BARBITURATE POISONING

Anna Jacob

Roll no 16

BARBITURATES

- Barbiturates are white, crystalline, odorless powders, with a faintly bitter taste.
- The barbiturates are derivatives of **barbituric acid (2,4,6-trioxohexahydropyrimidine)**
- Barbital became the first commercially available barbiturate in 1903
- USES

1.Sedative-hypnotic.

2. Pre-operative sedation.

3. Treatment of seizure disorders.

4.Neonatal jaundice

Classification

S.No	Class of Barbiturate	Onset of action	Duration of action	Major Examples
1.	Long acting	2 h	6-12 h	Barbitone, Diallylbarbituric acid, Mephobarbitone, Methyl phenobarbitone, Phenobarbitone, Phenytoin
2.	Intermediate acting	0.5-1 h	3-6 h	allobarbitone, Amobarbital [syn, Amobarbitone, Amylobarbital, Amylobarbitone, Pentymalum, Sodium amytal][Proprietary names Amal; Amytal; Eunoctal; Neur-Amyl; Stadadorm], Aprobarbital, Butobarbitone, Probarbitone, Vinbarbital
3.	Short acting	10-15 m	<3h	Cyclobarbitone, Ortal, Pentobarbital, quinalbarbitone, Seconal
4.	Ultrashort acting	immediate	5-10 m	Kemithal sodium, Pentothal sodium, Thiamylal sodium

- MOA
- CNS depressant

They facilitate and prolong the inhibitory effects of GABA and glycine by increasing the duration of chlorine channel opening.(Their actions are not antagonized by flumazenil)

- Toxicokinetic

(1)Barbiturates are rapidly absorbed from GIT including the rectum

(2)After ingestion, barbiturates are preferentially absorbed from the small intestine

(3)They are concentrated in the liver for a short time, and then evenly distributed in the body fluids

(4)Longer-acting barbiturates tend to be more lipid soluble, and more protein bound, a more rapid onset and shorter duration of action, and are metabolized almost completely in the liver.

(5)Barbiturates are eliminated by hepatic and renal systems. Metabolism of most of these drugs occurs by oxidation in the liver resulting in the formation of alcohols, ketones, phenols, or carboxylic acids which are excreted in the urine as such or in the form of glucuronic acid conjugates. Metabolism of barbiturates is more rapid in children and is slower in the elderly.

1) Fatal dose - (i) Short acting:1-2 g (ii) Medium acting:2-3 g (iii) Long acting:3-5 g

(2) Fatal blood levels - (i) Short acting:3 mg% (ii) Medium acting:7 mg% (iii) Long acting:10 mg%.

Fatal period - 1-2 days.

- Adverse Effects

- Residual depression
- Paradoxical excitement (especially in the elderly)
- Hypersensitivity reaction—localised swelling of eyelid, cheek, or lip, erythematous or exfoliative dermatitis.
- Synergistic action with ethanol and antihistamines.

Acute poisoning

- CNS – CNS depressant effect mimics that of ethanol.

[A] Symptoms

- drowsiness [usually the earliest symptom]
- Ataxia, Confusion
- Delirium , Excitement , Hallucinations
- Headache , nystagmus [lateral and vertical] , Paresthesias , Slurred speech , Vertigo , Visual disturbances
- Finally stupor progressing to deep coma.
- Coma may persist for a few hrs to a few days, and then the patient makes a gradual recovery.

[B] Signs -(i) Babinski toe sign +ve (ii) Loss of response to painful stimuli

(iii) Pupils – (a) slightly contracted (b) react to light (c) Dilate [may be unequal] during terminal stages [due to hypoxia]

(iv) Superficial and deep reflexes - inhibited or completely lost

- Respiratory

(i) Barbiturates cause a depression of the medullary respiratory center " induce respiratory depression " leads to (a) bronchopneumonia (b) respiratory acidosis [contributes to CVS depression]

(ii) COPD patients more susceptible [even at therapeutic doses].

(iii) (a) either rapid and shallow or (b) slow and labored

(iv) In terminal stages "irregular "Cheyne Stokes "stops completely ["death]

