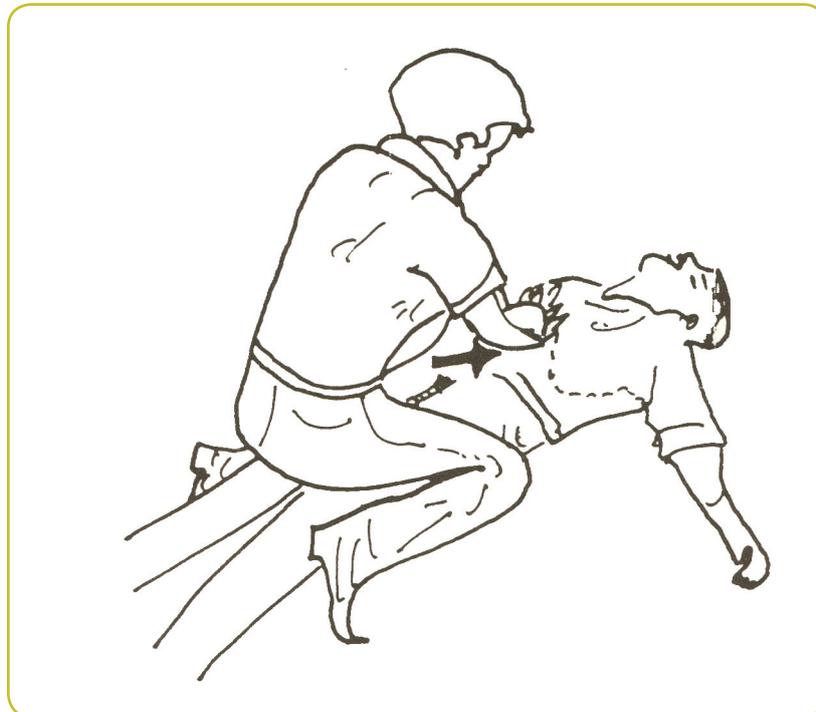


Figure 29 : Heimlich maneuver for unconscious

Summary

Cardiopulmonary Resuscitation (CPR) is a holding action for sudden cardiac or respiratory arrest until more advanced life support care can be made available.

CPR involves a combination of mouth to mouth rescue breathing and chest compression. It keeps some oxygenated blood flowing to the brain and other vital organs until appropriate medical treatment can restore normal heart action. The major factor that influences success is Speed. The

highest success rate has been achieved when PR was started within 4 minutes or less. In order to ensure fast action it is important to recognize the need for immediate action and perform the steps of CPR quickly and efficiently.

Cardiopulmonary Resuscitation includes three basic rescue skills, the ABCs of CPR : Airway, Breathing and Circulation to Assess the Victim's condition and to support life. This table Summaries the variation between Infant, Child, and Adult as regard CPR :

Table. 1: Variation between Infant, Child, and Adult CPR

Item	Infant 0-1 Year	Child 1-8 Years	Adult > 8 Years
Shake and Shout	Yes	Yes	Yes
Call for Help	Yes	Yes	Yes
Position Victim	Yes	Yes	Yes
Open Airway	Yes	Yes	Yes
Look, Listen and Feel for breath	Yes	Yes	Yes
Two breaths	Yes	Yes	Yes
Check Pulse	Brachial	Carotid	Carotid
Activate EMS	Yes	Yes	Yes
Locate Hand Position	Lower third sternum	Lower third sternum	Lower third sternum
Compress with	2-3 fingers	Heal of one Hand	Heal of one Hand other Hand on Top
Compression Depth	1.3-2.5 cm	2.5-3.8 cm	3.8-5 cm
Compression / minute	At least 100	80-100	80-100
Compression / Ventilation Ratio	5-1	5-1	5-2 or 5-1
Breathing	2 breaths 1-1.5 seconds each. 20/minute	2 breaths 1-1.5 seconds each. 20/minute	2 breaths 1.5-2 seconds each. 10- 12/minute

Burns and Scalds

Burn types:

- Scald/ steam
- Contact
- Chemical/ caustic
- Electrical
- Radiation

Clinical Assessment:

- Cause, size, and thickness.
- Use rule of nines.
- Partial thickness burns are painful, red & blistered.[Do not remove or rupture blisters].
- Full thickness burns are painless and white or gray.

Rule of Nines:

palm	1%
arm(all over)	9%
leg (all over)	18% (14%children)
front	18%
back	18%
head(all over)	9% (14% children)
genitals	1%

Action

- Ignore areas of erythema only.
- Remove clothes from affected area.
- Place under cold running water for 10 minutes or until pain is relieved.
- Do not burst blisters.
- Give analgesia.
- Check tetanus immunity give immunization and/or prophylaxis as necessary.
- Apply silver sulfadiazine or sterile Vaseline -

impregnated gauze and non adherent dressing and follow up, every 1-2 days (for healing & infection).

Refer

Refer The Following Cases:

1. Cases of more than 10% -children or 15%adults.
2. Burns affecting: face (eyes & ears), neck, both hands, both feet & perineum.
3. Type of burn: electrical, chemical & smoke inhalation.
4. Presence of associated injuries: soft tissue trauma, fractures & head injury.
5. Presence of medical problems: diabetes, heart disease, pulmonary disease & ulcer history.
6. Social problems such as suspected child abuse or neglect, self inflicted burns & psychological problems.

Prevention of Scalds & Burns

Health education is very important (in occupational & domestic accidents)

Domestic Accidents

- The leading causes of accidental deaths & injuries in the home for all age groups are:

- Falls
- Fires
- Burns
- Poisoning
- Suffocations

- All age groups are affected but children &

elderly are more susceptible (Risk group).

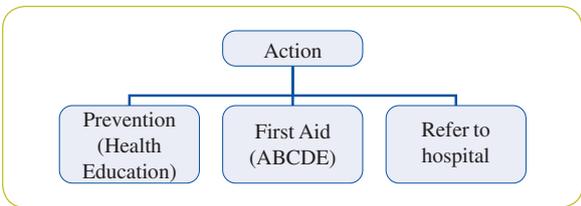
- Risk factors for accidents in the elderly group:

- Chronic illness
- Neurological abnormalities
- Psychological disturbances
- Poly pharmacy
- Visual impairment
- Osteoporosis
- Gait abnormalities

Domestic Accidents may present as :

Wounds, burns, scalds, fractures, eye injuries, shock, hemorrhage etc...

Action :-



Shock

Definition: the presence of inadequate tissue perfusion & oxygenation.

Compensated shock	Uncompensated shock
Vital organ perfusion is maintained by compensatory mechanisms	Associated with impairment of tissue perfusion when compensatory mechanisms fail

Types of Shock:

- Hypovolemic shock
- Cardiogenic shock
- Tension Pneumothorax
- Neurogenic shock
- Anaphylactic shock
- Septic shock
- Endocrinal shock

Recognizing Shock
Clinical findings
Vital signs
Peripheral perfusion
Color
Mental status
No reliable laboratory tests

Hypovolemic shock:

Caused by diminished blood volume secondary to loss of:

- blood, as in external or internal hemorrhage

(hemorrhagic shock)

- plasma, as in burns and peritonitis
- fluids, as in severe vomiting, diarrhea, intestinal obstruction or in a high output intestinal fistula.

Recognizing Shock
Hemorrhagic Shock
 Most common in trauma
 Not common in isolated head injury
 Aggressive management improves outcome

Recognizing Shock
Cardiogenic shock
 Myocardial dysfunction
 Cardiac tamponade

Recognizing Shock
Tension pneumothorax
 Clinical diagnosis
 Emergent needle decompression

Recognizing Shock
Neurogenic Shock
 Loss of sympathetic tone
 Hypotension without tachycardia
 No cutaneous vasoconstriction

Recognizing Shock
Septic Shock
 Uncommon in acute trauma
 Warm skin
 Wide pulse pressure

Management:

Shock Management
 Airway
 Breathing
 Circulation
 Disability
 Exposure

Shock Management
 Circulation
 Control external bleeding
 Obtain vascular access
 Fluid resuscitation(isotonic electrolyte solution- Ringer's lactate-Normal saline
 Adult 1-2 liters
 Children 20 ml/kg

Do ABCs and transfer into emergency unit in nearest hospital.

Hemorrhage

Definition: It is the escape of blood from a vessel damaged by injury or disease.

Types of Hemorrhage:

1. Traumatic hemorrhage
 - primary occurs immediately after trauma
 - secondary is complication of sepsis
 - reactionary occurs within the first 24 hrs, after cessation of the primary
2. Pathological hemorrhage
 - inflammatory, neoplastic, etc.
3. Spontaneous hemorrhage
 - defect in haemostatic mechanisms

Clinical types

Internal bleeding (concealed) e.g.	External bleeding (revealed) e.g.
<ul style="list-style-type: none"> • intracranial • haemothorax • haemoperitoneum • haemopericardium • retroperitoneal 	<ul style="list-style-type: none"> • wound • ulcer • fungating tumor • from natural orifice: <ul style="list-style-type: none"> o Epistaxis • Haemoptysis • Haematemesis • Haematuria <ul style="list-style-type: none"> o Melaena • Metrorrhagia

Management of hemorrhage:

Among all surgical emergencies, hemorrhage constitutes the most urgent problem as it rapidly threatens the patients' life & predisposes to serious local & general complications.

The principles of management of all forms of hemorrhage consist simply of:

- Immediate control of bleeding (stop hemorrhage)
- Timely replacement of the lost blood (restore blood volume)

In practice, the management of bleeding from external wound consists of 3 phases:

First-aid treatment: 3 P's

(Packing, Pressure & Position)

- Digital compression
- Pressure bandage or by sphygmomanometer
- Elevation of the limb above the level of the heart

1. Resuscitation by anti- shock measures
2. Definitive control of bleeding by operation.

Choking

1. Choking-Adult

If blockage of airway is only partial, the victim can usually be able to dislodge the foreign body by coughing, but if obstruction is complete urgent intervention is required to prevent asphyxia.

Conscious Adult:

Carry Out Back Blows:

- Stand beside & slightly behind the victim
- Support the chest with one hand & lean the victim forewards
- Give up 5 sharp blows between the scapulae with the heel of the other hand; each blow should be aimed to relieve the obstruction
- If the back blows fail, carry out abdominal thrusts.

Give 5 Abdominal Thrust (Heimlich Maneuver):

- Stand behind the victim
- Wrap your arms around victims waist
- Make a fist with one hand & place the thumb side just above victim's navel & below the tip of the sternum (xiphoid process)
- Grasp fist with your other hand
- Press fist into victim's abdomen with quick upward thrusts
- Each thrust should be a separate& distinct effort to dislodge the object
- After every 5 abdominal thrusts check the victim's mouth, coughs up object, or start to breath or cough forcefully.



Unconscious Adult:

A -Give up to 5 abdominal thrusts with the victim supine on the floor:

- Straddle victim's thighs
- Put heel of one hand against middle of victim's abdomen slightly above navel & well below sternum notch (fingers of hand should point towards victim's head)
- Put other hand directly on top of the first hand
- Press inward & upward using both hands with up to 5 quick abdominal thrusts
- Each thrust should be distinct & a real attempt made to relieve the airway obstruction.
- Keep the heel of hand in contact with abdomen between thrusts.

