

Mercury

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Portrait of A Slippery Metal

ORIGIN

Mercury comes from a mineral called cinnabar



PHYSICAL PROPERTIES

Mercury is the only metal that exists as a liquid at room temperature

PERIODIC SYMBOL

Hg

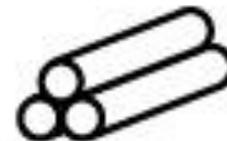
COMMON USES



Refining gold



Once common in dental fillings



In Chinese-made PVC pipe



Fluorescent lights

Mercury

- ▶ Mercury (Hg) is a naturally occurring metal that is mined chiefly as **Hg S** **cin** **nabar ore**.
- ▶ Approximately one-third of commercial mercury use is in the manufacture of **chlorine and caustic soda**

Uses

Industry

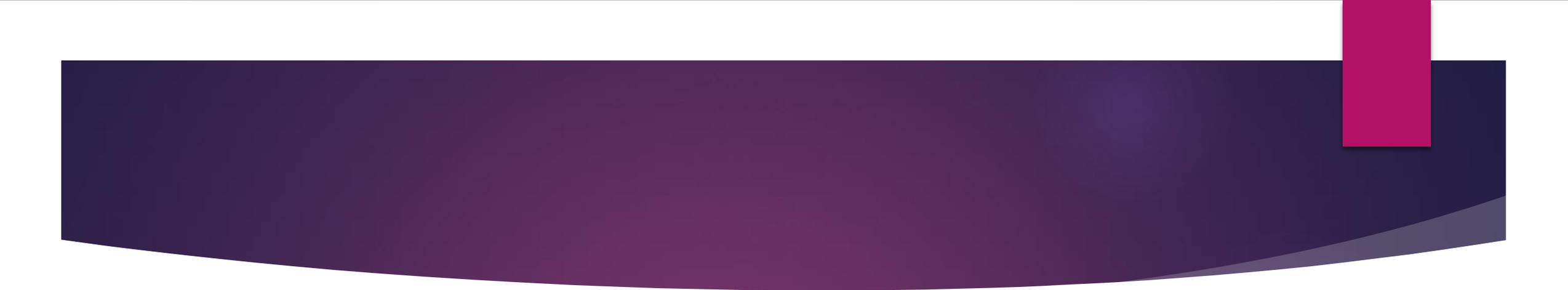
1. Barometer, thermometer, etc.
2. Ceramics
3. Dry cell batteries
4. Electrical appliances(mercury switches)
5. Explosives and fireworks
6. Felt hats
7. Fluorescent and mercury vapour lamps

Medicine and Dentistry

1. Antiseptic and disinfectant
2. Dental amalgam
3. Diuretic
4. Purgative

Miscellaneous

1. Electroplating
2. Embalming
3. Fabric softener
4. Fingerprint powder
5. Fungicide
6. Gold and silver extraction
7. Grain preservative
8. Paints
9. Pesticides
10. Taxidermy

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- ▶ **Mad hatter disease, or mad hatter syndrome or Erethism or erethism mercurialis ?????**

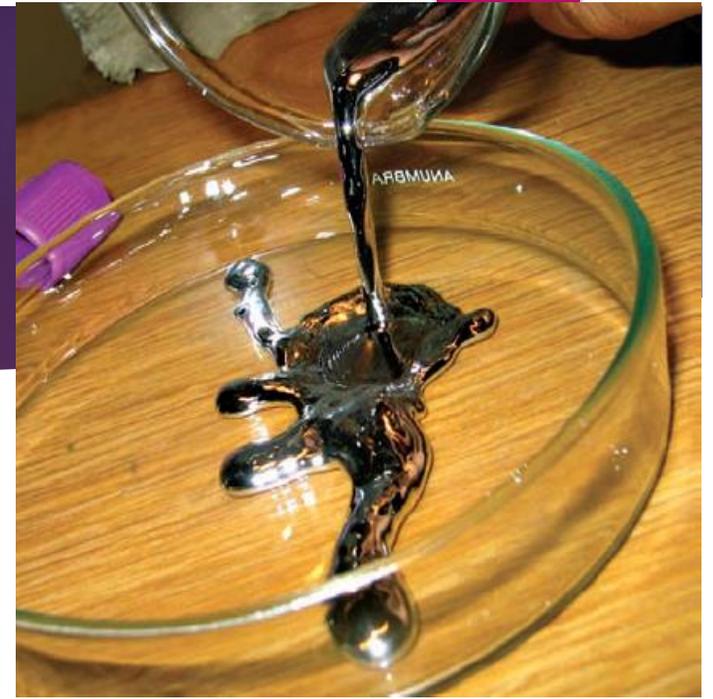
Introduction

Synonyms

- ▶ Quicksilver; Liquid silver

Physical Appearance

- ▶ Heavy, silvery liquid, per se non toxic but vapourises at room temperature to give off a toxic vapour: **mercuric mercury**.
- ▶ In its solid state, mercury is a tin-white, ductile metal that is malleable enough to be cut with a knife



Forms and Sources of Mercury



- Hg^0 – Elemental Mercury
 - The metal form; liquid and gas forms; dental amalgam
- Hg^{II} – Inorganic Mercury
 - The salt, formed by oxidation of Hg^0 in blood and mouth



- MeHg - Methylmercury
 - Organomercurial; found in fish; Also formed in gut from amalgam mercury



- EtHg - Ethylmercury
 - Synthetic organomercurial; antimicrobial
 - ***Ends up mostly as Hg^{II}***



Types/Forms

Salts or compounds of mercury may be

- ▶ Inorganic or
- ▶ Organic .

