
CONSULTATIO · ERUDITIO · INVESTIGATIO

TOXIC METALS IN PEDIATRICS

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TOXIC METALS IN PEDIATRICS
ALL METALS CAN BE TOXIC

- Sufficient quantities
- Low concentrations
  - lead, mercury, iron manganese, cadmium, arsenic, nickel, berylium

TOXIC METALS IN PEDIATRICS
SPECIAL FACTORS

- When compared to adults, the pediatric population is more susceptible or has increased risk for metal toxicity
- Can be either symptomatic or asymptomatic
- Normality or life threatening illness

TOXIC METALS IN PEDIATRICS
SPECIAL FACTORS (Cont)

- Increased surface area in proportion to body weight
- Proximity to ground-metal dust
- Hand to mouth activity
- Different metabolism - some detoxification, pathways not fully developed
- Long term effects - start younger
- Lack of knowledge - pediatric laborers

TOXIC METALS IN PEDIATRICS
FACTORS AFFECTING METABOLISM

- Dietary deficiencies enhance intestinal absorption
- The blood-brain barrier is incompletely developed
- Placenta limited barrier function
- Site of entry - Target organ i.e. Iron - GI-liver
- Highest concentration not in target organ i.e. Bone lead - Hematopathology - CNS
- Genetic factors may increase susceptibility i.e. Lead - G6PD, Thalassemia, sickle cell trait

TOXIC METALS IN PEDIATRICS
BASICS

- Genotype- environmental interaction
- Stage of development
- Threshold effects
- Properties of agent
- Dose-response curve
- Manifestations of teratogenesis

TOXIC METALS IN PEDIATRICS
BASICS

- GENOTYPE ENVIRONMENT INTERACTION
  - The genetic differences among species and individual subjects within a species account for variability of effects

TOXIC METALS IN PEDIATRICS
BASICS (Cont)

- STAGE OF DEVELOPMENT
  - Organogenesis from day 18 thru 60 of human gestation is the period of greatest sensitivity to teratogenic insults

TOXIC METALS IN PEDIATRICS
BASICS (Cont)

- THRESHOLD EFFECTS of MECHANISMS
  - Dosage or level of exposure below which the incidence of death, malformation etc is not statistically greater than that of a control population

TOXIC METALS IN PEDIATRICS
BASICS (Cont)

- DOSE RESPONSE CURVE
  - Correlates the magnitude of the effects to the dose of drugs or chemicals the embryo was exposed to

TOXIC METALS IN PEDIATRICS
BASICS (Cont)

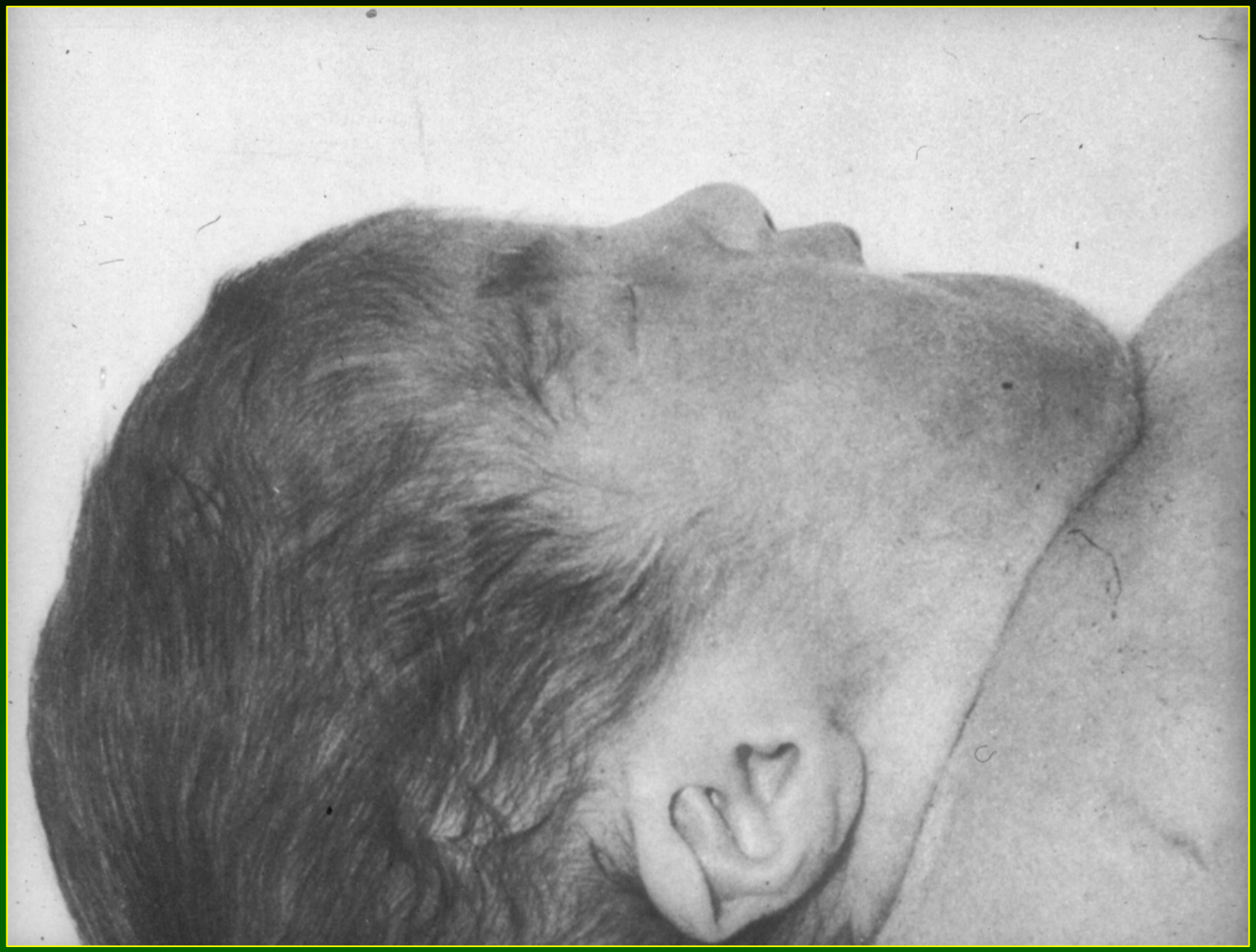
- PROPERTIES OF AGENT
  - Determine its access and effects on fetus

TOXIC METALS IN PEDIATRICS
BASICS (Cont)

- MANIFESTATIONS OF TERATOGENESIS
  - Deaths, malformation, growth retardation or functional deficit