B-Perform finger sweep:

- Use your thumb & fingers to grasp victim's jaw & tongue, lift the tongue away from back of throat & away from the foreign body
- Or use cross finger method by crossing the index finger & thumb and pushing the teeth apart.
- With index finger of other hand, slide finger down along the inside of one cheek deeply into mouth & use a hooking action across the

other cheek to dislodge foreign object

- If foreign body comes within reach, grab & remove it, do not force object deeper

C- Sequence the cycle:

- Give 2 rescue breaths
- Do up to 5 abdominal thrusts
- Finger sweep

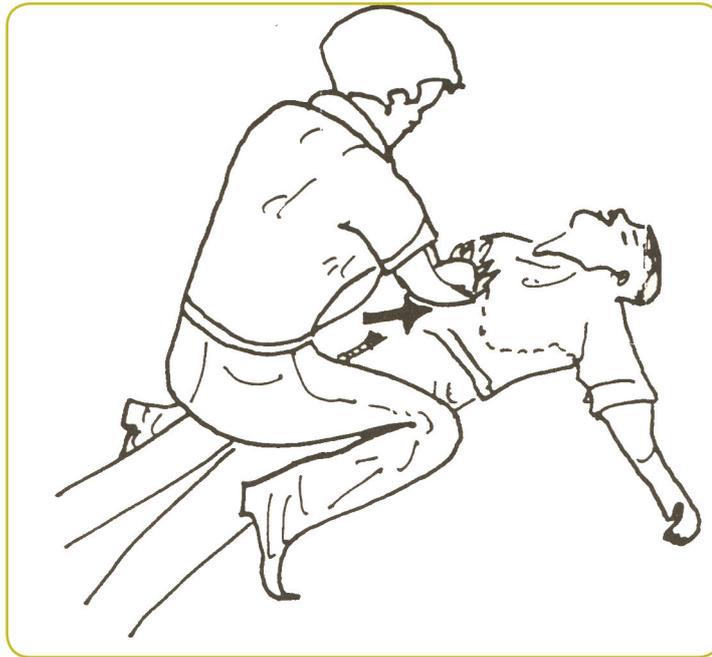
Choking- Child

(1-8 years)

- Look into mouth
- Remove foreign body only if seen with finger sweep
- Give up to 5 abdominal thrusts (Heimlich maneuver)

Choking Infant

(Under 1 year)



Note

A. If Infant is Conscious: (Can Cough, Breathe or Cry)

1. Shout for help
2. Give up to 5 back blows:
 - Lay infant face down over your forearm with head lower than his/her chest
 - Brace your forearm & infant against your thigh
 - Give up to 5 distinct & separate back blows between shoulder blades by the heel of your hand
3. Give up to 5 chest thrusts
By supporting the back of infant's head & start CPR
4. Repeat:
 - up to 5 back blows
 - up to 5 chest thrusts

Note

B. If Infant is Unconscious:

1. Give 2 slow breaths
 - Open the airway with head-tilt/ chin lift method
 - Seal your mouth over the infants mouth & nose
 - Give 2 slow mouth to mouth breaths 1-1½ seconds each
2. Activate emergency medical system for help
3. Give up to 5 back blows
4. Give up to 5 chest thrusts
5. Check mouth for foreign body (if object is seen use finger sweep)
6. Repeat the cycle until help arrives or object is expelled.

Fractures & Extremity Trauma

Identify

- Life threatening injuries
- Limb threatening injuries
- Disabling injuries
- Less serious injuries

How life threatening?

- Associated injuries
- Hemorrhage
- Crush syndrome
- Overwhelming infection
- Multiple injuries could add to risk of multi- system organ failure

How limb threatening?

- Vascular injury
- Compartmental syndrome
- Complete disorganization

Attention

- Documentation is important
- Do not allow the limb injury distract you, There may be a more serious & important injury
- Remember occult injuries
- Set priorities in assessment & management
- Activate Emergency medical system

Primary survey & Resuscitation

- Airway
 - Breathing
 - Circulation
 - Disability
 - Exposure
 - Splint
 - Restore distortion
 - Wound care
 - Refer to emergency unit of the nearest hospital
- NB:** X ray is not always urgent

Intestinal Obstruction

Intestinal obstructions is a common surgical emergency, because of its serious nature, it demands early diagnosis & speedy relief

Types:

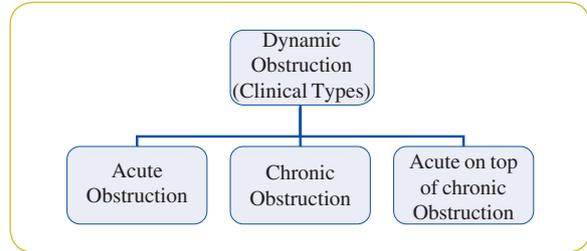
A Dynamic Obstruction

Peristalsis ceases & no propulsive waves occurs

Dynamic Obstruction

Peristalsis is working against obstructing agent (in the lumen, the wall or outside the wall)

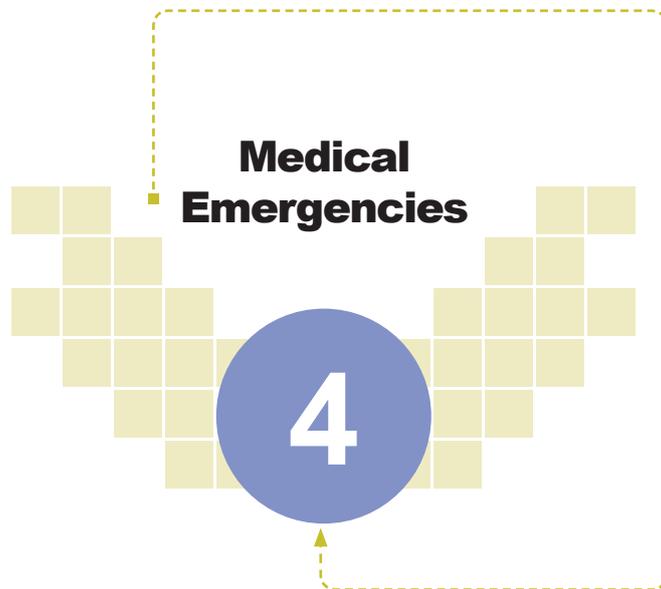
Clinical Types:



- Acute intestinal obstruction favors small gut, with immediate central severe, colicky abdominal pain, early vomiting, central distension, and constipation.
- Chronic obstruction favors the large bowel, with lower abdominal colic at first & absolute constipation. Distension comes later, and involves the periphery.
- Acute on top of chronic obstruction; spreads from the large bowel to involve the small intestine. It gives rise to pain & constipation on a variable time scale, later followed by general distension & vomiting.

Refer

- Refer all cases of intestinal obstruction to nearest hospital.



Management of Medical Emergencies

Unconsciousness and Coma

- Glasgow coma scale
- Disturbed level of consciousness
- Delirium
- Syncope
- Convulsions
- Stridor
- Abdominal pain: Acute

Unconsciousness and Coma

- Consciousness means a state of wakefulness with awareness of self and surroundings.
- Clouding of consciousness means reduced wakefulness and/or self-awareness.
- Confusion is the state of altered consciousness

in which the subject is bewildered and misinterprets his or her surroundings.

- Sleep is the state of normal mental and physical inactivity from which the subject can be aroused.
- Stupor is an abnormal, sleepy state from which the subject can be aroused by stimuli, applied vigorously or repeatedly.
- Delirium is a state of high arousal in which there is confusion and often visual hallucination.
- Coma is a state of unarousable unresponsiveness (The Glasgow coma Scale for grading coma).
- Syncope (drop attack) is a transient loss of consciousness (fall to ground) for less than 2 minutes and recovered when patient lies down.
- Glasgow Coma Scale

Table. 2: Glasgow Coma Scale

Eye opening (E)	Score	Verbal response (V)	Score
Spontaneous	4	Orientated	5
To speech	3	Confused conversation	4
To pain	2	Inappropriate words	3
No response	1	Incomprehensible sounds	2
		No response	1
Motor response (M)			
Obeys	6		
Localizes	5		
Withdraws	4		
Flexion	3		
Extension	2		
No response	1		
Glasgow Coma Scale = E + M + V (GCS minimum = 3 : maximum = 15)			

Disturbed level of consciousness (Coma or Stupor)

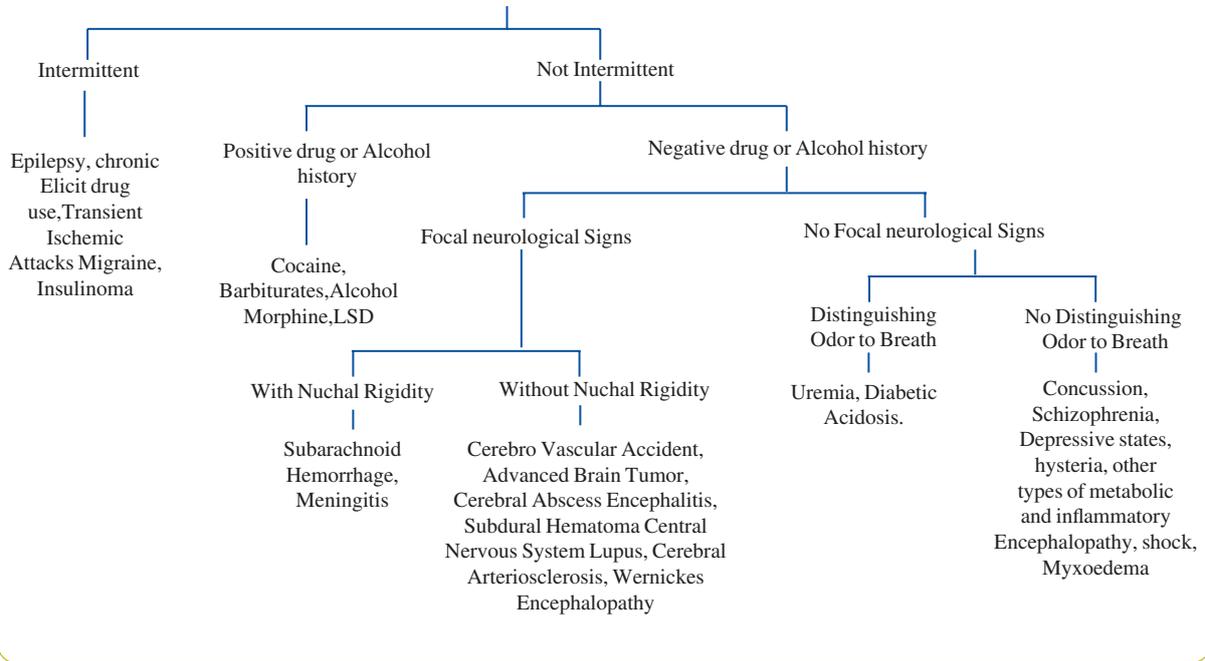


Figure "30": Flow-Chart Diagram for D.D. of Coma or Stupor

Disturbed Level of Consciousness

- First you have to exclude hypoglycemia.
- If you suspect hypoglycemia give oral or IV glucose

Coma:

is a state of unarousable unresponsiveness (The Glasgow coma Scale for grading coma).