- GIT

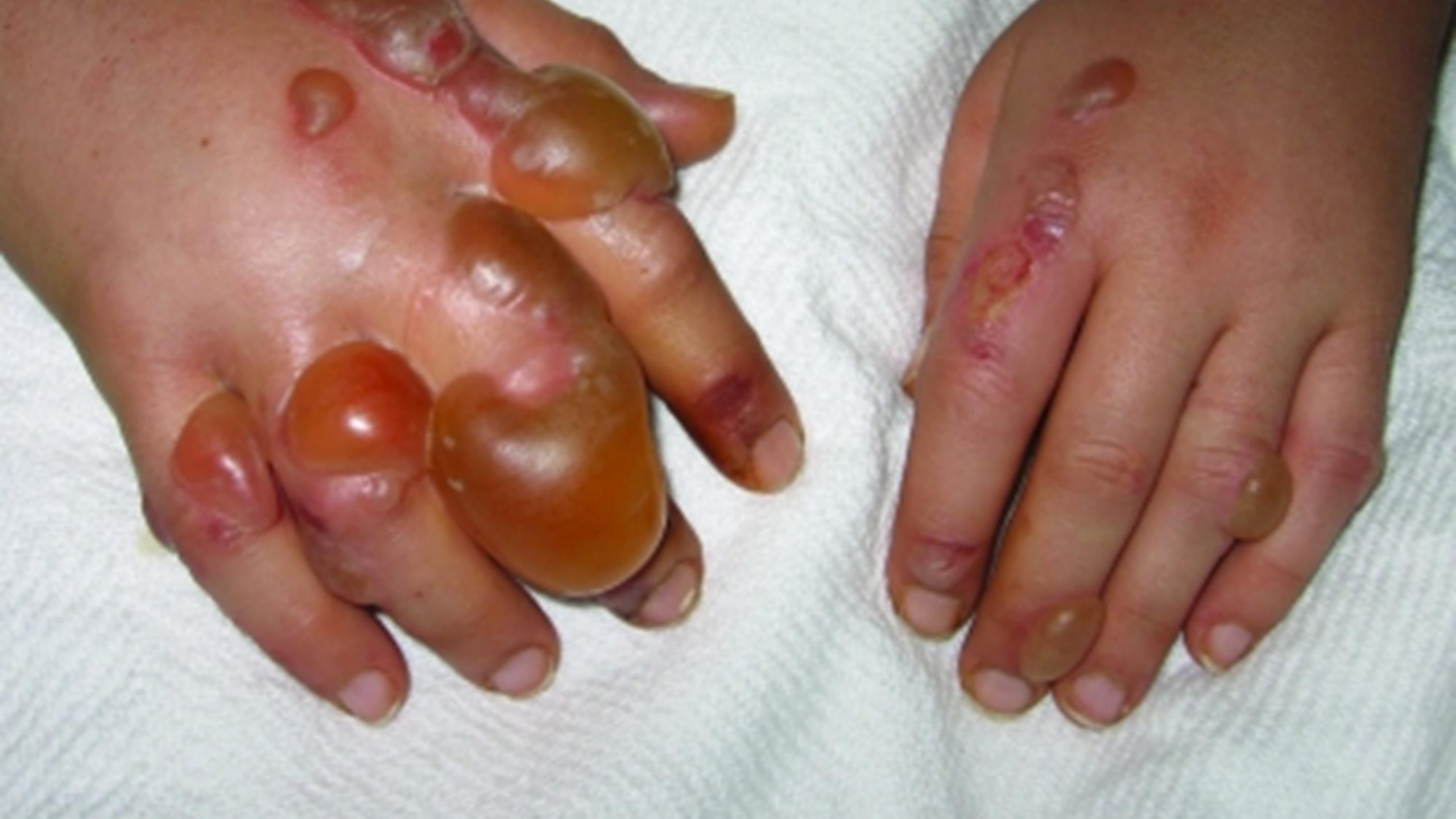
Decreased peristalsis
As condition improves " peristalsis returns to normal " -drug absorption " worsening of condition again " fluctuating levels of consciousness
Incontinence of fece

- CVS

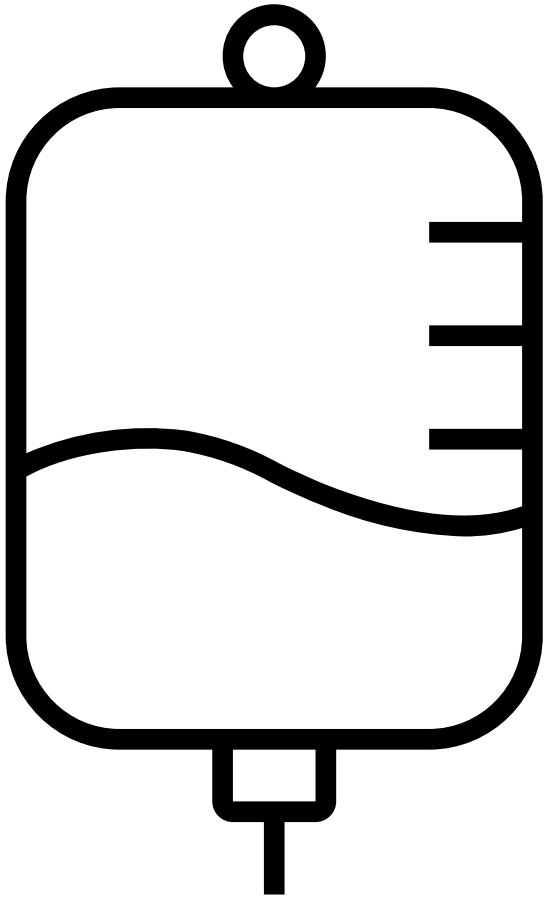
Progressive cardiovascular collapse- decreased output and increased capillary permeability
Signs of cardiovascular collapse [hypotensive shock] – (a) Cold, clammy skin (b) Cyanosis (c) Hypotension (d) Pulse – weak and rapid

Hypothermia, leucopenia,thrombocytopenia

Cutaneous bullae (“barb burns”, barbiturate blisters): These are clear, erythematous or haemorrhagic blisters, and occur in various areas of the body, most typically on the hands, buttocks, and between the ankles and knees, usually over pressure points and also over non-pressure points, such as dorsal surfaces of fingers and toes, and ocular conjunctiva.