TOXIC METALS IN PEDIATRICS

TERATOGENS



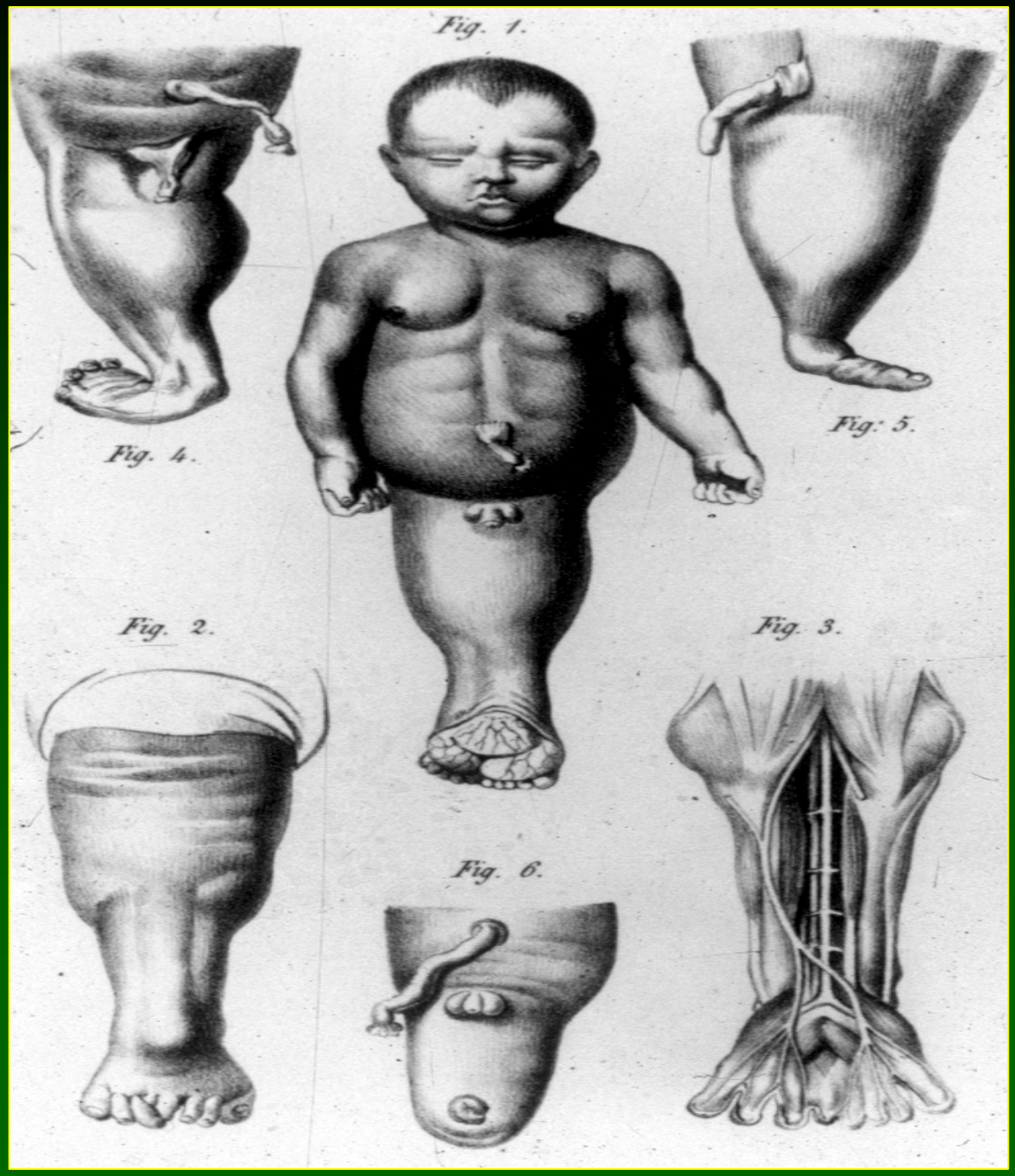

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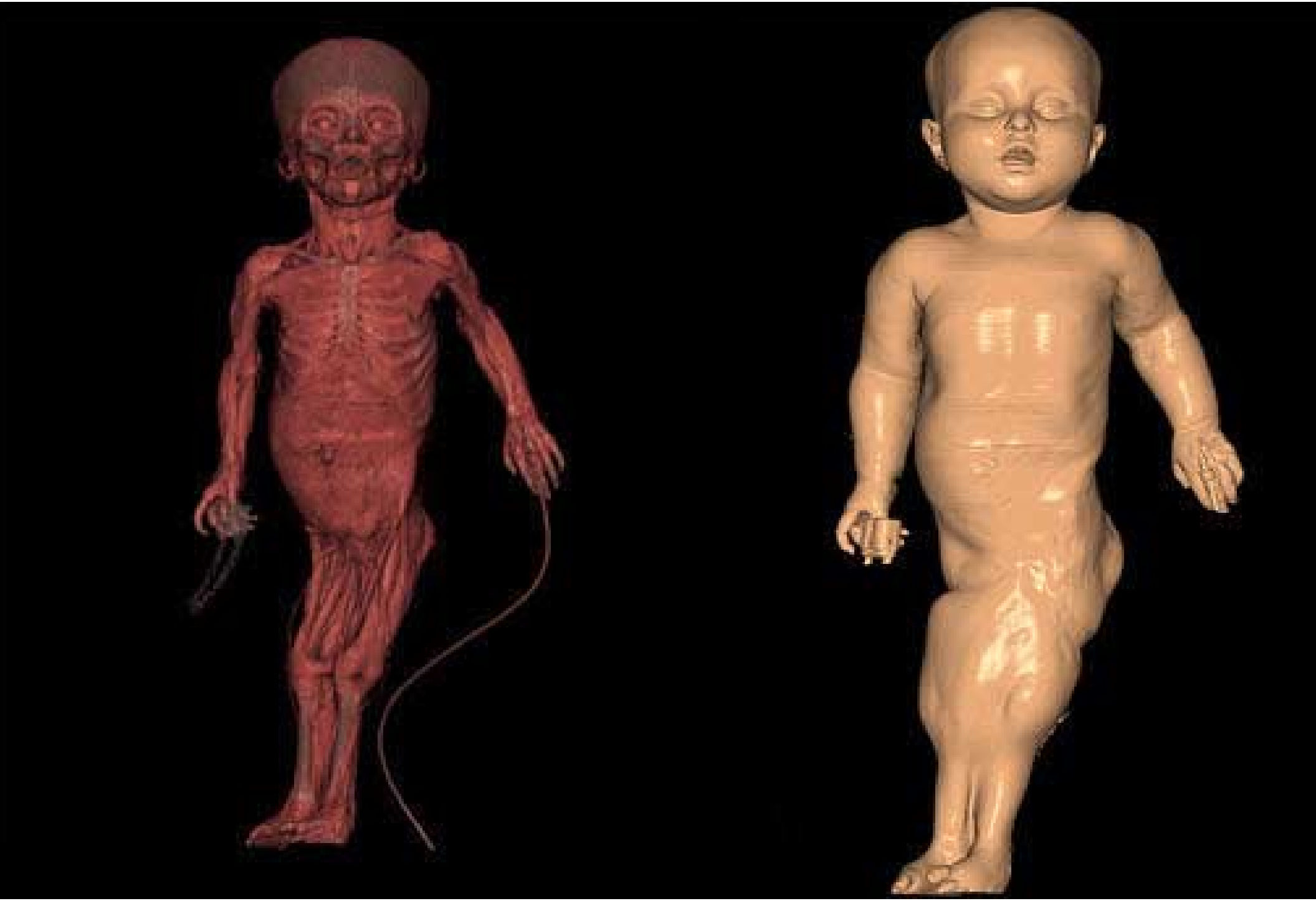
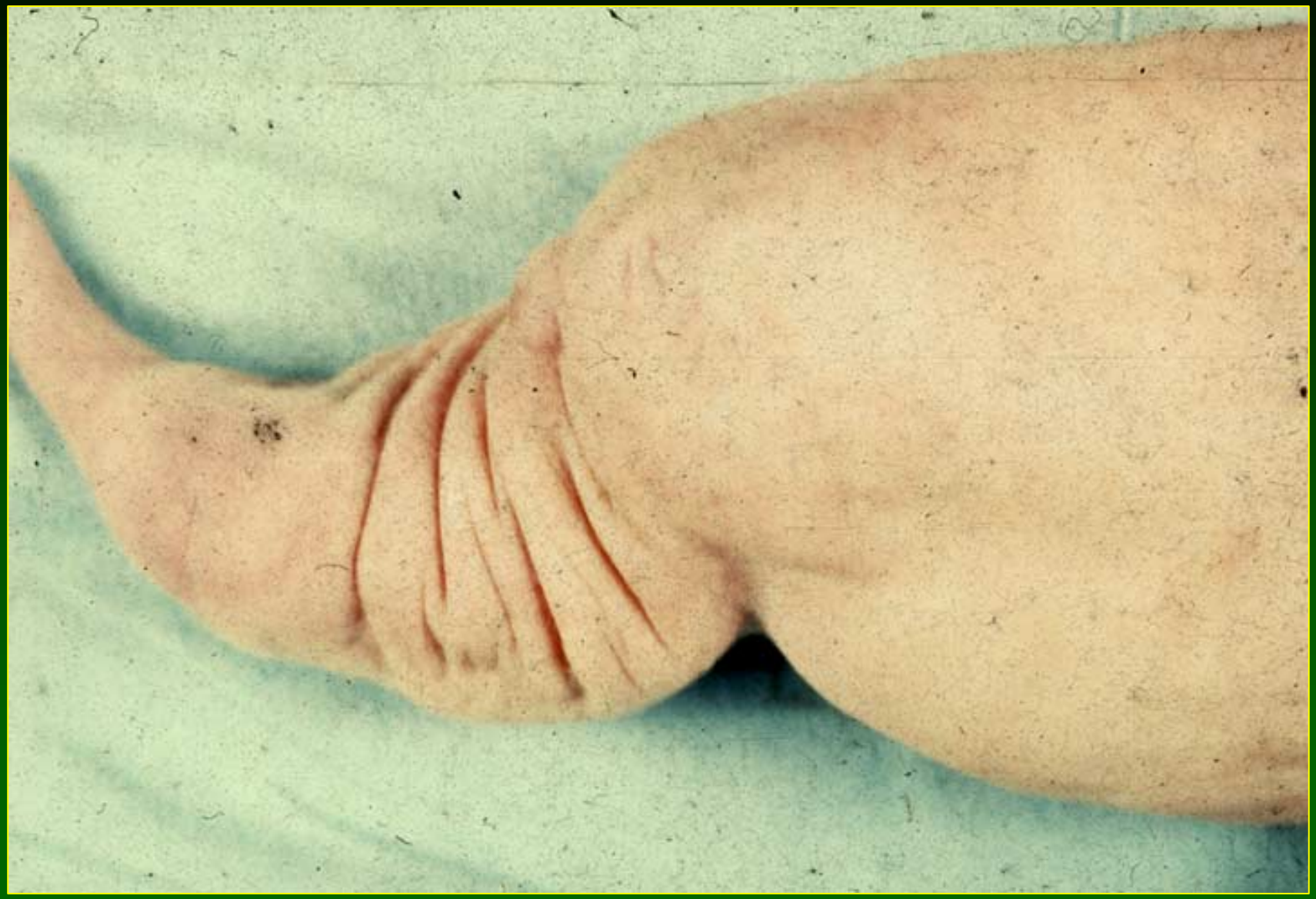
Fig. 4.
Fig. 5.
Fig. 2.
Fig. 3.
Fig. 6.






(AP/HOSPITAL DE SOLIDARIDAD)

TOXIC METALS IN PEDIATRICS
TERATOGENICITY

- Industrialized western countries
- 2-3% of births show morphologic abnormalities
- Underlying cause only know in 30-35% cases

TOXIC METALS IN PEDIATRICS

MECHANISMS OF TERATOGENSIS SUSPECTED

- Mutation
- Chromosomal aberrations
- Mitotic Interference
- Others

TOXIC METALS IN PEDIATRICS
TERATOGENESIS - ETIOLOGY

- Genetic
- Environmental
  - Drugs and Chemicals
- Unknown (polygenic)

TOXIC METALS IN PEDIATRICS

TERATOGENIC DRUGS

- Alcohol
- Aminopterin
- Androgens
- Antiacids
- Aspirin
- Barbiturates
- Estrogen