Inorganic salts are of two types—

- ▶ Mercuric (bivalent, i.e. Hg^{++}) →

mercuric chloride, mercuric oxide, mercuric sulfide

- ▶ Mercurous (monovalent, i.e. Hg^+). →

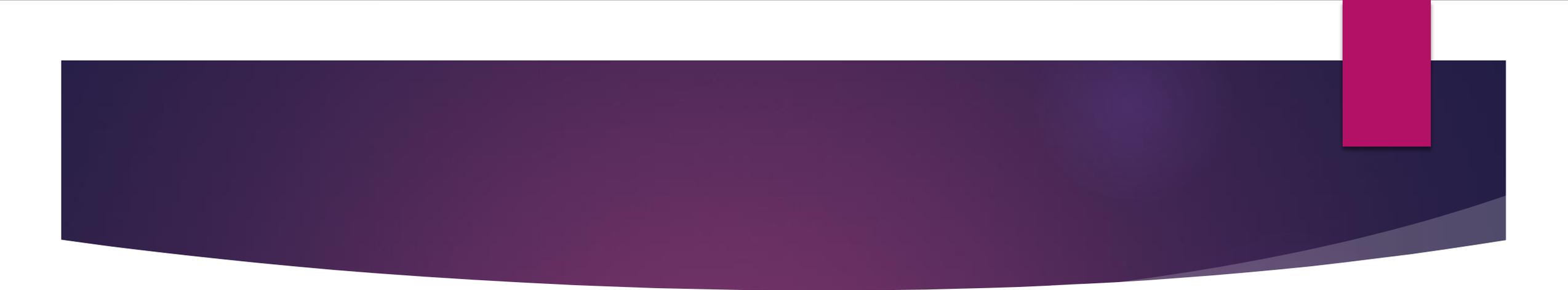
mercurous chloride

Source

- ▶ Breaking of mercury **fluorescent light bulbs**, heating of **mercury-gold** amalgams
- ▶ Use of mercury-containing **latex paint**
- ▶ Ingestion or handling of **liquid mercury from thermometers** or other mercury-containing devices
- ▶ Insertion or removal of **dental amalgam restorations** can generate mercury vapour
- ▶ **Bruxism, chewing, and tooth brushing** may increase amalgam release of mercury vapour

Source of poisoning

- ▶ **Occupations** which have the greatest exposure to mercury vapours
 - ▶ Mining and processing of cinnabar ore,
 - ▶ Chlor alkali industry
 - ▶ Mercury containing manufacturing instruments or materials.
- ▶ **Dietary exposure** to mercury (methyl mercury) from fish, shellfish and marine mammals

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- ▶ Organic mercurials are generally more toxic and comprise mainly compounds such as phenyl and methoxymethyl mercury, and alkyl compounds such as ethyl and methyl mercury.
 - ▶ The most toxic compound of mercury is methyl mercury.

Fatal Dose

- ▶ Fatal ingested mercury dose in man is estimated to be 100 grams
- ▶ Mercuric chloride: 0.5 to 1 gm/70 kg
- ▶ Mercurous chloride : 1.5 to 2 gm/70 kg

Methylmercury-

- ▶ Ingestion of 10–60 mg/kg may be lethal
- ▶ Chronic daily ingestion of 10 mcg/kg may be associated with adverse neurologic and reproductive effects

Dimethylmercury-highly toxic

- ▶ Exposure to a few drops has resulted in a delayed but fatal encephalopathy.

Summary of absorption and toxicity of mercury compounds

Form	Absorption		Toxicity	
	Oral	Inhalation	Neurologic	Renal
Elemental (metallic) mercury				
Hg ⁰ liquid	Poor	NA*	Rare	Rare
Hg ⁰ vapor	NA*	Good	Likely	Possible
Inorganic mercuric salts				
Hg ²⁺	Good	Rare but possible	Rare	Likely
Organic (alkyl) mercury				
RHg ⁺	Good	Rare but possible	Likely	Possible

Toxicokinetics

Absorption

DERMAL

- ▶ Intact skin (organic and inorganic mercurial)
- ▶ Elemental mercury may be readily absorbed if applied to the skin in suitable form

Absorption

	Elemental Hg	Ionic Hg	MeHg
Inhalation	75-85% of an inhaled dose of the vapor is absorbed by the body (human studies). 97% of absorption occurs through the lungs.	Data are limited. Absorption via inhalation is estimated at 40% (dog study).	Vapors of MeHg can be absorbed; the amount is unknown.
Oral	< 0.01% of an ingested dose is absorbed from the GI tract (rat study).	Absorption from the GI tract following oral dose is estimated at 7-15% (human study). A mouse study indicates that absorption is approximately 20%.	Approximately 95% of MeHg in fish is absorbed from the GI tract (human studies). The exact site of absorption is unknown.
Dermal	Dermal absorption rate = 0.024 ng Hg/cm ² skin for every 1 mg/m ³ in the air (human study). < 3% of total amount of elemental Hg absorbed by the body is from dermal exposure.	Approximately 2-3% of a dermally applied dose of mercuric chloride was absorbed during a 5-hour period (guinea pig study).	Approximately 2-3% of a dermally applied dose of mercuric chloride was absorbed during a 5-hour period (guinea pig study).

DISTRIBUTION

Elemental Hg

Absorption results in rapid diffusion across the lungs and entrance into the bloodstream, where it is distributed throughout the body (because it is lipophilic), including the blood-brain barrier and the placenta.

Ionic Hg

The ingested dose is rapidly distributed from the the GI tract to the blood and organs. Mercuric Hg has a high affinity for sulfhydryl groups in the RBCs and plasma. The highest concentration is in the kidneys. Mercuric mercury induces metallothionein production in the kidneys, which may contribute to the kidney's accumulation of mercuric mercury. It does not cross readily cross the blood-brain barrier or the placenta because of its ionic charge.