Stupor:

is an abnormal, sleepy state from which the subject can be aroused by stimuli, applied

vigorously or repeatedly.

Note

After exclusion of hypoglycemia, in all patients examine & assess Glasgow Coma Scale

- Ensure patent airway
- Put IV line with 5% glucose to keep veins open
- Refer to emergency unit

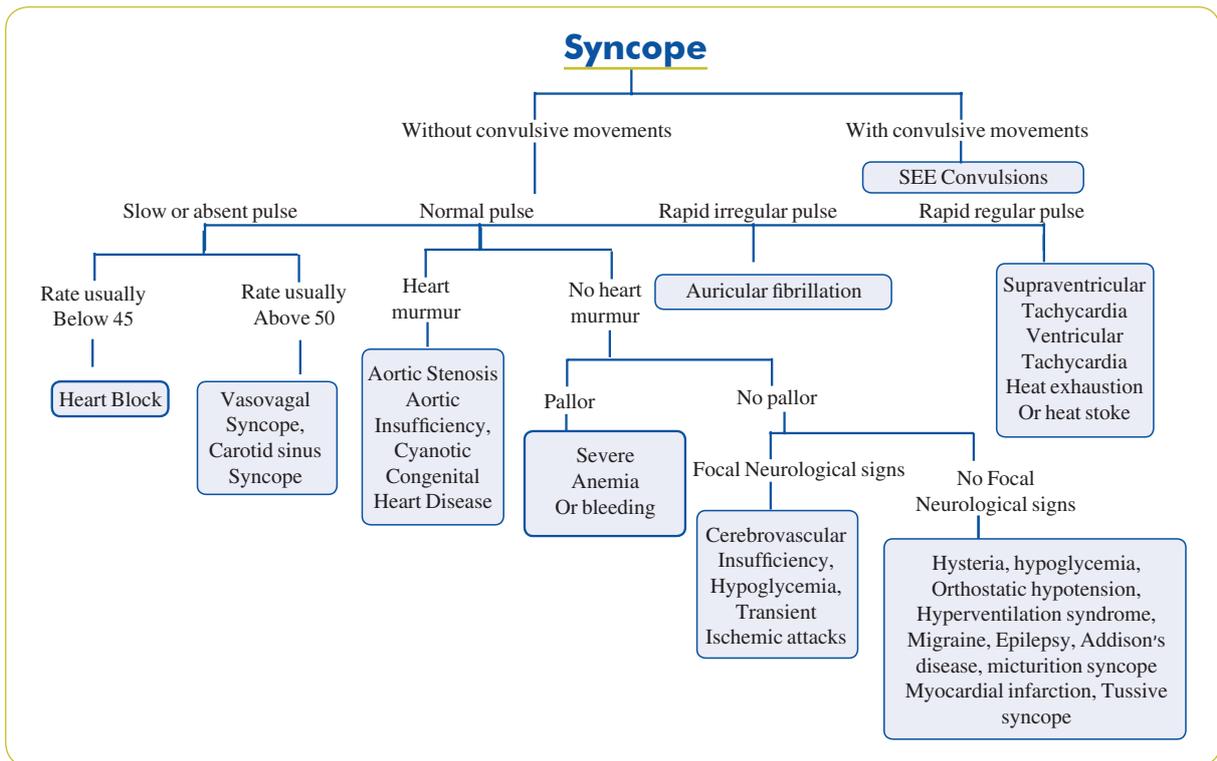


Figure "31": Flow-Chart Diagram for D.D. of Syncope

Syncope:

(drop attack) is a transient loss of consciousness (fall to ground) for less than 2 minutes and recovered when patient lies down.

Immediate management:

lay patient down & lift legs, Patient will recover consciousness

Then refer for further evaluation

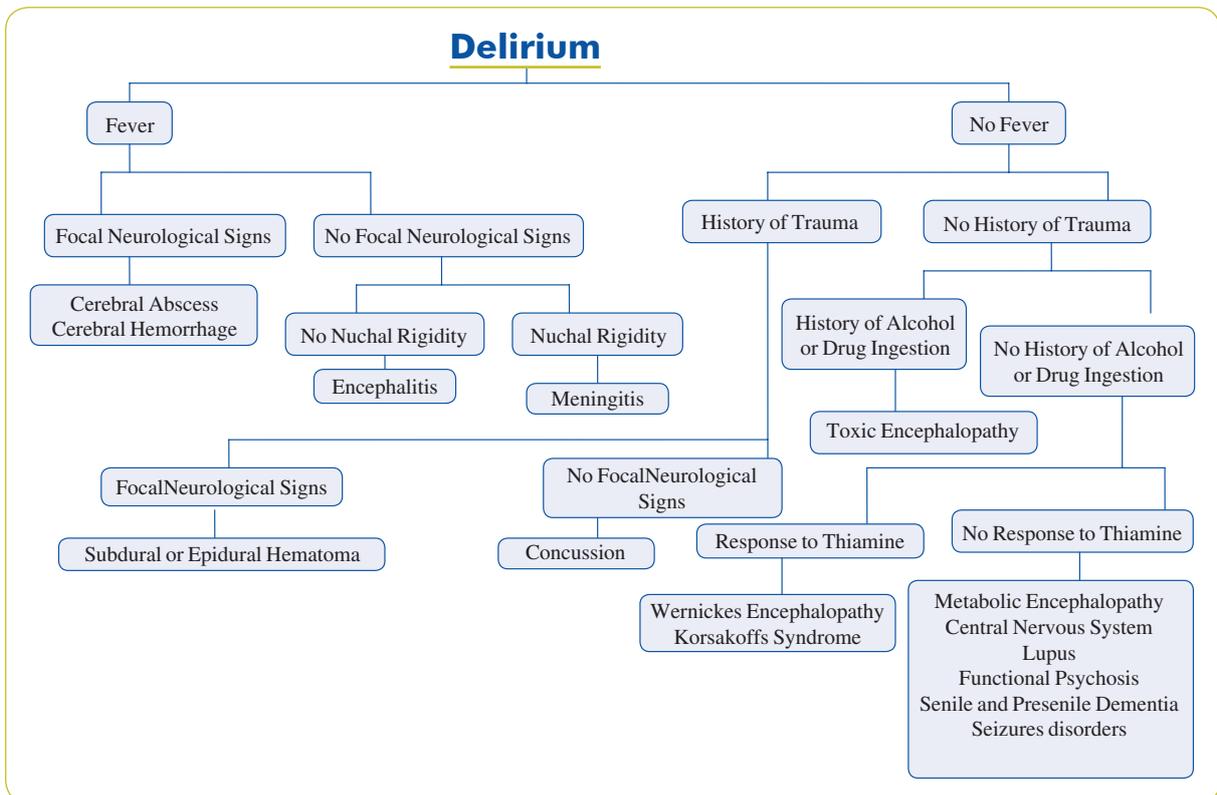


Figure "32": Flow-Chart Diagram for D.D. of Delirium

Delirium

Delirium is a state of high arousal in which there is confusion and often visual hallucination.

After exclusion of hypoglycemia, in all patients examine & assess Glasgow Coma Scale

Ensure patent airway

Put IV line with 5% glucose to keep veins open

Refer to emergency unit

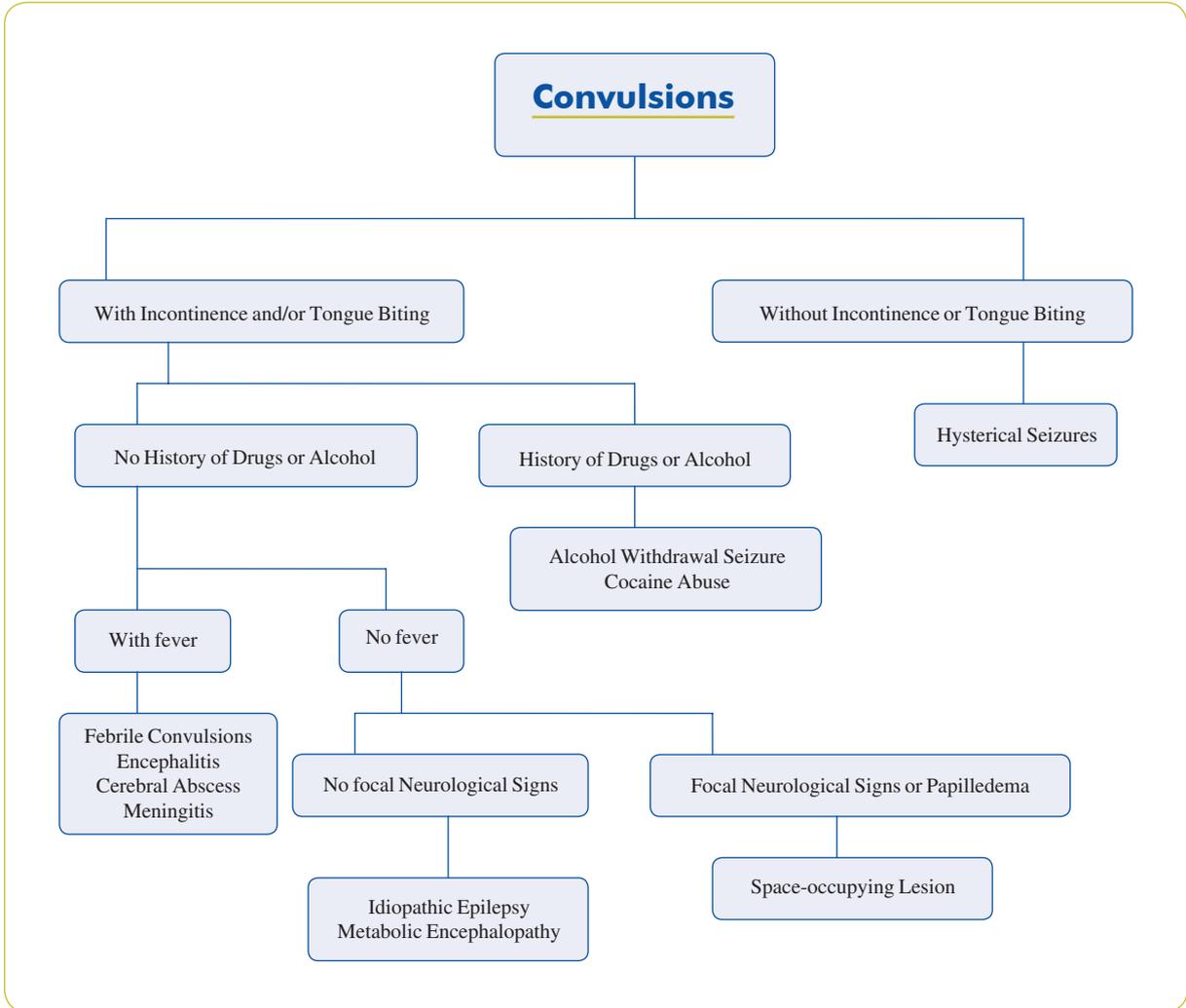


Figure "33": Flow-Chart Diagram for D.D. of Convulsions

In Case of Epilepsy:

Note

Emergency Measures:

- Maintain airway patent
- Avoid tongue biting
- Exclude hypoglycemia
- If prolonged seizure >3 min give IV diazepam

- Sleep deprivation
- Photosensitivity: flashing lights or flickering
- Drugs: Tricyclic Antidepressants, Phenothiazines
- Withdrawal of anticonvulsant drugs
- Metabolic abnormalities

Refer for EEG & CT

In Case of Hysterical Seizures:

Reassure and refer to a psychiatrist

In the other Cases Refer for Proper Diagnosis.