TOXIC METALS IN PEDIATRICS

DRUGS CONSUMED IN PREGNANCY

- Alcohol
- Analgesics
- Antacids
- Antiemetics
- Antihistamines

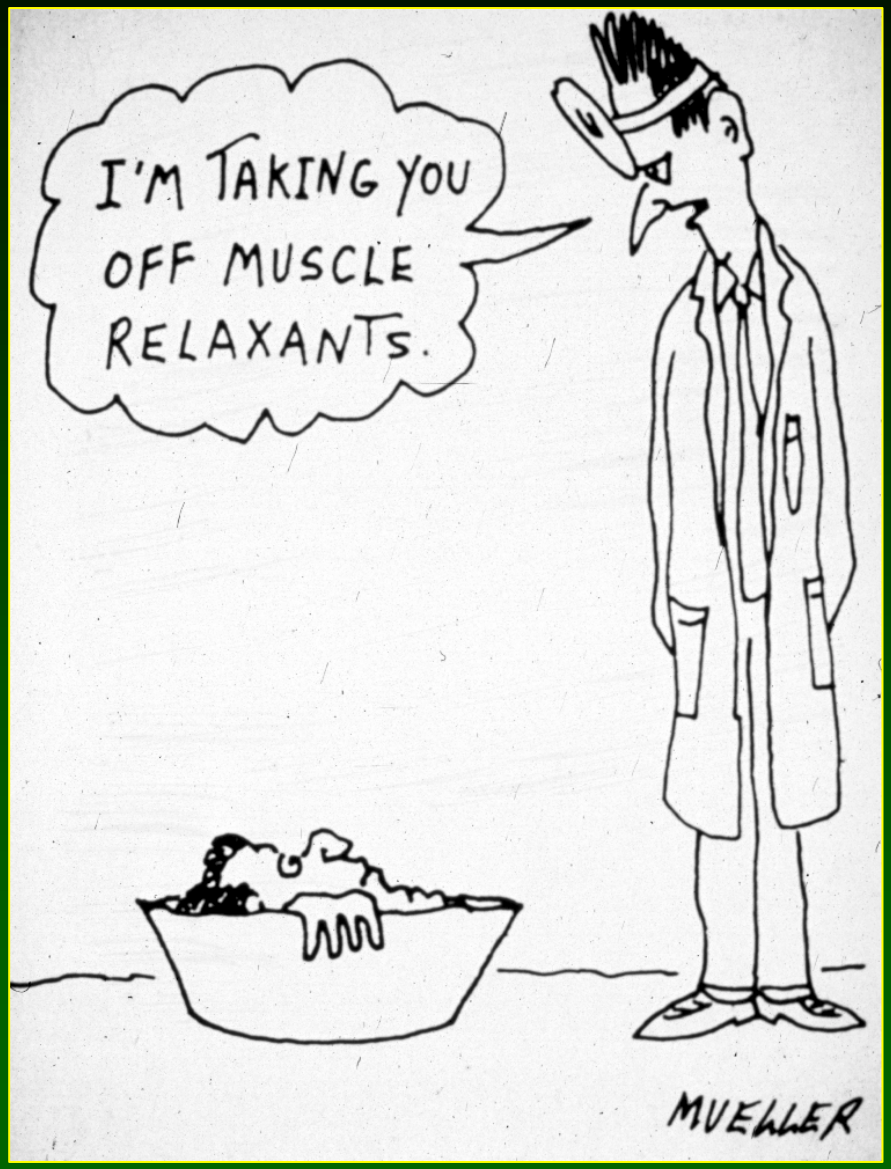
TOXIC METALS IN PEDIATRICS
QUESTIONS

- Can the agent produce the malformations?
- Likelihood in a particular patient?

TOXIC METALS IN PEDIATRICS

QUESTIONS (Cont)

- TO ANSWER WE NEED:
  - Methodology
  - Epidemiologic studies
  - Clinical studies
  - Basic science knowledge


I'M TAKING YOU OFF MUSCLE RELAXANTS.
MUELLER

COPPER

- Disordered biliary excretion - Cu accumulates
- Menke’s syndrome or Wilson’s disease

MENKE'S CLINICAL FINDINGS

- Described in1962, Copper role in 1972
- Symptoms as in Cu deficiency
  - Neuropathy (Central degeneration, developmental delay)
  - Vessel abnormalities
  - Steely hair, hypopigmentation
  - Bony changes, Osteoporosis, fractures
- Survival: 3 months to 3 years