MeHg

The percentage of absorbed MeHg from the GI tract that is distributed to the blood ranges from 1% to 10% About 5% is absorbed into the bloodstream and is distributed to all tissues within a few days. The concentration in RBCs is roughly 20X the concentration in plasma. Maximum levels (~10%) occur in the brain, in 5-6 days. It is also readily transferred to the fetus and the fetal brain. The high mobility of methyl mercury in the body is not due to lipid solubility. It is present in the body as water-soluble complexes mainly attached to the sulfur atom of thiol ligands. MeHg transport across the blood-brain barrier occurs via a MeHg-L-cysteine complex, which is transported by the L-system (leucine preferring) amino acid carrier.

Metabolism

Elemental Hg

Elemental Hg is oxidized in the red blood cells by catalase and hydrogen peroxide to divalent ionic (mercuric) Hg.

Ionic Hg

Mercuric Hg is unstable in vivo and has been shown to convert to elemental Hg (rat study). It can also be methylated by intestinal flora, but cannot be methylated in body tissues.

MeHg

MeHg is stable in the body compared to other species. It is slowly demethylated to mercuric Hg in tissue macrophages, intestinal flora, and the fetal liver. Although these sites of demethylation are known, the enzymes in mammalian tissues responsible for the biotransformation have not yet been identified. It is metabolized to ionic mercury at a rate of around 1% of the body burden per day. The mercuric Hg resides for long periods of time in the CNS, probably in an inert form.

Excretion

Elemental Hg	Ionic Hg	MeHg
<p>Approximately 7-14% of inhaled mercury vapor is exhaled within a week after exposure. The rest of the elemental Hg is either excreted via sweat and saliva, or is excreted as mercuric Hg.</p> <p>Approximately 80% is excreted as mercuric Hg via feces and urine. Half-life elimination is approximately 58 days. This is slightly more than 1% of the body burden/day.</p>	<p>Approximately 85% of an oral dose is excreted via feces within a couple days. Most of the absorbed ionic Hg is excreted in urine. Smaller amounts are excreted in saliva, bile, sweat, exhalation, and breast milk. Half-life excretion ranges from 49-96 days.</p>	<p>The major routes of excretion are bile and feces. MeHg undergoes enterohepatic cycling where it is secreted into bile, and then partly reabsorbed and returned to the liver. Most MeHg is eliminated by demethylation and then excretion of the ionic form in the feces (~90% in feces as mercuric Hg). This process does not occur in nursing infants due to incomplete development; their process of elimination is not understood. Breast milk is also a route of excretion.</p> <p>The range of half-life elimination has been estimated at 45-90 days (although much faster for lactating females). Individuals who are exposed regularly to MeHg reach a steady-state body burden in about 5 half-lives (~1year).</p>

Mechanism of toxicity

- ▶ Mercury reacts with **sulfhydryl (SH) groups**, resulting in enzyme inhibition and **pathologic alteration of cellular membranes**.
- ▶ **Inactivation of various enzymes and structural proteins, and alterations of cell membrane permeability**, are believed to contribute to the severe toxicologic effects.
- ▶ Increased oxidative stress, disruption of microtubule formation, interference with protein synthesis, DNA replication, and Calcium homeostasis are purported pathways.

Metallic mercury vapor

1. Altering the tertiary and quaternary structure of proteins and by **binding with sulfhydryl and selenohydryl groups**
2. Potentially **impair function of any organ, or any subcellular structure**
3. Chief target organ of mercury vapor is the **brain**, but peripheral nerve function, renal function, respiratory function, immune function, endocrine and muscle function, and several types of dermatitis have been described

Inorganic mercury

All three Binds with sulfhydryl groups

1. Acute poisoning with mercuric salts (typically HgCl_2) generally targets the **gastrointestinal tract and the kidneys**.
2. Extensive precipitation of **enterocyte proteins of gut occurs with potential necrosis of the gut mucosa**. This may produce death
3. **Surviving patients** commonly develop **renal tubular necrosis**
4. Immune dysfunctions include **hypersensitivity reactions to mercury exposure**
5. **Thyroid dysfunction** seems associated with inhibition of the **5' deiodonases**

Organic Mercury

1. Methyl mercury reacts with **sulfhydryl groups throughout the body**, therefore potentially **interfering with the function of any cellular or subcellular structure**.
2. **Interfere with DNA transcription and protein synthesis**, including protein synthesis in the developing brain, with destruction of endoplasmic reticulum and disappearance of ribosomes
3. **Disruption of numerous subcellular elements in the central nervous system and other organs and in mitochondria**;

Metallic mercury vapor

4. Metallic mercury vapor is also a **pulmonary irritant**.

Inorganic mercury

6. Inorganic mercuric salts are **corrosive to the skin, eyes**.

Organic Mercury

4. **Disruption of heme synthesis**, cell membrane integrity, free radical generation, neurotransmitter disruption, and stimulation of neural excitotoxins, resulting in damage to many parts of the brain and peripheral nervous system

5. **Imbalance in Th2 : Th1 ratios favoring autoimmunity**

6. Methylmercury is associated with **neurodevelopmental disorders**.

Inorganic and organic mercury compounds may cause **contact dermatitis**.

Elemental and methylmercury are particularly **toxic to the CNS**.