- Death
- (i) In early stages due to – respiratory failure ,ventricular fibrillation.
- Death is rapid if alcohol or antihistamines are ingested simultaneously
- (ii) In late stages due to –bronchopneumonia , pulmonary edema , acute renal failure or cerebral edema.



- TREATMENT

✓Scandinavian method- airway , artificial respiration, oxygen supplementation , stomach wash(1:1000 KMnO4),Activated charcoal , prophylactic antibiotics , IV Fluids

✓Forced alkaline diuresis- sodium bicarbonate in 5% dextrose slow IV infusion or Mannitol 100-200 mi of 25% solution IV first 3 hrs,then next 3 hrs- 500 ml of 5% solution

✓Haemodialysis

✓Exchange transfusion

✓Symptomatic treatment- management of prolonged coma (deep vein thrombosis, orthostatic pneumonia)

✓Emesis is contraindicated

✓No specific antidote

others- THAM, ILE , Hemoperfusion , immunotherapy(Bovine Gamma Globulins[BGG])

- PM appearances

(1) Signs of asphyxia – congestion of all internal organs, cyanosis, petechial hges in lungs and on pleura and pericardium

(2) Nose and mouth - Froth

(3) Skin - Barbiturate blisters

(4) Lungs (i) Intensely congested. May even be turned completely black [full of dark deoxygenated blood] (ii) Show edema and bronchopneumonia in late deaths

(5) Esophagus – lower end may show erosion from regurgitation

(6) Stomach – (i) congested. (ii) erosions. (iii) White particles on ingested barbiturates seen (iv) Fundus – thickened, granular, hemorrhagic

(7) Kidneys – degeneration of convoluted tubules

(8) Brain – edematous, especially in late deaths. In delayed deaths there is symmetrical necrosis of globus pallidus and corpus callosum, focal areas of necrosis in cerebrum and cerebellum and a variety of vascular lesions.

- Laboratory detection

(1) Dille-Koppanyi Test - Two solutions are used. (i) Soln 1 - 1% cobalt acetate in methanol . (ii) Soln 2 - 5% isopropylamine in methanol

(iii) Add two drops of Soln 1 to the drug, followed by one drop of Soln 2"If barbiturates are present a lavender-blue color will develop.

(2) Calorimetric method

(3) GC-HPLC.

Diagnosis

1. Serial plasma levels

Plasma levels exceeding 8 mg/ dL are generally associated with some degree of coma.

In the absence of tolerance, plasma levels exceeding 2 to 3 mg/dL may be associated with CNS depression.

2. EEG:

alpha coma indicates poor prognosis.

Chronic poisoning

- Etiology

(i) Prolonged therapeutic use - Unintended addiction (Dependence - psychic and physical)

(ii) Prolonged recreational use.

- Signs and symptoms –

Physical deterioration - Ataxia , cerebral function impaired , depression ,Dysarthria , hypertonia and tremors of Parkinsonian type ,Tendon reflexes depressed

Social deterioration – Impairment of mood, behavior and intellectual functions.

- Barbiturate abstinence syndrome

withdrawal syndrome on the 2nd to 4th day after the drug is suspended.

Symptoms -(a) anxiety ,Disturbances of vision , dizziness ,Hypotension , insomnia , Nausea and vomiting ,psychosis ,restlessness ,rhythmic intention tremor , convulsions, seizures and Weakness.

May persist for 2 wks. If the syndrome is not recognized and correctly treated- hyperthermia, circulatory failure, and death may ensue.

Treatment - Administration of barbiturates

Medicolegal importance

- 1) Popular drug as an agent of **suicide**
- (2) **Euthanasia** - Barbiturates are a popular drug for euthanasia. In Switzerland, oral pentobarbitone for the purpose.
- (3) **Barbiturate automatism**
- (4) Drug of **abuse**, recreational use (i) Popular drug of abuse because of psychological symptoms it produces. Short acting and intermediate-acting barbiturates are preferred [amobarbital (Amytal), pentobarbital (Nembutal), secobarbital (Seconal), combination of amobarbital and secobarbital (Tuinal)]. Known in drug world as barbs, bluebirds, blues, dolls, downers, goofballs and tooties. (ii) Physical and psychological dependence develops with repeated use. (iii) Sometimes used to alleviate adverse or withdrawal effects of other illicit drugs.
- (5) Used in **narcoanalysis** – As truth serum
- (6) **Judicial Execution** - Used in judicial execution by injection. A sequential drug combination of sodium thiopental [CNS depression], pancuronium bromide [paralysis of respiratory muscles], and potassium chloride [cardiac arrest] is used.
- (7) Barbiturates resist putrefaction.

Thank you

- References

Forensic medicine and toxicology for mbbs- anil aggrawal

Textbook of forensic medicine and toxicology- Ignatus 5th edition

Modern medical toxicology- VV pillay 4th edition