TOXIC METALS IN PEDIATRICS

Mercury Exposure in Pediatrics

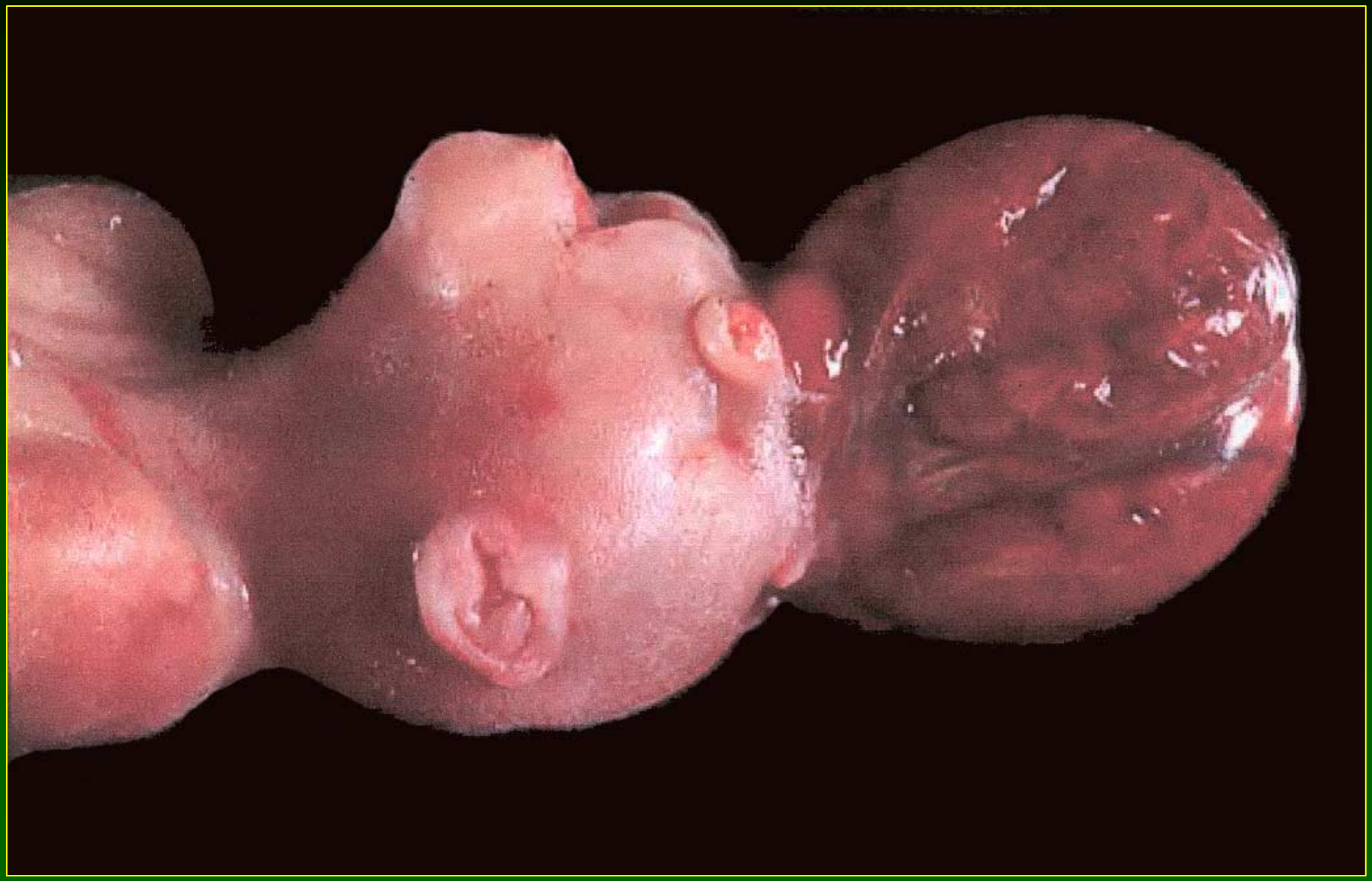
TOXIC METALS IN PEDIATRICS

MERCURY

- Can pass through placenta
- Deliveries usually uneventful
- Can pass through breast milk
- Affects developing nervous system
- Affects proximal renal tubules

MERCURY-AUTOPSY

- Atrophic brains
- Decreased neurons
- Architectural disrupture
- Exencephaly
- Encephalocele
- Hydrocephalus



TOXIC METALS IN PEDIATRICS
METHYLMERCURY

- Fetal – Infants – Intrauterine exposure
- Post natal – Children – Post natal exposure
- Adults

TOXIC METALS IN PEDIATRICS
METHYLMERCURY

Transplacental Effects:

- Embryotoxic – acting before the third month of pregnancy
- Fetotoxic – acting in or after the third month of pregnancy

TOXIC METALS IN PEDIATRICS
METHYLMERCURY

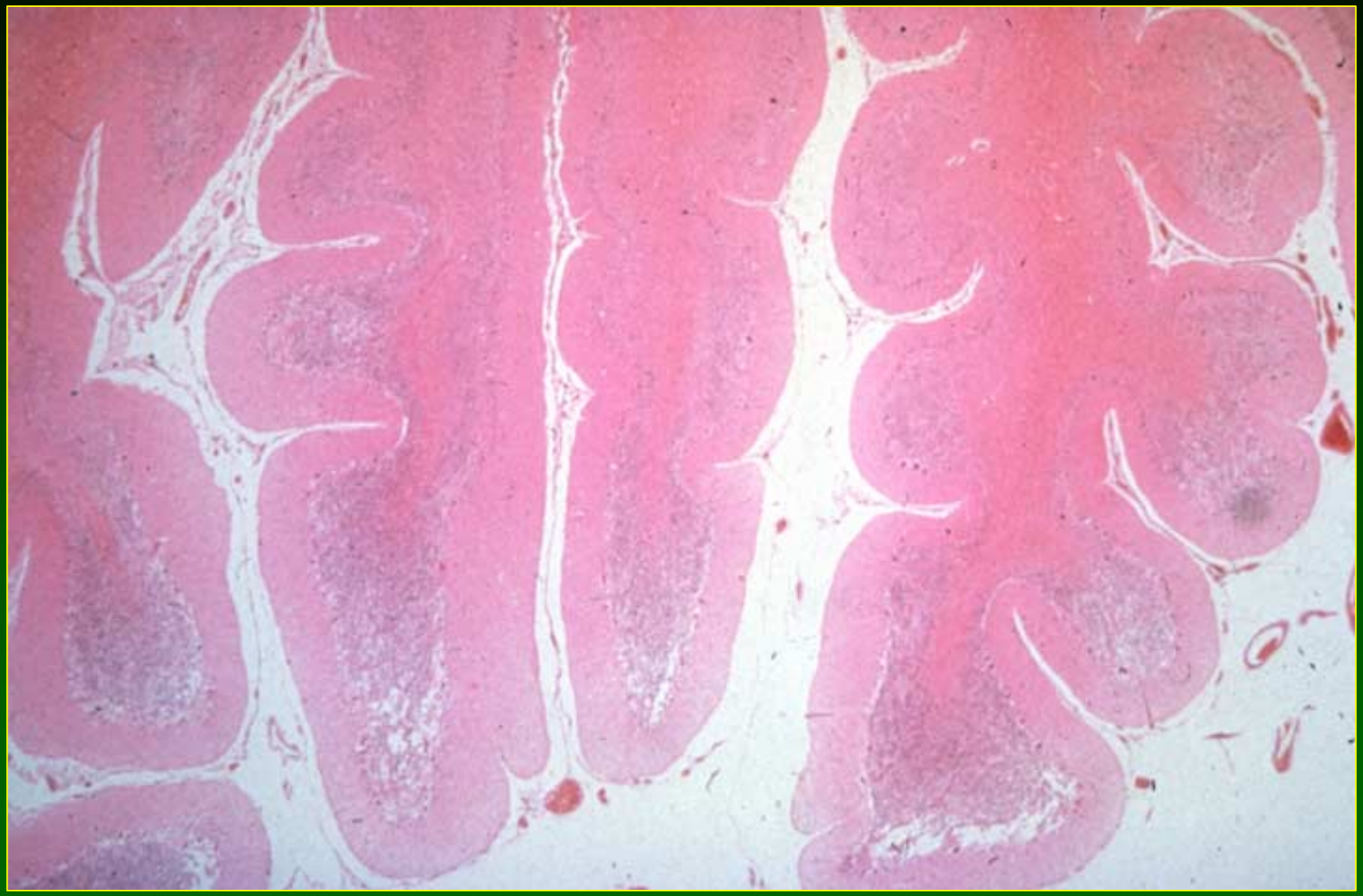
- Minamata, Japan-polluted bay-fish
- Iraq-contaminated bread
- Canadian Cree indian infants
- New Zealand