Clinical presentation

Acute Poisoning-elemental and inorganic

Inhalation:

**Delayed upto 4 hrs
dyspnoea, cough, fever, headache,
chills, GI disturbances, metallic
taste, and blurring of vision.
Stomatitis, swelling of the salivary
glands and gingivitis,
Severe- non-cardiogenic
pulmonary oedema, dyspnoea,
convulsions. conjunctival
congestion, fever, reddened palms
and soles, deep red oral mucosa
with “strawberry tongue, skin
cervical lymphadenopathy**

Ingestion:

**abdominal pain, vomiting,
diarrhoea, and shock.
Haematemesis.

severe-renal failure,
pulmonary oedema, and coma.
Urine may appear pinkish**

Injection:

**Subcutaneous or intramuscular
injections
Abscess, ulceration,
thrombophlebitis,
granuloma formation, and
pulmonary embolism.
Repeated haemoptysis

Intra-arterial injection-peripheral
embolisation with ischaemia,
gangrene, abscess
formation and ulceration.**

Strawberry tongue



Skin rash – Mucocutaneous lymph node syndrome



Clinical presentation Chronic Poisoning-elemental and inorganic

Inhalation:

Tremor

Danbury tremor

Hatter's shakes

Concussio mercurialis

Ataxia, reeling gait, Fasciculations of the tongue and

Parkinsonian syndrome

**Metallic taste, anorexia, nausea,
increased salivation, Gingivitis, halitosis, blue line on
gums**

**Erethism, Mercuria lentis, membranous
glomerulonephritis with hyaline casts and fatty casts in
the urine.**

Ingestion:

Colitis.

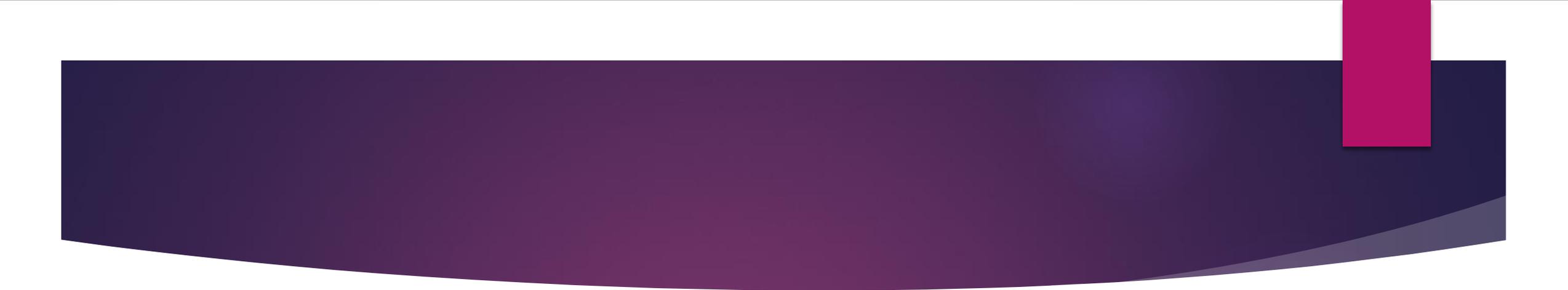
Melanosis coli.

Dementia.

Tremor.

Renal failure.

Acrodynia (Pink disease)

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- ▶ Acrodynia (Pink disease)-mainly in children
 - ▶ with anorexia, insomnia, profuse sweating, skin rash, and photophobia. The hands and feet become puffy, pinkish, painful, paraesthetic, perspiring and peeling (child pees!). Teeth may be shed, with ulceration of gums. Antisocial behaviour, insomnia, aching extremities, and Alopecia
 - ▶ Exposure to mercury at an early age is suggested as a possible factor in the aetiology of autism

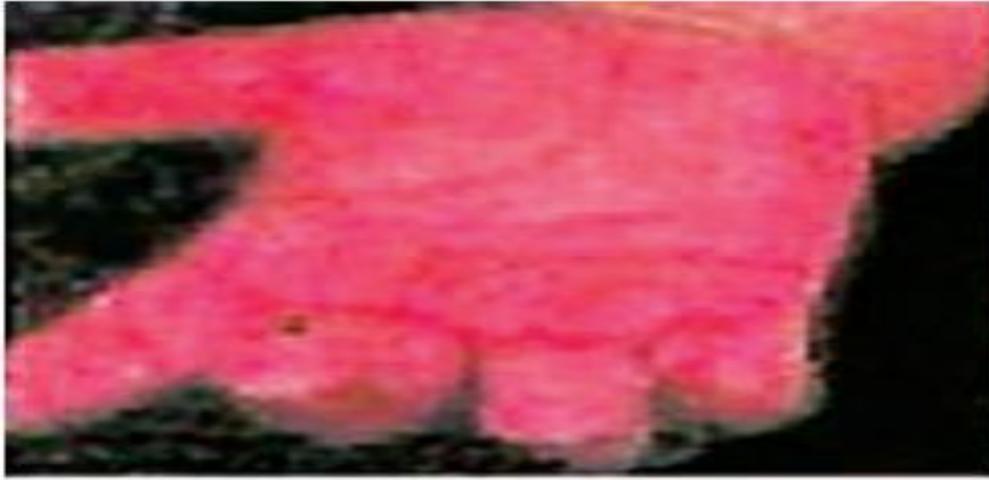


Fig 9.17: Pink disease (Acrodynia)

organic mercurials:

- ▶ Between 1953 and 1970, on the island of **Kyushu around Minimata Bay in Japan**, more than 2000 people were diagnosed to be suffering from a curious cluster of **neurological symptoms** comprising paraesthesiae, narrowing of vision, dysarthria, diminution of hearing, amnesia, ataxia, staggering gait, weakness, and emotional instability.
- ▶ Some developed paralysis and became stuporous, and out of all the people afflicted nearly a **hundred died**.
- ▶ The condition came to be known as the **Minimata disease**
- ▶ it was caused by consumption of **fish** contaminated with methyl mercury