Avoid Precipitating Factors:

- Pyrexia: in children <5 yrs.

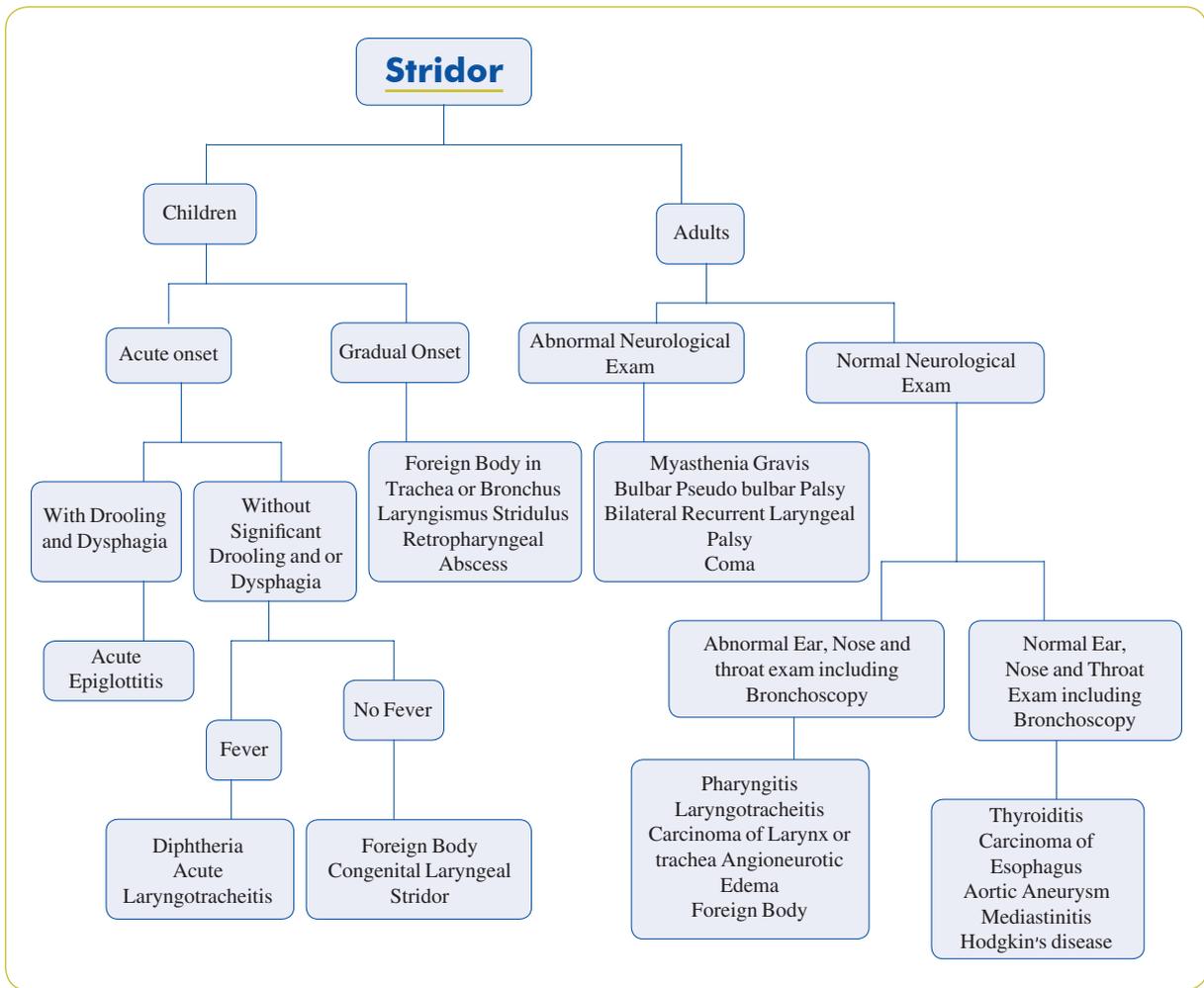


Figure "34": Flow-Chart Diagram for D.D. of Stridor

Stridor: is difficulty in respiration (inspiratory) or due to pathology in upper respiratory tract.

Note

Management:

- Give oxygen
- Insert IV line
- Give IV Corticosteroid
- Refer immediately to emergency unit

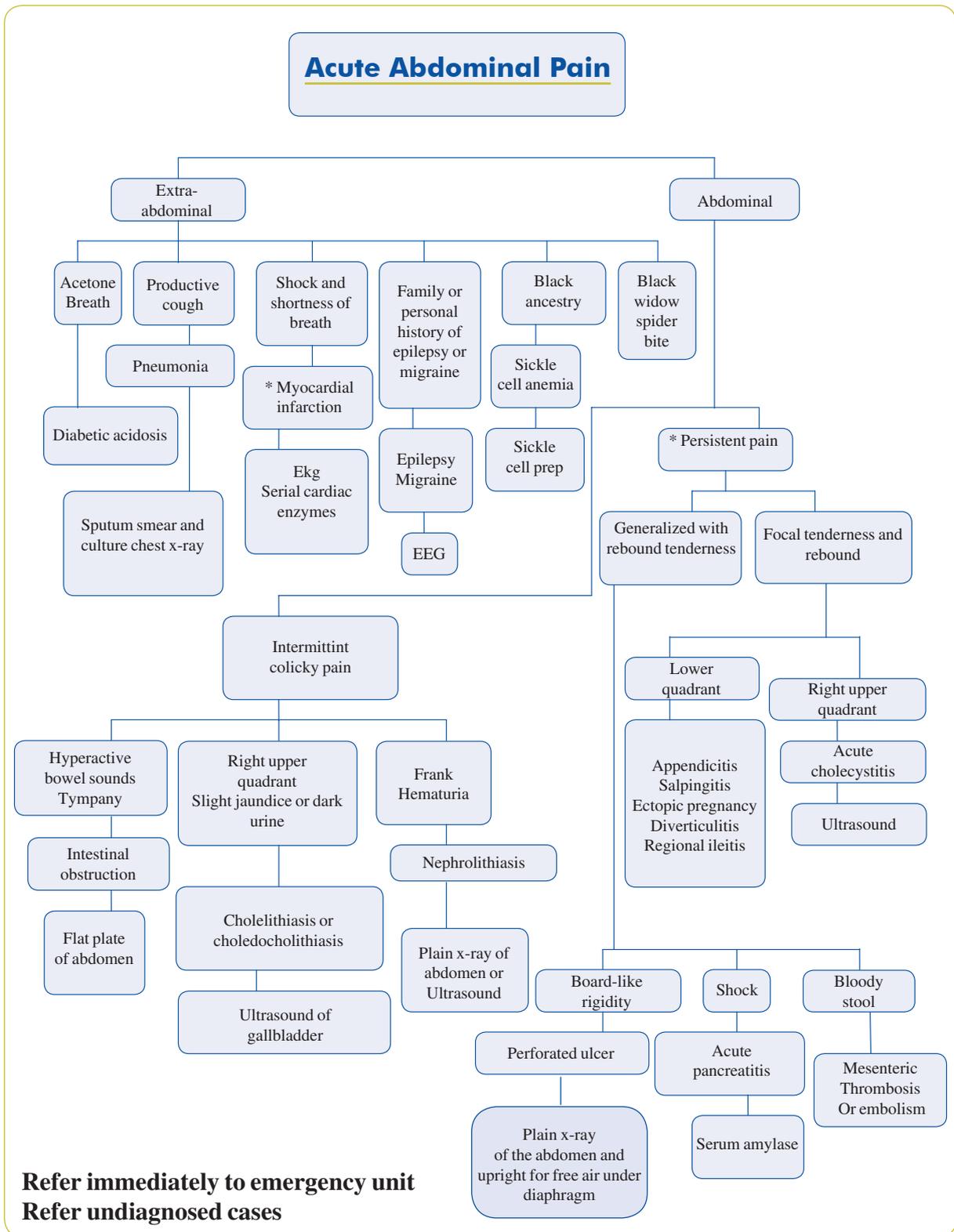


Figure "35": Flow-Chart Diagram for D.D. of Acute Abdominal Pain

Acute Abdominal Pain

In medical causes of acute abdomen there is NO rigidity or rebound tenderness.

N.B. Familial Mediterranean Fever is characterized by recurrent attacks of

- Fever
- Arthritis: monoarticular

- Serositis: abd.pain due to peritonitis or pleurisy
- Attacks last for up to 1 week

Refer to confirm diagnosis

Appendicitis produces more gradual onset of pain and pain may be made worse by movement.

Vomiting may accompany any acute abdominal pain but, if persistent, it suggests an obstructive lesion of the gut.

All other cases with rigidity and /or rebound tenderness should be referred to surgical emergency unit.

Other rare medical Cause of Acute Abdomen are acute porphyria and familial hypertriglyceridemia.

Refer A sudden onset of severe pain suggests:

- Perforation e.g. duodenal ulcer
- Rupture e.g. of an aneurysm
- Torsion e.g. of an ovarian cyst
- Acute pancreatitis

Refer immediately to emergency unit

Colicky pain can be due to an obstruction of Gut

- Biliary system
- Urogenital system
- Or uterus.

These will probably initially require conservative management along with analgesics and antispasmodic.

If colicky pain changed into constant pain → inflammation supervene. This will be supported by:

- Raised temperature.
- Tachycardia
- And/or raised white cell count

Add broad spectrum antibiotics, IV line and transfer to emergency unit

Back Pain Suggests:

- Pancreatitis
- Rupture of an aortic aneurysm

- Renal tract disease
- **Diabetic Ketoacidosis** (refer to Diabetic section)
- **Myocardial infarction:** refer to chest pain & IHD section
 - o Give sublingual nitrate tablet every 5 min for 3 tablets
 - o Chew aspirin tablet
 - o Refer to emergency unit
- **Sickle Cell Crisis:**
 - o IV fluid
 - o Oxygen
 - o Antibiotics
 - o Adequate analgesia
 - o After attack give pneumococcal vaccine
 - o Hemophilis influenza vaccine
 - o Refer to further evaluation

Scorpion Bite:

1. analgesic
2. antivenom

Snakes Bite :

1. observation for 12-24h
2. no excision of bite area
3. no arterial tourniquet
4. diazepam for anxiety
5. I.V fluids & volume expander for hypotension
6. Antivenoms as early as possible by slow IV
7. usually these is allergy adrenalin (1 in 1000) & continue antivenoms
8. antibiotic of wound is infected
9. antitetanus prophylaxis

Tetanus:

1. clean wound & debridment
2. give tetanus Ig 250u + tetanus toxoid "booster"
3. if not vaccinated before: give tetanus toxoid:

day zero	0.5ml IM
8 wks	0.5ml IM
6-12 m	0.5ml IM

 boosterevery 5 years



Food Poisoning

Disease of an infective or toxic nature caused by consumption of food and water

Food poisoning may also be caused by organic & non-organic toxins.