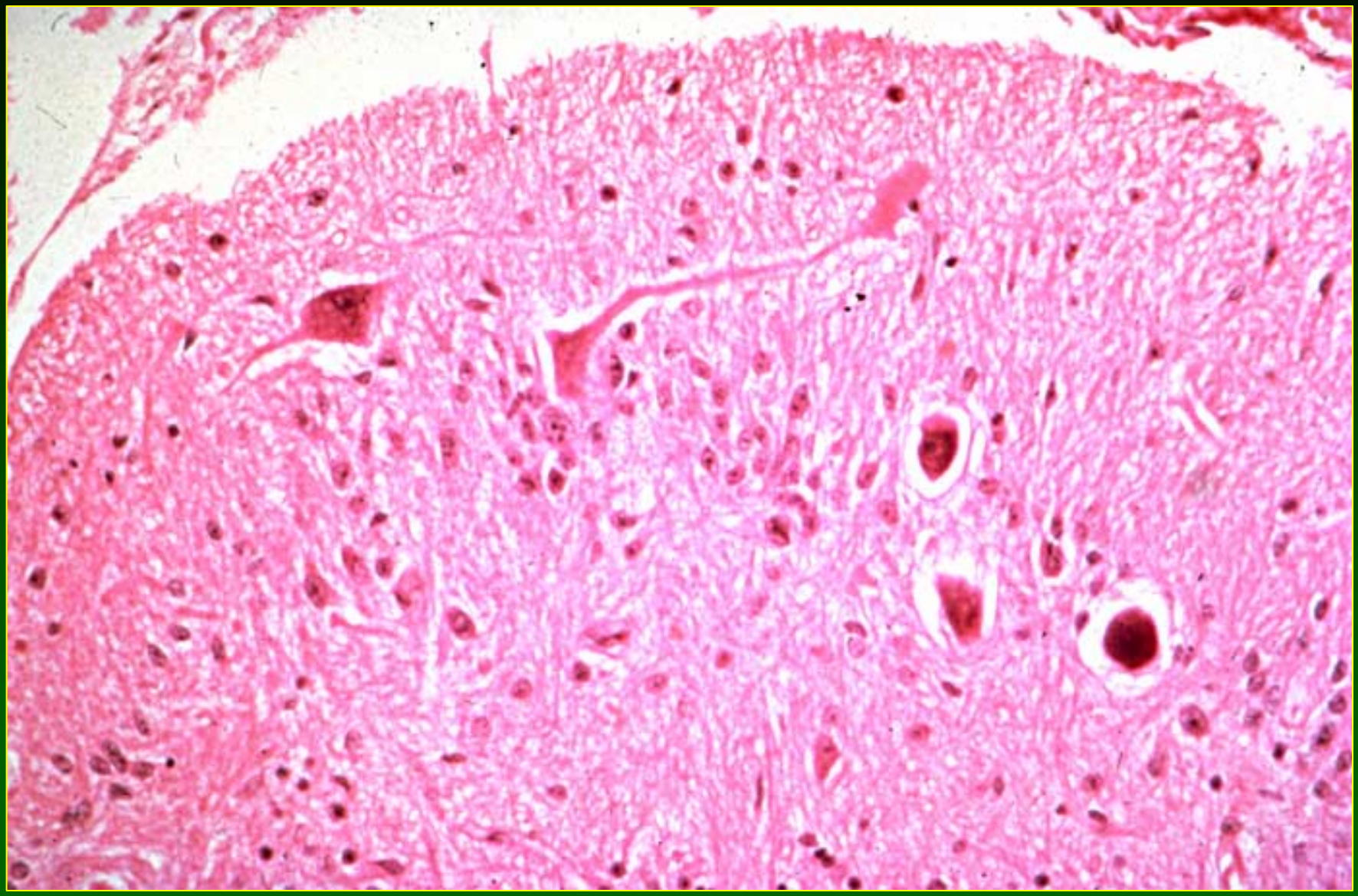
TOXIC METALS IN PEDIATRICS

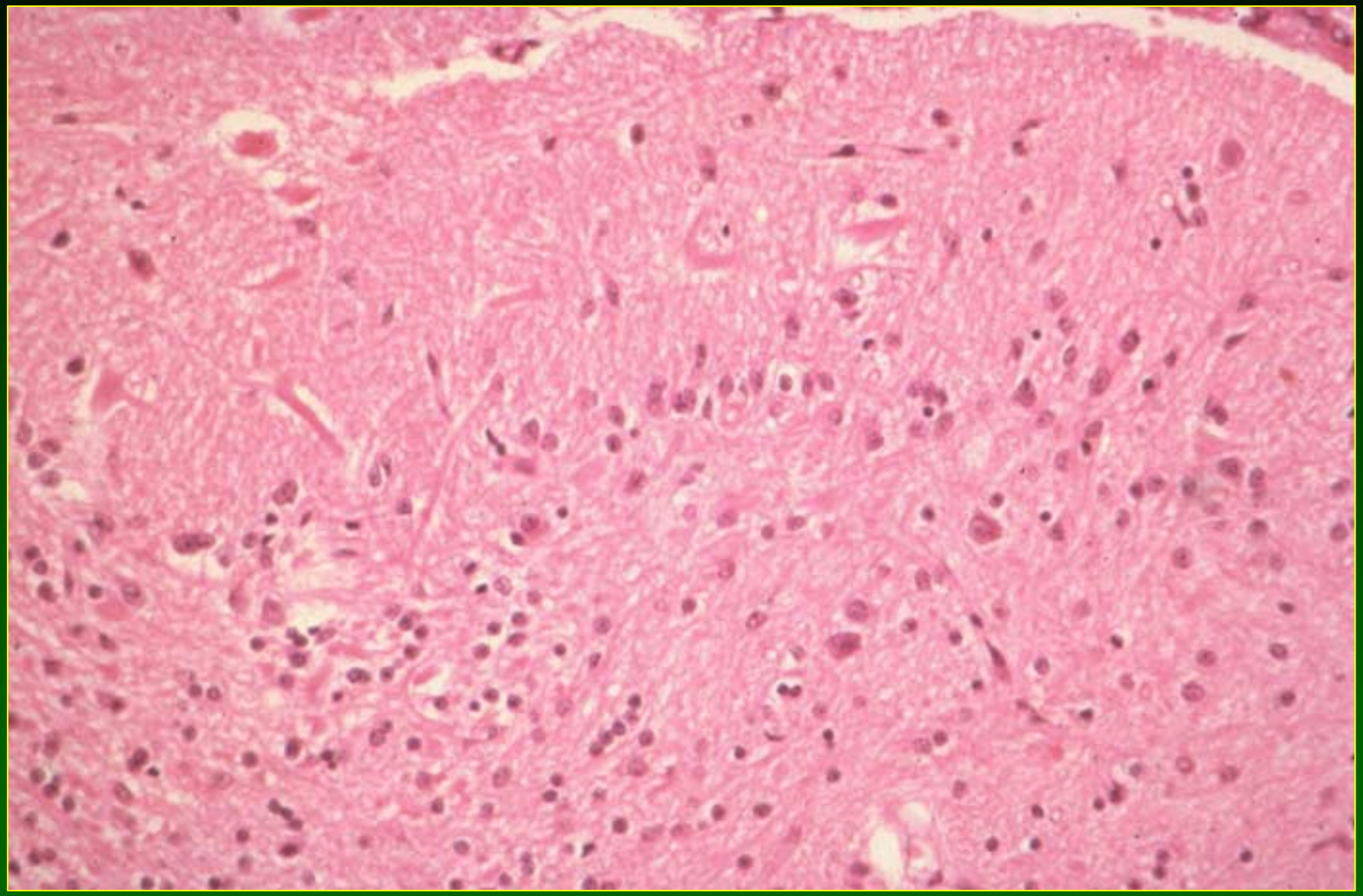
MINAMATA

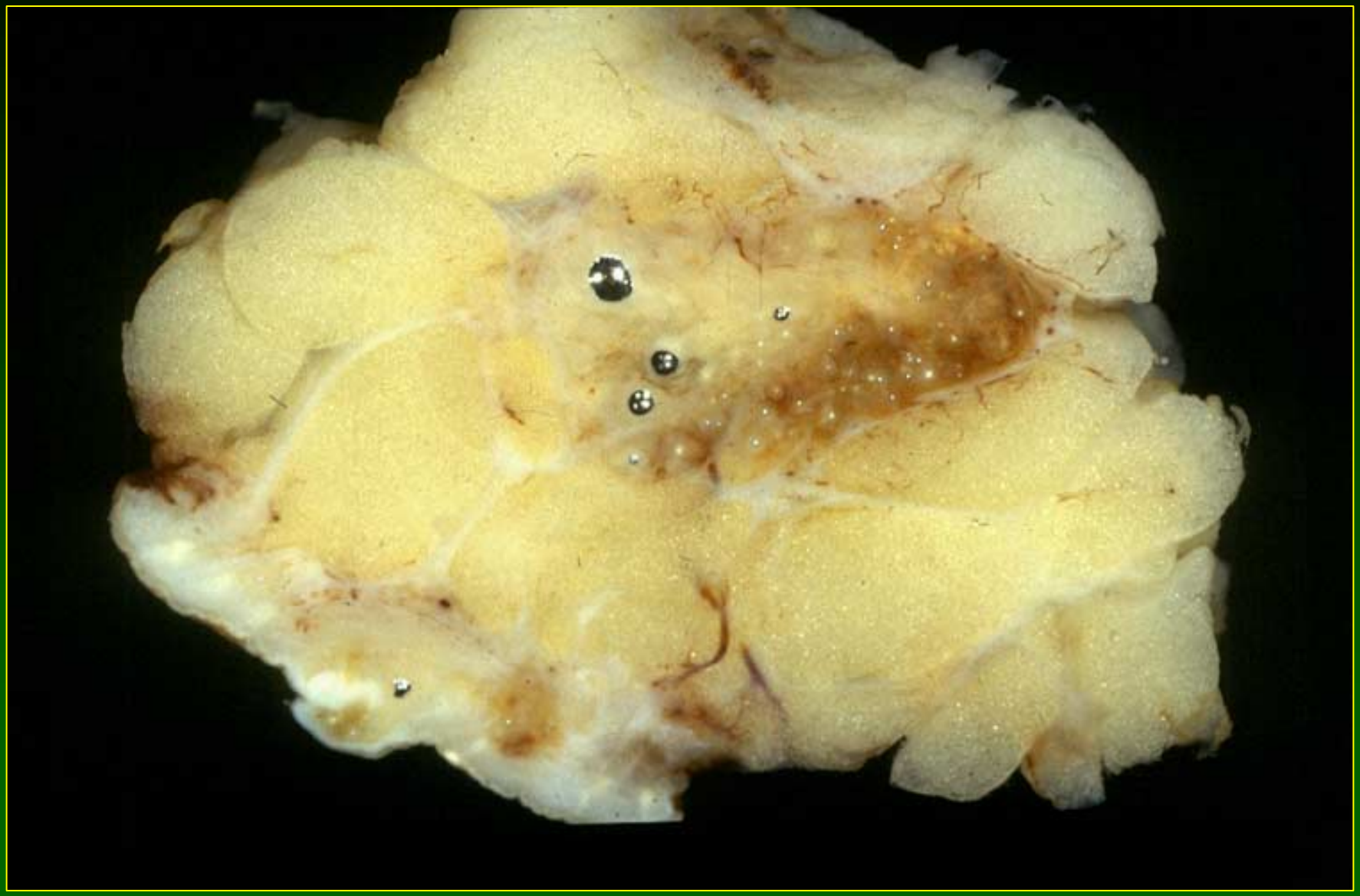
- Lethargy
- Uncoordinated suching
- Convulsions
- Cerebral palsy