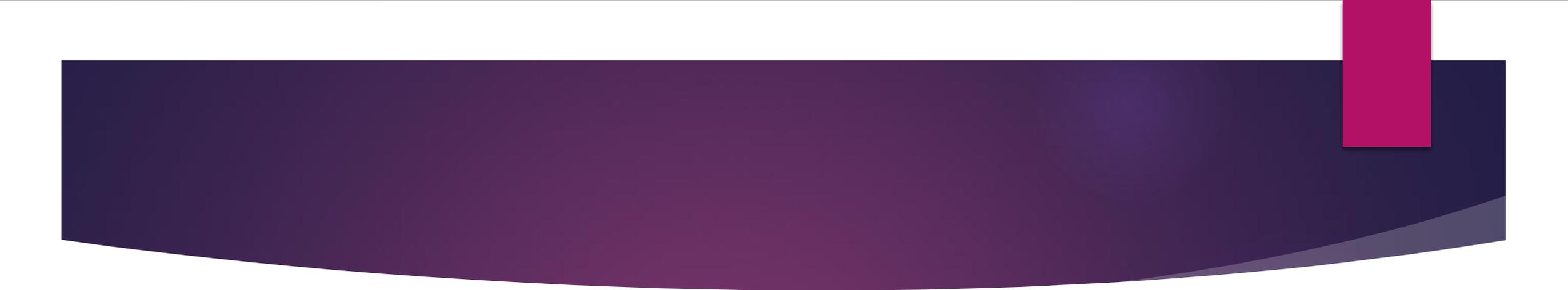
Fig 9.18: Minimata disease

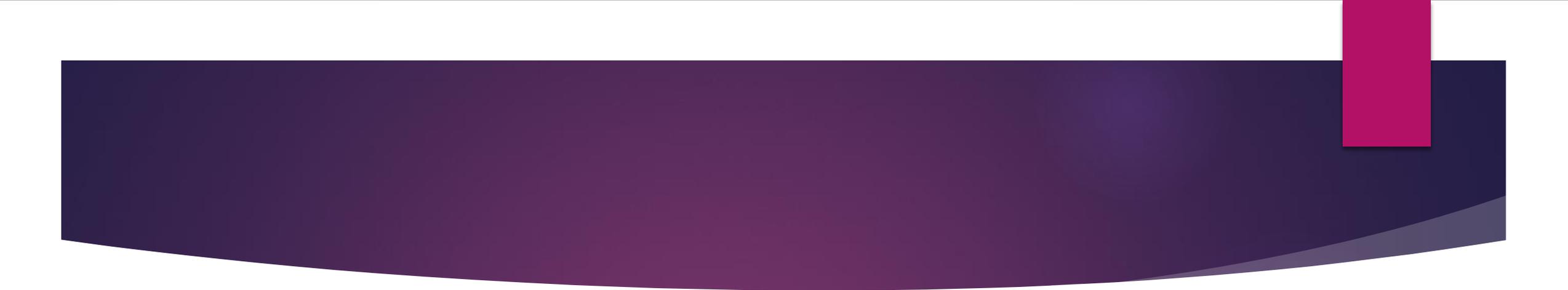
Minimata Disaster



► Minamata disease was first discovered in Minamata city in Kumamoto prefecture, Japan, in 1956. It was caused by the release of methylmercury in the industrial wastewater from the Chisso Corporation's chemical factory, which continued from 1932 to 1968. This highly toxic chemical bioaccumulated in shellfish and fish in Minamata Bay and the Shiranui Sea, which, when eaten by the local populace, resulted in mercury poisoning. While cat, dog, pig, and human deaths continued for 36 years, the government and company did little to prevent the pollution. The animal effects were severe enough in cats that they came to be named as having "dancing cat fever".

► As of March 2001, 2,265 victims had been officially recognised as having Minamata disease (1,784 of whom had died)[2] and over 10,000 had received financial compensation from Chisso. By 2004, Chisso Corporation had paid \$86 million in compensation, and in the same year was ordered to clean up its contamination.[4] On March 29, 2010, a settlement was reached to compensate as-yet uncertified victims

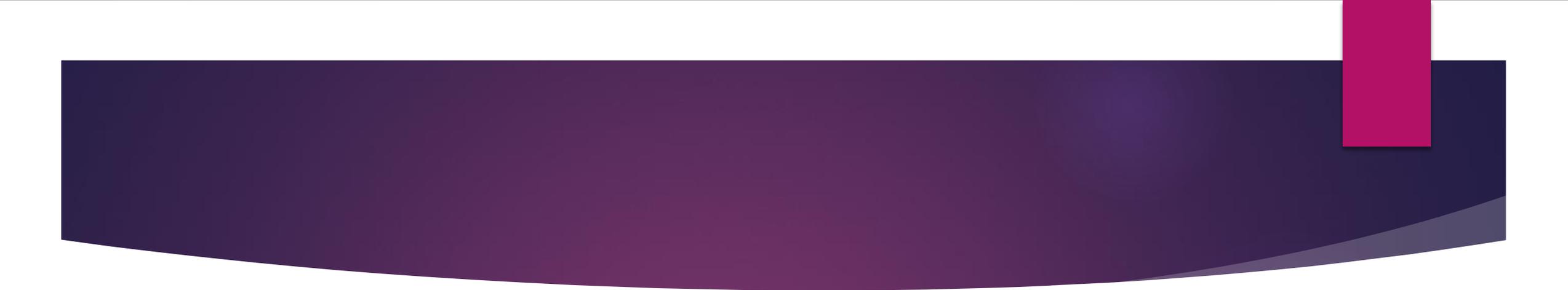
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- ▶ Methyl mercury is a subtle, **difficult to detect, long lasting poison**.
 - ▶ When large quantities of **industrial waste and agricultural fungicides** containing mercury are released into the ocean apart from volcanic discharges,
 - ▶ **Methylation** of this relatively inoffensive metal results in the production of methyl mercury which then **enters the algae-fish-human food chain**
 - ▶ This biological methylation is accomplished by a deep sea bacterium called **methanobacterium omelanskii**
 - ▶ These **bacteria are consumed by plankton** which in turn are **eaten by fish**.
 - ▶ Fish eaten by human.