Table 3: Bacterial Causes of Food Poisoning:

Organism	Source	IP	Symptoms	Diagnosis	Recovery
Staph.aureus	Contaminated food & water	2-4 h	Diarrhea, vomiting & dehydration	Culture organism in vomitus of food	< 24 h
E.coli	Cattle meat, milk	12-48 h	Watery diarrhea (± bloody diarrhea)	Stool culture	10-12 days
Bacillus cereus	Contaminated food	1-6 h	Diarrhea, vomiting & dehydration	Culture organism in faeces and food	Rapid
Clostridium perfringes	Contaminated food	8-22 h	Watery diarrhea & cramping pain	Culture organism in faeces and food	2-3 days
Clostridium botulinum	Bottled or canned food	18-24 h	Neuromuscular paralysis	Demonstrate toxin in food or faeces	10-14 days
Salmonella	Cattle and poultry eggs, meat	12-48 h	Diarrhea, vomiting & fever	Stool culture	3-6 days, up to 2 weeks
Campylobacter	Cattle and poultry meat, milk	48-96 h	Diarrhea ± blood, fever, malaise & abdominal pain	Stool culture	3-5 days
Shigella	Man- contaminated food& water	24-48 h	Watery, bloody diarrhea	Stool culture	7-10 days

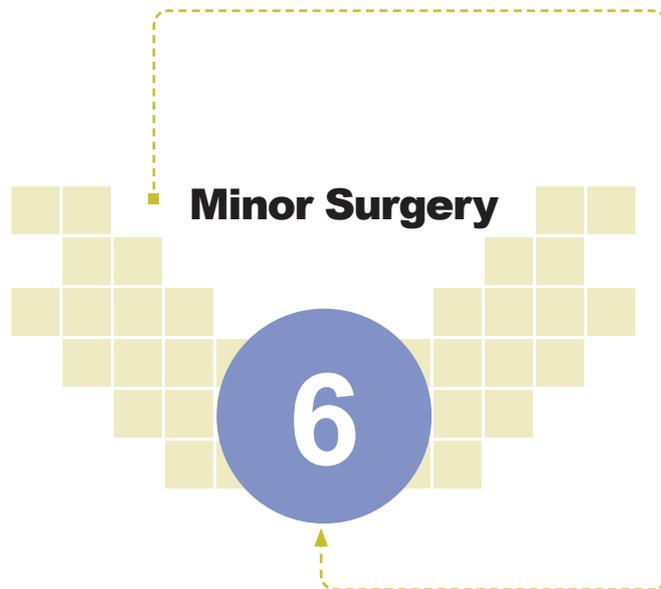
Prevention:

Improvement in food handling & preparation

Treatment:

Give oral fluid + empirical antibiotic

If patient is dehydrated IV line → refer to secondary care



Minor Surgery

Guidelines of Minor Surgery for Family physician

1. Assess the case (history taking, physical examination...)
2. Follow basic principles of surgery:
 - Asepsis
 - Haemostasis
 - Local anesthesia
 - Suturing
 - Cautery
3. Follow up for healing & infection
4. Referral to Hospital for other surgery requiring general anesthesia & admission over night.

Types of Minor Surgery:

1. Nail extraction
2. Abscess drainage
3. Cut wound suturing
4. Male circumcision
5. Removal of skin lesion (sebaceous cyst, dermoid cyst, callosity, warts & small subcutaneous lipoma)

Acute Abscess Drainage:

- Once pus forms, the only treatment should be free drainage.
- Incision & drainage is the standard method.. The incision should be situated over the pointing part of the abscess & should be dependent; otherwise a counter incision over a dependant area is necessary.
- The loculi inside the abscess are broken to ensure adequate free drainage.
- A specimen of pus could be sent for culture & sensitivity.
- A rubber drain or a wick of gauze is left protruding from the abscess cavity. **The drain serves two purposes**; it allows escape of discharge, and prevents premature closure of the skin wound before abscess cavity is obliterated by granulation tissue.
- Adequate free drainage is usually enough for most abscesses and antibiotics are required in only in overwhelming infections or in immunocompromised patients.
- In dangerous area, e.g. the neck, a sinus forceps is used to open the abscess after skin incision (Hilton's method) this avoids injury of important structures in the area.

Wounds

1. Assess the wound (history, physical examination).

History: ask about type of trauma, onset, duration, and treatments tried etc..

Physical Examination

- Examine while using sterile technique
 - Assess the size, the depth of the wound
 - Explore for foreign body
 - Assess the circulation, sensation, and movement distal to the wound
 - Palpate the underlying bones & parts surrounding the wound site.
 - Assess the range of motion & strength against resistance of all body parts surrounding the wound.
2. Preparation of wound site
 - Clip hair, do not shave surrounding hair as close to skin surface as possible. Eye brow should never be shaved.
 3. Wound cleaning with normal saline
 4. Prevention of tetanus is important (If person is immunized ---> give booster dose of the toxoid, if not immunized give immunoglobulin & start immunization)
 5. After preparing the wound, decide whether to apply sutures

Refer

Wounds for Urgent Referral:

- Avulsion flaps: results in a sizable amount of non viable tissues that may not be apparent initially
- Amputated fingers if properly reserved can be re- implanted
- Stab wounds of the neck and the abdomen, even if apparently simple very commonly hide a serious injury
- Wounds involving nerve, tendon, or bone damage
- Facial and hand wounds if not small and /or superficial

Special Wound Conditions:

- Old wounds
- Non accidental violent injury e.g. abused children, mentally retarded negligence, domestic accidents against women & self inflicted wounds.

In wounds Antibiotics

Prophylactic antibiotics should be given in the

following cases:

- Most mammal bites
- Puncture wounds
- Patients with cardiac valve disease or implants
- Heavily contaminated wounds
- Wounds with delayed treatment
- Wounds with tissue necrosis

Removal of Skin Lesions

- Ensure that you have practiced the techniques
- Better remove benign lesions- refer suspicious lesions to a specialist
- Take care with lesions on the face & lip, the scare may be very noticeable
- Explain to the patient the possible complications & possibility of keloid
- Clean & anaesthetize the area
- Make incision in the skin lines if possible
- Send all excised lesions for histopathology, place in formalin & carefully label the site and side.
- Be careful with diabetic patients.

Sebaceous (Epidermoid) Cyst

Complete excision of the cyst with an ellipse of overlying skin containing the punctum is performed to avoid recurrence.

Dermoid Cyst

- The only way of treatment is by surgical excision.
- In children with a dermoid cyst in the scalp it is better to wait until closure of the skull sutures because some cysts may have communication with dura.
- Surgery for a dermoid cyst is more difficult than that for a sebaceous cyst, because a dermoid cyst is deeper.

Callosity

The patient should avoid the causative agent if possible. The callosity should be shaved with a razor blade & repeatedly painted with an ointment containing salicylic acid.

Corn

A corn is similar to a callosity but a combination of friction & pressure. Treatment is the same. excision & sutures are rarely necessary.

Wart

- This is due to virus infection.

Treatment Options Are:

- Curettage & Diathermy
- Repeated application of glacial acetic acid

Lipoma

A subcutaneous lipoma is usually excised for cosmetic reasons. The operation is easy & depend on enucleation of the tumor from the inside its capsule.

Circumcision

Circumcision is the most commonly performed operation for Egyptian males

There is nothing called female circumcision, it is forbidden & considered female genital organ mutilation.

Indications:

- Circumcision can be done at any age, better after 40 days post delivery
- It can be performed without anesthesia in the first two months
- Local infiltration anesthesia at age 2-6 months (fine needle & injecting 3-4 ml xylocaine 2% without adrenaline in the midline spot at the base of the shaft of the penis to block the dorsal nerve of the penis)
- Age 6 months & older give general anesthesia

Contraindication:

- Bleeding disorders
- Hypospadias
- Epispadias

Postponement:

- Presence of inguinal hernia
- Premature & unstable child
- Presence of local infection or extensive rash (napkin rash)

Techniques

- Aseptic preparation
- The method depends on the age of the patient:
- Crush- excision is the method of choice in infants & children
- Dissection- excision is necessary in adolescents & adults

Do not forget

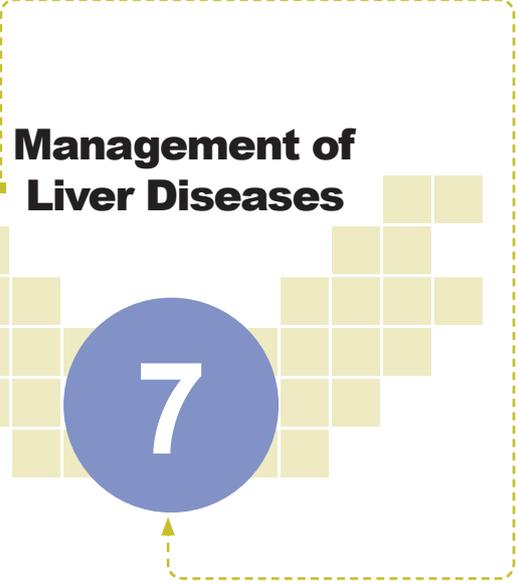
Do not forget parent / patient education

Think in complications (post-operative bleeding, stricture injury of the glans penis & external urethra and gangrene of the glans) Try to avoid them.



**Management of
Liver Diseases**

7



Management of Liver Diseases

Liver Disease

- Acute liver disease
- Chronic liver disease
- Jaundice

Acute Liver Disease

Symptoms of Acute Liver Disease:

The patient may be:

Asymptomatic and anicteric or

Symptomatic: generalized symptoms of malaise, anorexia, fever then jaundice appear.

Signs of Acute Liver Disease:

Jaundice

Enlarged tender liver

Pale stool

Dark urine

Treatment:

If Hepatitis A:

No specific treatment.

Bed rest till liver enzymes return normal.

Small frequent light diet.

If Hepatitis B:

Prevention & prophylaxis:

- Standard safety precautions
- Avoid risk factors
- Vaccination: see vaccination section
- Active immunization:
 - o Combined prophylaxis (vaccination & immunoglobulin)
 - o Staff with accidental needle-stick injury
 - o All newborn babies of HBs-positive patients.