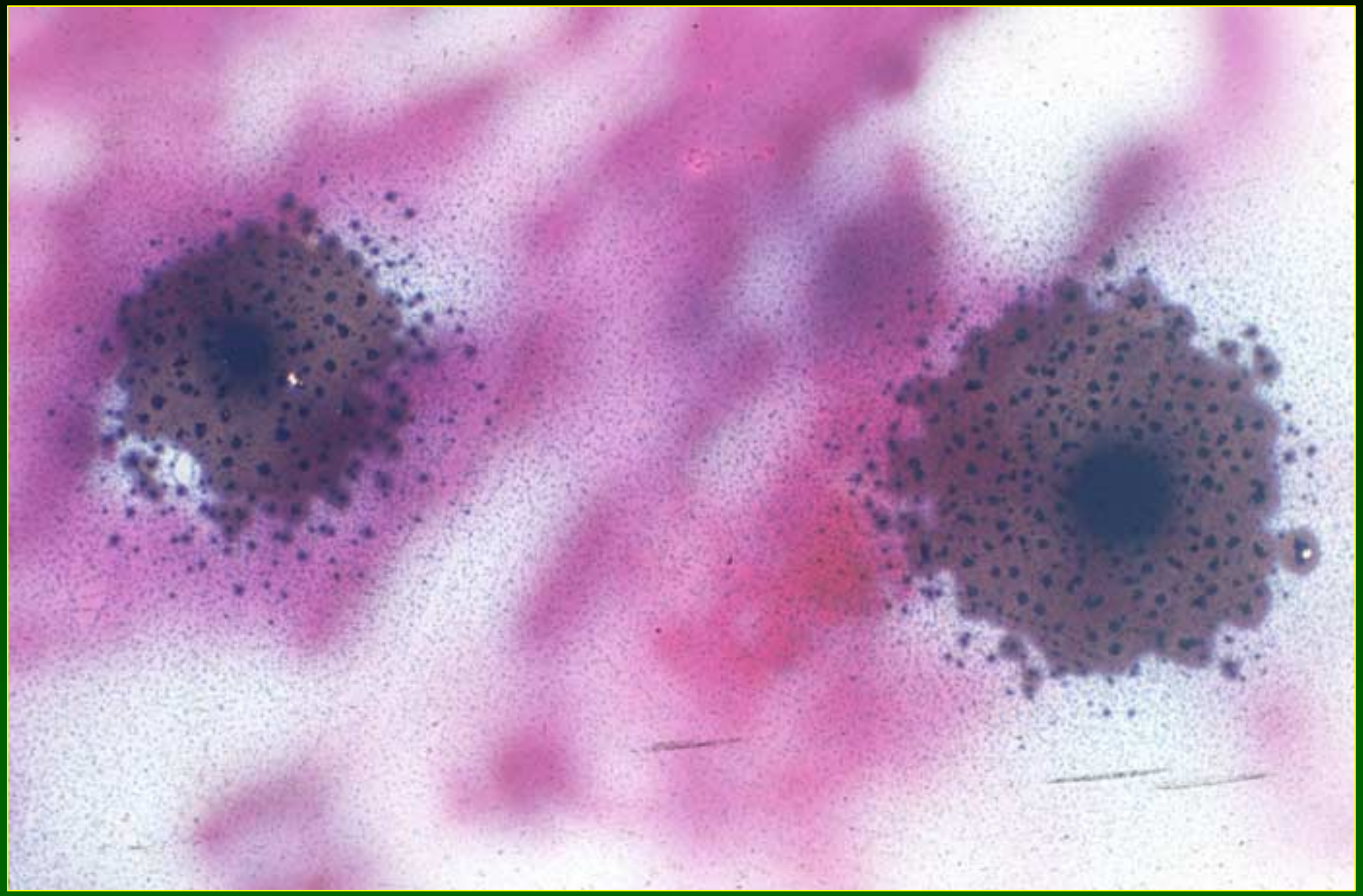
- A 5 y/o Japanese girl developed signs of acute methyl mercury poisoning after eating contaminated fish. She died at age 23 years after suffering what was described as the “apallic syndrome”