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- ▶ In 1964, a similar outbreak of poisoning was reported from another part of Japan: Niigata along the Agano river. Forty three cases were diagnosed as having the Minimata disease out of whom six died.
 - ▶ Shocking tragedy in Iraq in 1971–72, when 500 people died out of a total of 6530 victims due to consumption of imported wheat and barley meant for sowing, treated with methyl mercury
 - ▶ Nearly 95,000 tonnes of seed grain treated with methyl mercury was baked into bread.

1971 Iraq poison grain disaster

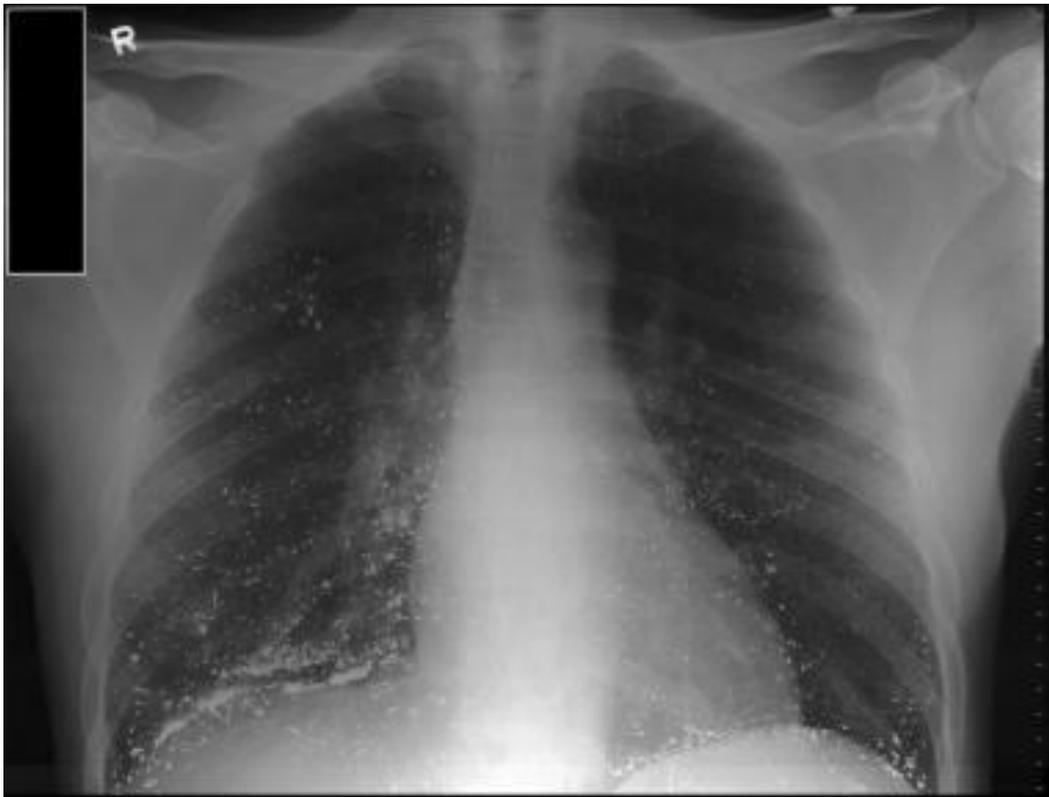


- ▶ **The 1971 Iraq poison grain disaster was a mass methylmercury poisoning incident that began in late 1971. Grain treated with a methylmercury fungicide and never intended for human consumption was imported into Iraq as seed grain from Mexico and the United States. Due to a number of factors, including foreign-language labelling and late distribution within the growing cycle, this toxic grain was consumed as food by Iraqi residents in rural areas. People suffered from paresthesia (numbness of skin), ataxia (lack of coordination of muscle movements) and vision loss, symptoms similar to those seen when Minamata disease affected Japan. The recorded death toll was 459 people, but figures at least ten times greater have been suggested. The 1971 poisoning was the largest mercury poisoning disaster when it occurred,[2] with cases peaking in January and February 1972 and stopping by the end of March.**

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- ▶ In the human body **methyl mercury is bound by haemoglobin** and circulates in this form in the bloodstream for **several weeks or months**
 - ▶ **Excretion is very slow** and the estimated half life in man is **70 days**, While in fish it is 200 days
 - ▶ It passes easily into the CNS where it selectively and irreversibly **damages** the cells of the **granular layer of cerebellum and cerebral cortex**
 - ▶ Especially injurious to the CNS of infants and children.

Diagnosis

- ▶ X-ray
- ▶ Blood mercury level-Normal level is less than 3 mcg/100 ml
- ▶ Urine mercury level: Urinary mercury is the best biological marker for chronic elemental or inorganic mercury exposure.
- ▶ Normal level is less than 10 to 15 mcg/100 ml.
- ▶ A 24-hour urine collection is recommended
- ▶ Hair analysis: Done by cold vapour atomic absorption spectrometry



Emergency and supportive measures

1. Inhalation. Observe closely for several hours for development of **acute pneumonitis and pulmonary edema**

2. Mercuric salt ingestion. Anticipate severe gastroenteritis and **treat shock aggressively** with intravenous fluid replacement.

Vigorous hydration may also help maintain urine output.

Acute renal failure is usually reversible, but **hemodialysis** may be required for 1–2 weeks.

▶ 3. Organic mercury ingestion. Provide **symptomatic supportive care**.