Treatment as in Hepatitis A

If Hepatitis C:

- **Prevention & Prophylaxis:**
 - o Standard safety precautions.
 - o Avoid risk factors

Treatment as in Hepatitis A

In case of acute liver disease, refer patient for liver functions & viral markers

Chronic Liver Disease

Symptoms of Chronic Liver Disease:

The patient may be:

Asymptomatic, or

Nonspecific symptoms particularly fatigue, or

Specific symptoms:

- Right hypochondrial pain
- Abdominal distension due to ascites
- Ankle swelling due to fluid retention
- Hematemesis and melena
- Pruritis due to cholestasis
- Gynecomastia, loss of libido and amenorrhea
- Confusion and drowsiness due to neuropsychiatric complications (hepatic encephalopathy)

Signs of Chronic Liver Disease:

- May be normal, or
- Spider naevi over chest, upper body (above nipple line)
- Palmer erythema
- Clubbing
- Dupuytren's contracture
- Parotid enlargement
- Shrunken liver
- Splenomegaly
- Gynecomastia, testicular atrophy
- Hepatic flap
- Foetor hepaticus
- Drowsy and coma
- Ascites, dilated veins on abdomen, lower limb oedema

In case of chronic liver disease, refer patient for diagnosis by for liver functions test & abdominal sonar.

Treatment:

- Salt restriction
- Avoid aspirin & NSAIDS

No treatment will arrest or reverse cirrhotic changes.

In case of complications, refer.

Jaundice

Definition yellowish discolorations of skin and mucous membrane due to ↑ serum bilirubin

Table 4: D.D of Jaundice

	Hemolytic	Hepatocellular	Obstructive
Causes	Hemolytic anaemia	Acute: Viral hepatitis Toxic : gold CCL4 Chronic: Ch. Hepatitis Cirrhosis	Extra hepatic : Stone Malignancy Hepatic: Drugs:anabolic steroids, largactil, Cholangitis
Depth	Mild (lemon)	Moderate (orange)	Deep (olive green)
Bilirubin	↑ Indirect	↑ Both	↑ Direct > 20%
Urine	- Normal on voiding - Darken on standing	- Slightly dark	- Dark, frothy
Stool	Dark brown	Slightly pale	Clay colour
Itching	-	+	+++
Abd.Pain	- In acute hemolytic crisis - In sickle painful crisis	- In acute hepatitis	- Biliary stones - Malignancy
Associated	- Anaemia - Splenomegaly - + Leg ulcers	- Chronic liver cell failure - Portal hypertension	- Brady cardia - Coagulation defects - Fat malabsorption
Liver function tests	Normal	Impaired	- Early: normal except ↑↑alkaline phosphatase - Late : impaired

Jaundice

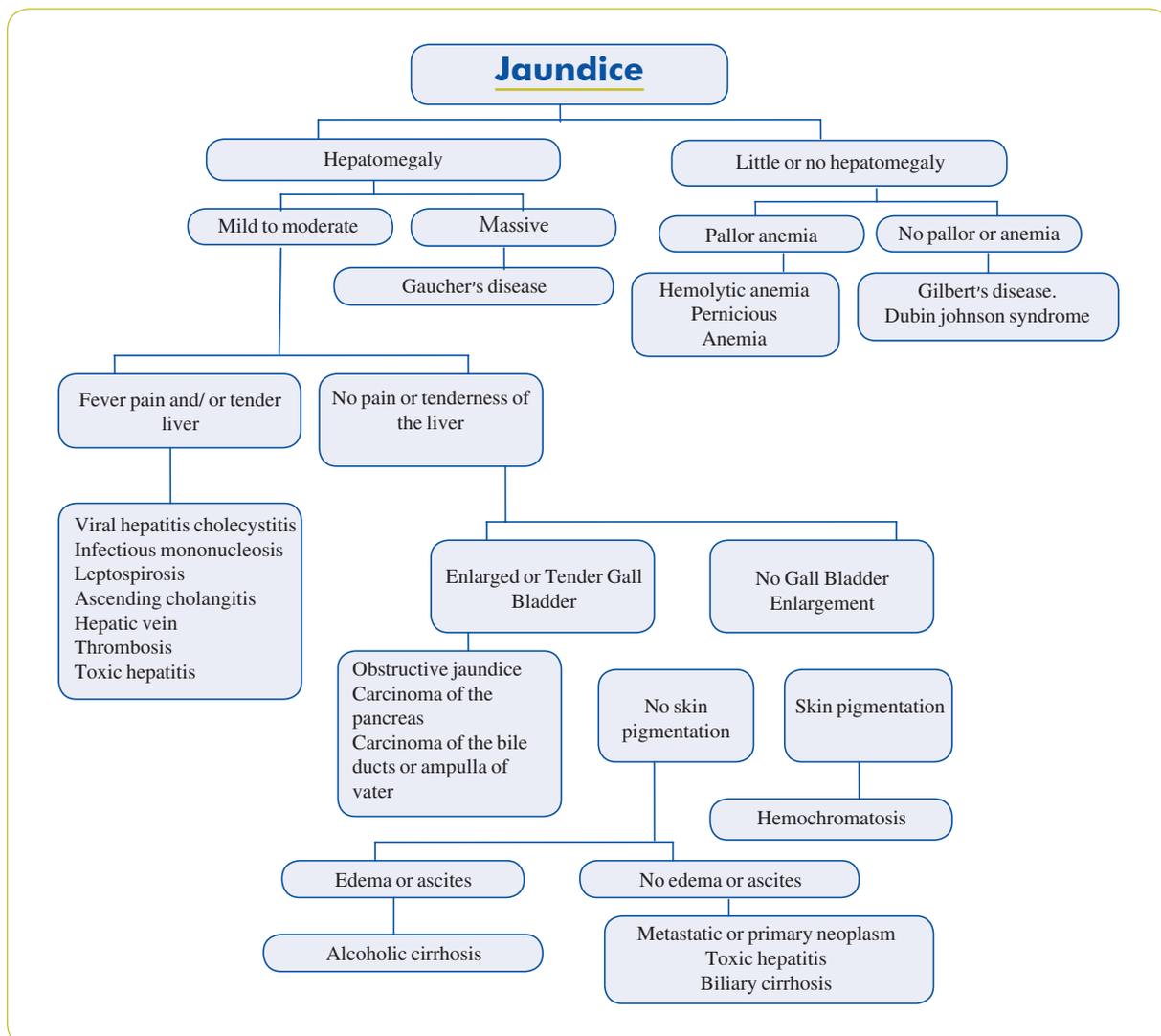


Figure "36": Flow-Chart Diagram for D.D. of Jaundice

Prescribing in Hepatic Patients

- The main site of biotransformation is the liver, but it can occur in other tissues like; kidney, lungs, GIT flora, wall etc..
- The use of drugs in patients with liver disease is an art, requiring common sense, and it should be based on the evolving science of pharmacokinetics and pharmacodynamics
- Because of the liver's strategic location between the portal and systemic circulations and its extensive enzyme activity, the liver plays a vital role in drug metabolism.

Role of The Liver in Dealing with Drugs:

- Inactivation of most of the drugs.
- Activation of some drugs.
- Detoxification of most of the drugs.
- Production of more toxic metabolites of some drugs.
- Synthesis of plasma proteins mainly albumin, with its well known Drug binding ability (see before).
Drug binding ability (see before).
- Secretion of drugs with bile, with consequent enterohepatic recycling (what is its clinical significance)?
- The function of the liver is to transform lipophilic substances into hydrophilic ones to be eliminated in urine or bile, or other aqueous media.
- This is achieved by two types of reactions:

Phase I: it includes: oxidation, reduction, and hydrolysis reactions.

Aiming at introduction of a functional group to render the molecule polar

Phase II: includes conjugation reactions with: glucuronic acid, acetyl Co-A, glutathione, glycine, phosphoadenosyl 1-phosphosulfate (sulphate conjugation), S- Adenosyl Methionine (Methylation).

N.B. The two phases are not sequential, and any of them may precede or come after the other.

- Drug biotransformation is achieved by the cytochromes (Microsomal and non-microsomal enzyme systems).

- More than 100 members of these cytochromes are known and identified. They are involved in drug metabolism.
- They are members of four gene families; (P450-I, II, III, IV).
- Individual p450s have distinct catalytic properties, and can metabolize many drugs and have unique binding sites and have substrate specificity.
- Genetic polymorphism of enzymes can lead to altered drug handling by liver, e.g. Slow and fast acetylation of INH due to polymorphism of acetylation enzyme. (See more details later)
- Genetic difference in their catalytic properties may lead to idiosyncratic response to drugs.
- Abnormal reactors for drug metabolism can be identified by PCR amplification of mutant genes.

Factors Affecting Bio-Transformation of Drugs

1. Inducers and inhibitors of the CYP, MES.
2. Hepatic blood flow; esp. For drugs with high hepatic first pass metabolism.
3. Malnutrition.
4. Age: young age: decreased due to deficient enzyme synthesis
Old age: aging enzymes, decrease Hepatic B.I.F. & Hepatic volume.
5. Sex: more activity in males than females.
6. Liver diseases; impaired metabolism is proportionate to HC affection. It decreases clearance of some but not all drugs.
7. Genetic factors
 - Drug biotransformation is impaired in presence of liver diseases. In patients with acute or chronic liver disease, drugs depressing CNS may precipitate encephalopathy.
 - Glucuronidation is relatively spared. Hence degradation of drugs by conjugation is less affected. This may be because there are extra hepatic glucuronidation pathways or the glucuronyl transferases may be so located in the interior of microsomes that they are protected from injury.
 - Benzodiazepines such as diazepam and

chlordiazepoxide undergo oxidative biotransformation and hence clearance is impaired in liver disease, whereas oxazepam and lorazepam are inactivated by glucuronidation and hence clearance may not be affected in stable cirrhotics.

- Hepatic acetylation is also impaired in patients with liver disease. INH acetylation is hence impaired.
- No reliable marker of hepatic drug metabolizing function that predict changes in hepatic clearance, analogous to CrCl in renal drug clearance. PT & S. Albumin may help.

Mechanisms of Impaired Drug Disposition in Liver Disease

- 1.Reduced enzyme activity
- 2.Parenchymal cell mass reduced
- 3.Reduced sinusoidal perfusion and capillarisation of sinusoids
- 4.Porto systemic shunting
- 5.Impaired bile flow
- 6.Changes in protein binding
- 7.Associated decreased renal clearance, malnutrition, Endocrine changes.

- **Hepatic clearance of drugs depends upon:**

- a. Efficiency of drug metabolizing enzymes.
- b. Hepatic blood flow(hepatic perfusion).
- c. Intrinsic clearance(extraction) of drugs by the liver.

D. Extent of protein binding of drugs.

- Drug bioavailability is also controlled by the liver's capacity to clear the drug from the circulation.
- This depends on both hepatic blood flow and the efficiency of drug removal by hepatocytes (extraction ratio).
- If the latter is very high, drug clearance primarily depends on hepatic blood flow (e.g., Propranolol, Lidocaine), whereas flow has relatively little effect on drugs that are slowly cleared by the liver (e.g., Theophylline, Warfarin, Diazepam).

- Most drugs are cleared at intermediate rates, which are affected by alterations in both hepatic flow and extraction capacity.