Treatment -Acute Poisoning

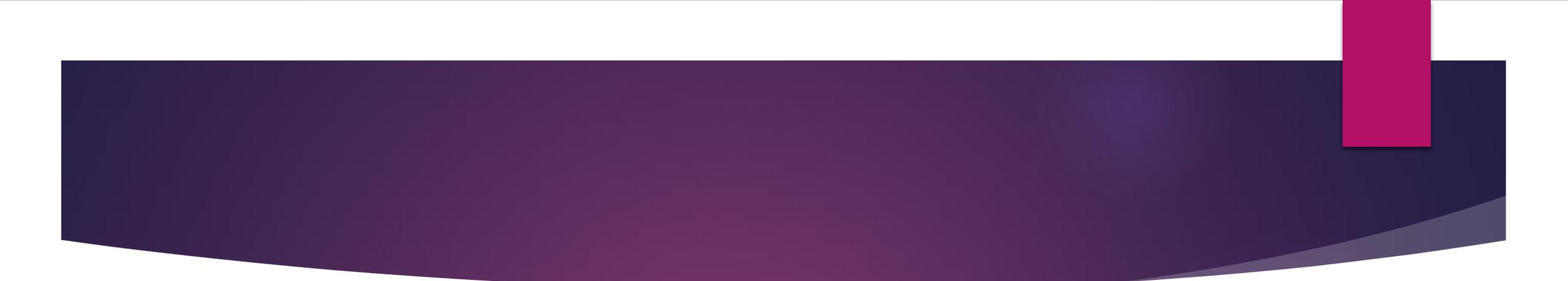
Metallic mercury & inorganic compounds

Inhalation:

- ▶ Supportive measures-give supplemental oxygen if needed.
- ▶ Chelation

Ingestion:

- ▶ In elemental mercury ingestion, take x-ray and repeat it to study the progression. If mercury gets lodged in the appendix, **perform appendectomy**.
- ▶ Administer **laxatives**.
- ▶ **Demulcents** for corrosive compounds such as mercuric chloride.
- ▶ **Stomach wash**: It may be advisable to add **egg white or 5% albumin** or just plain **milk** to the lavage fluid to bind the mercury.
- ▶ Elemental - **Multiple-dose cathartics, whole-bowel irrigation**.

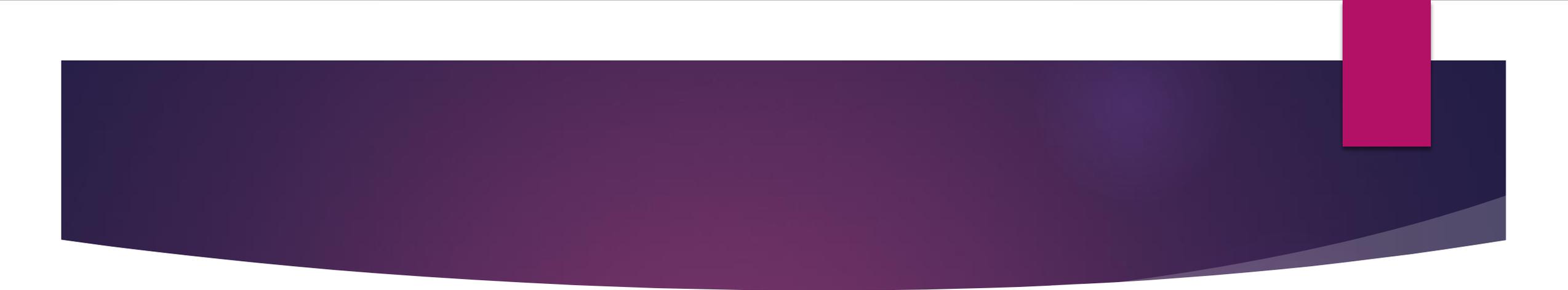


Inorganic- **Administer activated charcoal** if available. **Do not induce vomiting** because of the risk of serious corrosive injury.

Perform **gastric lavage**. Administer activated charcoal, although it is of uncertain benefit.

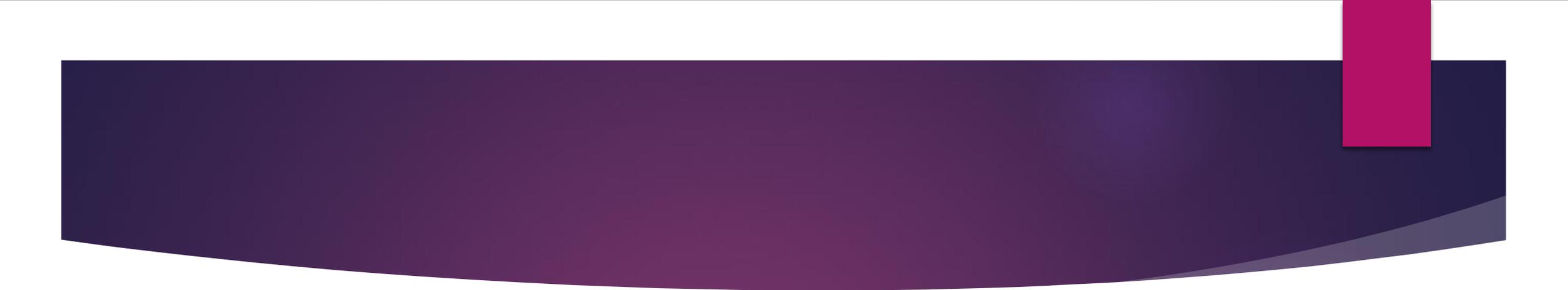
Chelation-

- ▶ Elemental-oral succimer DMSA, oral unithiol (DMPS), penicillamine (less effective)
- ▶ inorganic compounds-intravenous unithiol (DMPS), intramuscular BAL

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- ▶ Injection:
 - ▶ If there is abscess formation, perform **repeated incisions to remove the mercury**.
 - ▶ If the globules are very minute and widely distributed in the intercellular spaces, **excise the affected tissue**.
 - ▶ **Monitor the CNS and renal** functions for evidence of toxicity and treat accordingly.
 - ▶ **Chelation**.