- $CL_H = QH \{C_A - C_V / C_A\} = QE$ (extraction ratio)

[Q is the hepatic blood flow = 90 l/hr]

- If hepatic Cl > hepatic blood flow, Bioavailability is low, and v.v.
- If hepatic blood flow is decreased e.g. CHF, Cirrhosis, Beta Blockers, Cimetidine, etc... there will be increased systemic effects of Hepatic first pass drugs; e.g. Lidocaine, verapamil, propranolol, INH, Morphine, several Tricyclic Anti-Depressants.

CYP₄₅₀ Inducers:

- They increase synthesis of cyp enzymes. or: decrease degradation of these enzymes, e.g. Troleandomycin.
- Examples: Barbiturates except Secobarbital, Rifampicin, Phenytoin, Phenylbutazone, Griseofulvin, Smoking, Troleandomycin, Insecticides, Hydrocarbons, Androgens.
- Ethyl alcohol in small dose is enzyme inducer, meanwhile, it is enzyme inhibitor in large doses.
- Omeprazole (Proto Pump Inhibitor, used in treatment of peptic ulcer), is an inducer of CYP 1A_{1&2}, meanwhile it is an inhibitor of other CYPs.
- The effect of enzyme inducers is slow, unlike enzyme inhibitors whose effect is rapid.

Clinical significance of enzyme inducers:

- Decrease the response to the inducer itself. (This may explain tolerance to some drugs e.g. Barbiturates).
- Decrease the bioavailability and hence the response to concomitant drugs e.g. Oral anti-diabetics (leading to hyperglycemia), oral anti-coagulants (leading to thrombosis) & oral contraceptives (leading to pregnancy and break-through bleeding).
- Increase toxicity of metabolite induced tissue toxicity e.g. INH, Paracetamol.

CYP₄₅₀ Inhibitors

- Examples: Allopurinol, Chloramphenicol, Isoniazid, Cimetidine, Dicumarol, Disulfiram,

Ethanol, Ketoconazole, Nortriptyline, Oral Contraceptives, Secobarbital, Troleandomycin, Macrolides, Quinolones, Anti-histaminics. Bio-flavonoids of grape-fruits juice. ---> **They act through:**

- Competitive inhibition. (Cimetidine, Ketoconazol)
- Catalytic Inhibition through complex formation (Troleandomycin)
- Alkylation of the protein of the enzyme (Allopurinol, INH)
- Alkylation of the heme of the enzyme (Oral Contraceptives, Ethanol).
- Alkylation of the heme and protein of the enzyme (secobarbital).

Clinical significance of enzyme inhibitors:

- o Increase bioavailability and hence effect of concomitant drugs e.g. Oral anticoagulants (leading to bleeding) oral hypoglycemics (leading to hypoglycemia).
- o Increase toxicity of Concomitant Drugs, e.g. Grape fruit juice causes the arrhythmias if combined with Macrolides or Quinolones.
- o Decrease metabolite induced toxicity, e.g. Cimetidine reduces toxicity of acetaminophen.

Genetic determinants of drug metabolism and drug interactions

There are several enzymes that are responsible for the hepatic metabolism of drugs. There is inherited variability in their concentration and metabolic activity (Polymorphic Metabolism): N-Acetyltransferase N-Acetyltransferase (NAT) is responsible for the transformation of procainamide to its active metabolite N-Acetylprocainamide (NAPA) and for the metabolism of other drugs such as isoniazid and hydralazine. About 50% of Caucasians and African-Americans are "Slow" Acetylators, a Phenotype that is rare among Asians. This pattern arises because of the existence of two NAT isoforms which are products of different genes. NAT_1 is expressed in virtually all individuals, while NAT_2 is expressed only in rapid acetylators.

Slow Acetylators of Procainamide have higher parent drug concentrations and lower NAPA concentrations that do fast Acetylators. This is

probably not important for antiarrhythmic activity, since NAPA exerts some electrophysiologic actions of its own which are different from those of procainamide (i.e., Class iii versus class ia activity). Drug-induced lupus accumulation of procainamide may have deleterious effects due both to the native drug and to subsequent metabolism to toxic metabolites such as procainamide hydroxylamine. This explains why slow acetylators of procainamide are at greater risk for the development of drug-induced lupus during procainamide therapy than rapid acetylators. Similar considerations apply to isoniazid and hydralazine. In comparison, there is little or no antinuclear antibody formation or symptomatic lupus following the administration of NAPA.

Cytochrome P₄₅₀:

Historically, cytochrome P₄₅₀ has been conceptualized as one enzyme or an enzyme complex with the capacity to metabolize a number of drugs by a variety of routes.

More recent information has shown that there are over 100 isoenzymes of Cytochrome P₄₅₀, and the capacity of these enzymes is more clearly delineated with current research.

Nomenclature for the P₄₅₀ enzymes is based upon amino acid sequence Homology.

Enzymes that have 40% or more homology are assigned the same arabic numerical, those with 55% or more homology are assigned the same letter. As an example, the sterol 27-hydroxylase and vitamin D3 24 hydroxylase enzyme are more than 40%, but less than 55% homologous, and are assigned to the CYP₂₇ family as CYP_{27a} and CYP_{27b} respectively.

The importance of characterizing the functions of different CYP (P₄₅₀) isoenzymes is twofold:

- First, it allows studies of population of patients to discern different phenotypes of drug metabolism.
- The second role of characterization of substrate specificity of cytochrome p450 isoenzymes is its importance in drug interactions. In particular, specific inhibitors of some isoenzymes have been identified.

CYP_{2d6} Isoenzyme

- This is one of the best-characterized CYP₄₅₀ isoenzymes.

- It metabolizes a variety of drugs as will be discussed subsequently.
- There are clear phenotypes of this enzyme, and there are racial differences in this expression. as an example, up to 8-10% of Caucasians are deficient in this enzyme and are called poor metabolizers of those drugs metabolized through this mechanism.
- In contrast, the Asian populations have a very low incidence of poor metabolizers (≥ 1%).

Multiple molecular mechanisms have been identified in subjects who are poor metabolizers, resulting in the production of reduced amounts of nonfunctional CYP_{2d6} protein. In such "poor metabolizers", the functional consequences of enzyme deficiency depend upon the presence of other routes of drug metabolism and on the activity of any metabolites whose formation requires functional CYP_{2d6}. On the other hand, individuals have been described in whom two or more copies of the CYP_{2d6} gene are present. CYP_{2d6} activity may be exaggerated in these "hyperextensive metabolizers".

- CYP_{2d6} is a major route of biotransformation of a number of drugs including:
 - o Antiarrhythmic agents: Propafenone, Flecainide
 - o Beta-Blockers: Timolol, Propranolol, Metoprolol, Labetalol.
 - o Antidepressants: SSRIS as Fluoxetine, Paroxetine, Fluvoxamine, and some Tricyclic Antidepressants as Imipramine, Desipramine, Amitriptyline and Nortriptyline.
 - o Statins- Simvastatin and some other members of this class, analgesics such as Codeine.

The importance of the CYP_{2d6} polymorphism vary with the different drugs:

- o Increased drug activity with β-blockers, the CYP_{2d6}-dependent metabolites are less active than the parent drugs. As a result, poor metabolizers, who have higher concentrations of the parent

drug, display a greater degree of β-blockade than extensive metabolizers. Similarly, propafenone, but not its metabolites, exerts β-blocking activity in vitro. Thus, at any given dose, the plasma propafenone concentration and therefore the degree of β-blockade are greater in poor compared to extensive metabolizers. The importance of CYP_{2d6} phenotype is also seen with Simvastatin as it can affect both the degree of lipid lowering and tolerability.

- o Little change in drug activity the clinical significance of CYP_{2d6} is less with Flecainide. Although Flecainide biotransformation to inactive metabolites is CYP_{2d6}-dependent, the unchanged parent drug can undergo renal excretion. As a result, the CYP_{2d6} polymorphism is ordinarily unimportant during Flecainide therapy, except in subjects with renal failure. In this setting, marked Flecainide accumulation and potential cardiotoxicity may occur in poor metabolizers.
- o Reduced drug activity Codeine undergoes CYP_{2d6}-dependent biotransformation to a more active metabolite, Morphine. Thus, Codeine has less pharmacological activity in poor metabolizers than extensive metabolizers.
- Drug inhibition of enzyme activity a number of drugs are potent inhibitors of CYP_{2d6}, including ultra low dose of Quinidine (e.g. 50mg) and some ssris (Paroxetine, Fluoxetine). Extensive metabolizers receiving these drugs will display the phenomenon of "Phenocopying" behaving as if CYP_{2d6} activity were absent. This can be illustrated by the following observations: blockade of CYP_{2d6} by ssris can increase the incidence of side effects associated with Tricyclic Antidepressants. Blockade of CYP_{2d6} by Quinidine can increase the degree of β-blockade in extensive metabolizers receiving Timolol eye drops and in those treated with Propranolol or Propafenone.

These drug interactions are genetically determined, occurring only in extensive metabolizers in whom functional CYP_{2d6} is present

to inhibit. Inhibition of drug activity can also occur competitively when two drugs metabolized by CYP_{2d6} are given concurrently. In one study (Holtzman, et al, 1987), healthy subjects were given both flecainide and propranolol; the plasma levels were increased by 20% for flecainide and 30% for propranolol.

CYP_{3a4} isoenzyme

- It is the most important hepatic enzyme for drug metabolism. It is responsible for the biotransformation of many commonly used drugs such as quinidine, lidocaine, statins, calcium channel blockers, theophylline and cyclosporine. It has received considerable attention, largely because this isoenzyme is the major route of metabolism for cyclosporine as well as for other frequently used drugs, which can therefore inhibit the metabolism of cyclosporine. In contrast to CYP_{2d6}, genetically determined "poor metabolizers" with absent or low CYP_{3a4} activity have not been identified. However, the activity of the enzyme varies considerably among individuals for reasons that are incompletely understood.

Ingestion of a Number of Drugs Can Affect CYP_{3a4} Activity:

- Enzyme activity is reduced by erythromycin, clarithromycin, ketoconazole, itraconazole and large quantities of grapefruit. Grapefruit juice or unprocessed grapefruit appears to act by down regulating intestinal CYP_{3a4}.
- Enzyme activity is increased by rifampicin, anticonvulsants such as phenytoin and phenobarbital, and dexamethazone. These drugs appear to activate the nuclear pregnane X receptor (PXR), which binds to a response element in the CYP_{3a4} promoter. The ability of CYP_{3a4} to be induced and its broad substrate specificity are responsible for its drug interactions. It is also possible that endogenous substances modulate the expression or function of CYP_{3a4}, resulting in a wide variation in enzyme activity. Some of the interindividual variability may be genetically determined.

Competitive inhibition of CYP_{3a4} can lead to clinically important drug interactions. The effects are most pronounced when there is no alternative

pathway for the metabolism of a potentially toxic drug. The most spectacular example is the development of torsade de pointes during the administration of terfenadine or cisapride and a potent inhibitor of CYP_{3a4}. These drugs block cardiac potassium channels and normally undergo extensive presystemic biotransformation to metabolites that have no electrophysiologic activity. The ingestion of CYP_{3a4} inhibitors (e.g. Erythromycin or Ketoconazole) or the presence of a drug overdose or liver disease results in the accumulation of the native drug, resulting in QT prolongation and the potential for torsade de pointes.

The use of a potent CYP_{3a4} inhibitor, especially cyclosporine, can increase the plasma concentrations of simvastatin and most other statins, enhancing the risk of myopathy. Weaker inhibitors, such as the ccb's, have less risk. A similar type of drug interaction explains the increased cyclosporine concentration seen with co-administration of Ketoconazole, Diltiazem, or grapefruit juice. On the other hand, drugs that increase enzyme activity (e.g. Anticonvulsants) can reduce cyclosporine concentrations, requiring an increase in the cyclosporine dose.

CYP_{2c} Isoenzyme

This isoenzyme metabolizes the following drugs: -anticonvulsants: phenytoin, mephenytoin, methobarbital. -Antimalarials: proguanil, cycloguanil -oral hypoglycemic: tolbutamide - anticoagulants: warfarin CYP_{2c} is absent in about 3% of caucasian patients, and in substantially higher numbers of asian (greater than 10%). Cimetidine inhibits this isoenzyme, although it may also have effects on other cytochrome p450 isoenzymes. Thus, the administration of cimetidine with one of the above drugs may lead to a clinically important drug interaction.

CYP_{2c9} Isoenzyme

This isoenzyme inactivates the S-enantiomer (most active) of warfarin. There are multiple genetic polymorphisms of CYP_{2c9}. The maintenance doses required to reach a target INR can vary according to the genotype. Amiodarone inhibits CYP_{2c9}. This explains the potentiation of warfarin effect by amiodarone.

CYP_{2c19} Isoenzyme

Omeprazole, lansoprazole, and to a variable

degree, other proton pump inhibitors are primarily metabolized via CYP_{2c19} isoenzyme. The activity of CYP_{2c19} is determined to some extent by gene polymorphism, and two known inactivating mutations that occur most commonly in asian populations have been described. Five percent of caucasians are homozygous for this mutation. As a result, metabolism of drugs by this route may be delayed in these individuals. In addition, about two-thirds are homozygous for the wild type gene. Such persons rapidly metabolize drugs, while heterozygotes are intermediate metabolizers.

The activity of CYP_{2c19} affects the likelihood of success in the treatment of both helicobacter pylori and gastroesophageal reflux disease (GERD):

- The effect of variable metabolism of omeprazole in the treatment of helicobacter pylori was examined in japanese patients (Furuta, et. al,1998). While eradication was achieved in all individuals homozygous for a CYP_{2c19} mutation, successful treatment was achieved in only 60 and 29% of heterozygotes and wild type homozygotes, respectively. Another report from japan (Furuta, et. al, 2002) evaluated the efficacy of lansoprazole in the treatment of gerd. Poor metabolizers were much more likely to be cured on endoscopic examination than heterozygotes and wild type homozygotes (85 versus 68 and 46 % respectively). The cure rate was only 16% in wild type homozygotes who had severe GERD. Wild type homozygotes had the lowest plasma lansoprazole concentrations.

The CYP_{2c19} genotype also affects the metabolism of sertraline. Plasma sertraline concentrations are significantly elevated in patients with a CYP_{2c19} mutation. The clinical significance of this difference is uncertain.

N.B: a drug like Rifampicin induces a variety of hepatic enzymes, and, within the Cytochrome P₄₅₀ isoenzymes, produces a variable degree of induction. In an in vitro study of human hepatocytes (Rae, et al, 2001), Rifampicin substantially induced the CYP_{3a} family, CYP_{2c9}, CYP_{2a6}, and a number of non-P₄₅₀ enzymes but had little effect on CYP_{2d6} or CYP_{2e1}. Further research will undoubtedly identify other isoenzymes of Cytochrome P₄₅₀ and will refine our knowledge as to specific substrates or inhibitors. This will allow more precise prediction of clinically important

drug interactions in humans.

Pseudocholinesterase Deficiency

The paralytic agent succinylcholine is metabolized by the circulating enzyme pseudocholinesterase. The enzyme is functionally absent in approximately 1 in 3000 individuals. In such patients, prolonged paralysis may occur following ordinary doses of succinylcholine.

Thiopurine Methyltransferase

Thiopurine methyltransferase (TPMT) is responsible for the biotransformation of antimetabolites such as 6-mercaptopurine and azathioprine to less active metabolites. Rare cases of mutations in the tpmt gene have been described; during treatment with one of the above drugs, affected subjects display prolonged agranulocytosis that can be fatal or develop lower leukocyte counts necessitating drug discontinuation. In one series, for example 6 of 67 patients receiving azathioprine for rheumatic disease where heterozygous for mutant tpmt alleles (Black et. al., 1998). Five of these patients had to discontinue therapy within one month because of leucopenia, while the sixth did not adhere to therapy. In comparison the median duration of therapy was 39 weeks in those with wild type alleles. Some data also suggest that increased activity of tpmt may be associated with a decreased antitumor efficacy of thiopurine drugs.

Similar considerations apply to the use of 6-mercaptopurine. In a series of 180 children with acute lymphoblastic leukemia, the cumulative incidence of dose reductions in 6-mercaptopurine due to drug toxicity was 7% in the 161 children with two wild-type alleles, 35% in the 17 children with one mutant allele, and 100% in the two children with two mutant allele. Lowering the 6-mercaptopurine dose in the last two groups permitted administration of the full chemotherapy protocol.

P-glycoprotein

p-glycoprotein (P_{gp}), also called multidrug resistance glycoprotein, is a drug transport system that was initially identified in certain tumor cells that displayed the phenomenon of drug resistance because the cells were able to pump various anticancer drugs out of their cytoplasm. In addition to tumor cells, P_{gp} is expressed on the luminal aspect of enterocytes, on the canalicular aspect of hepatocytes, the luminal aspect of renal tubular cells, and in the capillaries of the blood-

brain barrier. Substrates for P_{gp} include anticancer drugs, digoxin, quinidine, cyclosporine, and many others.

P_{gp} expression may have a number of clinically important effects:

- Animal and in vitro studies suggest that poor central nervous system penetration of HIV protease inhibitors may be due to P_{gp} mediated efflux at the capillaries of the blood-brain barrier.
- The elevation in serum digoxin induced by a variety of drugs (quinidine, verapamil, cyclosporine, erythromycin, ketoconazole) is probably due to inhibition of P_{gp} mediated digoxin transport; especially since digoxin does not undergo significant metabolism prior to excretion. The administration of agents that inhibit P_{gp} by reverting the multidrug resistance phenotype (e.g. Quinine), by inhibiting the activity and maturation of P_{gp} (e.g. Cyclosporine), may increase the response to chemotherapeutic agents.

Pharmacokinetic and Pharmacodynamic

Changes in Drug Disposition in Hepatic Impairment

• Absorption:

It is impaired from GIT due to several factors:

- o Nausea and vomiting with hepatic or biliary dysfunction.
- o Dyspepsia and indigestion which interfere with drug absorption.
- o Non-healthy mucosa of GIT.
- o Intestinal mucosal congestion in cases of portal Hypertension&CHF.
- o Defective biliary secretion with consequent pancreatic enzyme Dysfunction, which interfere with activation of some drugs.
- o Use of polypharmacy with possible hazardous interactions, or interference with intestinal flora.

• Protein Binding:

- Liver is the site of synthesis of plasma proteins, particularly Albumin. Thus with liver impairment, there will

be hypoalbuminemia, and free parts of drugs will increase, needing dose adjustment.

• Distribution:

- o In cases of portal hypertension with ascites, and in cases of generalized oedema with liver cirrhosis, the volume of distribution is increased especially for hydrophilic drugs, which necessitates dose adjustment.
- o Decreased hepatic blood flow with CHF, and liver cirrhosis, will increase the systemic bioavailability of drugs known to undergo first pass hepatic metabolism (flow dependent drugs).

• Biotransformation:

- o Impairment of biotransformation of drugs metabolized in the liver.
(This point is detailed beforehand).
- o Increased susceptibility of the liver to drug insults.

• Elimination:

- o Decreased biliary elimination of drugs eliminated by this route.
- o Co-morbidity of the other organs of elimination e.g. Kidneys, may occur.

• Organ sensitivity:

- o Hepatic patients are more susceptible to CNS depressants.

Effect of Liver Disease on Some Pharmacologic Agents

1. Tranquilizers and sedatives: alprazolam, diazepam, chlordiazepoxide, midazolam- half life is increased by 50% to 400 % and clearance reduced by 30%-60%. Barbiturates if albumin levels normal no dosage adjustment required

2. Antidepressants and anticonvulsants:
*phenytoin - no change in drug disposition in acute viral hepatitis. *Amitriptyline, fluoxetine, valproic acid - half life is increased and clearance decreased

3. Analgesics and NSAIDs:

• **Ibuprofen and phenyl butazone** - no change in drug disposition dextropropoxyphene and pentazocine-clearance is impaired phenacetin-caution in use in alcoholic liver disease

4. Cortico Steroids: no change in drug disposition

5. Cardio Vascular Drugs:

- **Antiarrhythmics** - clearance is decreased and half life increased.
- **Beta blockers:** - labetalol and metoprolol no change -propranolol clearance is decreased, half life increased calcium channel blockers - clearance is decreased half life increased
- **Anti hypertensives** ACE inhibitors, NO change, diuretics half life and clearance altered especially in presence of renal failure. Digoxin, NO change

6. Gastric Acid Suppressants: only proton pump inhibitors have low clearance and increased half life.

7. Xanthines: Theophylline, clearance decreased with increased half life.

8. Antibiotics: Chloramphenicol, Clindamycin, Vancomycin, Erythromycin, Cefoperazone, Rifampicin, Half life is increased consequent to decreased clearance

9. Anticoagulants: clearance unchanged but bioavailability increased

10. Oral Hypoglycemics: Hypolipidemics such Gemfibrosil, Colchicine, Metoclopramide, Bioavailability is increased.

Note

Drug utilization in hepatic patients:

- Prodrugs of ACEI, are better avoided. Use Captopril or lisinopril.
- Antacids: avoid sodium containing prep. In ascites. Avoid Alum. Prep. Which may precipitate coma due to constipation.
- Azithromycin, Clarithromycin are better avoided for fear of jaundice (common).
- Cimetidine increases risk of confusion.
- Dantrolene causes severe liver damage.
- Reduce dose of Cal. Channel Blockers.
- Ketotifen increases risk of sedation.
- Reduce dose of Metronidazole, give it once/day in liver diseases.
- Neomycin is absorbed in liver disease from GIT, with increased risk of Ototoxicity.
- Pyrazinamide may lead to idiosyncr. Hepatic toxicity in liver diseases.
- Quinolones: avoid Ciprofloxacin, no Rfloxacin, Nalidixic acid. Reduce dose of Ofloxacin.
- Valproate: better avoided in liver diseases.

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