Organic mercurial

- ▶ Supportive measures.
- ▶ Chelation is not very effective.
- ▶ In severe manifestations with acute renal failure resulting from any type of exposure, the following may be tried: **haemodialysis, haemofiltration, or plasma exchange.**
- ▶ **Haemoperfusion is said to be ineffective.**
- ▶ Perform **gastric lavage and administer activated charcoal**
- ▶ **Polythiol is a nonabsorbable resin** that can theoretically help in facilitating the removal of methylmercury (short chain alkyl organic mercury), which is then excreted in the bile after enterohepatic circulation.
- ▶ Exchange transfusion has been used as a treatment of last resort.

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- ▶ In methylmercury intoxication, limited data suggest that **oral succimer oral N-acetylcysteine (NAC)** may be effective in decreasing Hg levels in tissues, including the brain
 - ▶ Because **BAL** may redistribute mercury to the brain from other tissue sites, **it should not be used** in poisoning by metallic or organic mercury, because the brain is a key target organ.

Treatment -Chronic Poisoning

Chelation therapy—

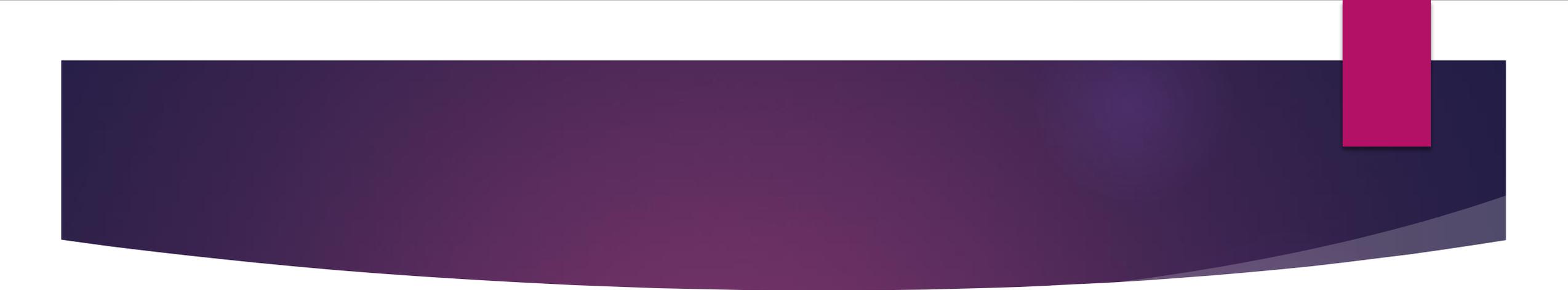
- ▶ BAL (British Anti Lewisite) - 100 mg by deep IM, every 4 hours for 48 hours, followed by 100 mg every 8 hours for 8 to 10 days.

OR

- ▶ – DMPS (2,3 DiMercapto Propane-1-Sulfonate) - 5 mg/kg IV, or 6 infusions of 250 mg/day, followed by 100 mg orally twice a day for 24 days.

OR

- ▶ – DMSA (Meso 2,3 DiMercapto Succinic Acid, or Succimer)-30 mg/kg/day orally for 5 days, followed by 20 mg/day for 14 days

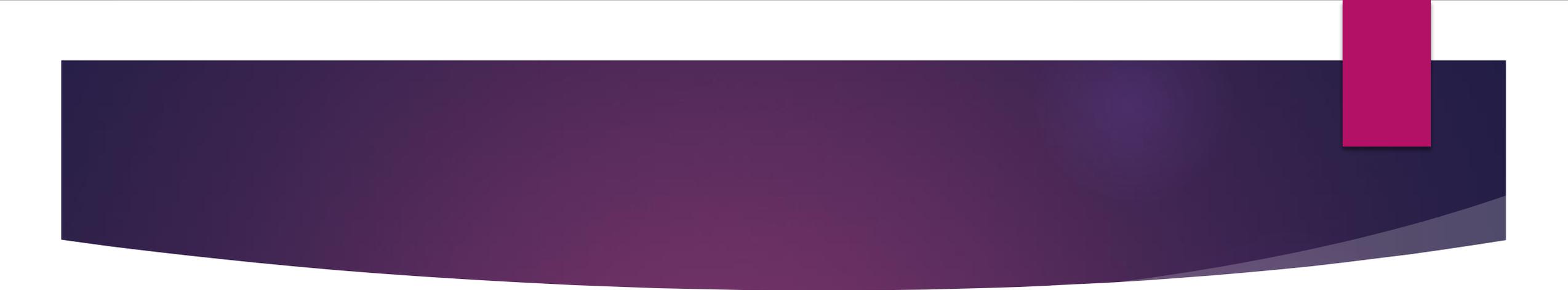


OR

- ▶ D-Penicillamine - 250 mg qid, for adults, (20 mg/kg/day) for 5 to 10 days.
- ▶ Supportive measures.
- ▶ In patients with chronic methylmercury intoxication, **repeated oral administration of an experimental polythiol resin was effective in enhancing Hg elimination** by interrupting enterohepatic recirculation



▶ **THANK YOU**

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- ▶ A 36-year-old woman presented to the ED with a three-day history of abdominal pain, diarrhea and fever.
 - ▶ One week ago her daughter had brought mercury in the liquid form from the school.
 - ▶ She had put it on the heating stove. One day later, her 14-month old sister baby got fever and died before admission to the hospital.