TOXIC METALS IN PEDIATRICS
LEAD METABOLISM

- Absorbed through gastrointestinal tract
- Bloodstream 95% bound to erythrocytes
- Plasma and extracellular fluid contain 1-5%
- Transfer to bone from blood
- Excreted mainly in urine

TOXIC METALS IN PEDIATRICS
LEAD EFFECTS

- Adverse effects at blood concentration of 0.10ppm (10ug/100dl)
- Asymptomatic to life threatening
- Drowsiness, irritability and vomiting
- Brain and kidney damage
- Colic
- Anemia microcytic, hypochronic
- Electrocardiographic abnormalities

TOXIC METALS IN PEDIATRICS

LEAD ENCEPHALOPATHY

- Blood lead concentrations of 80-100ug/dl
- Higher cognitive functions affected
- Irritability
- Motor impairment
- Dullness
- Convulsions
- Coma

TOXIC METALS IN PEDIATRICS
LEAD-FETUS

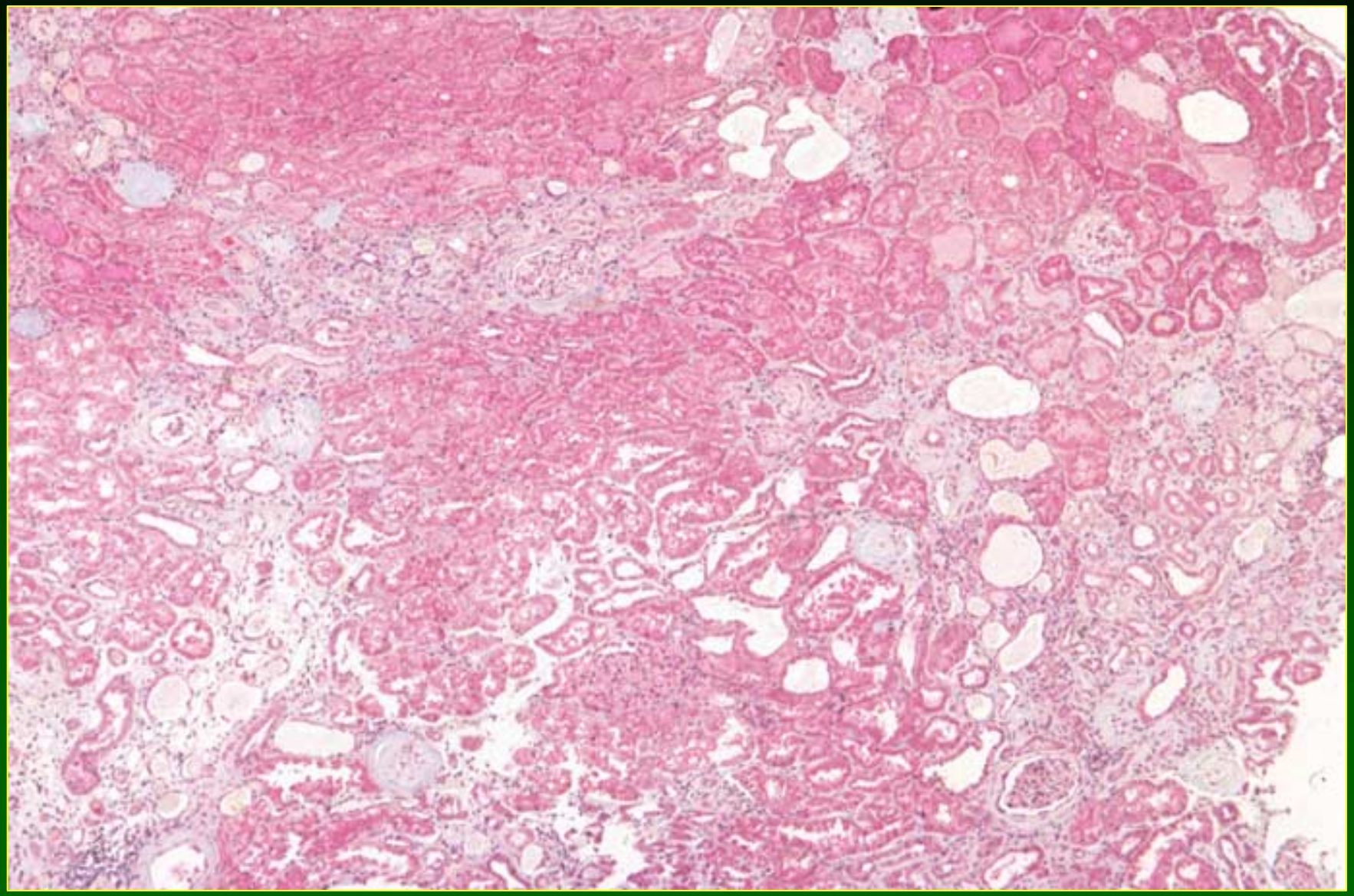
- Crosses placenta
- Fetal uptake begins at week 12 until birth
- Decreased growth
- Neurobehavioral deficits
- Reductions in gestational age
- Preterm labor
- Abortion

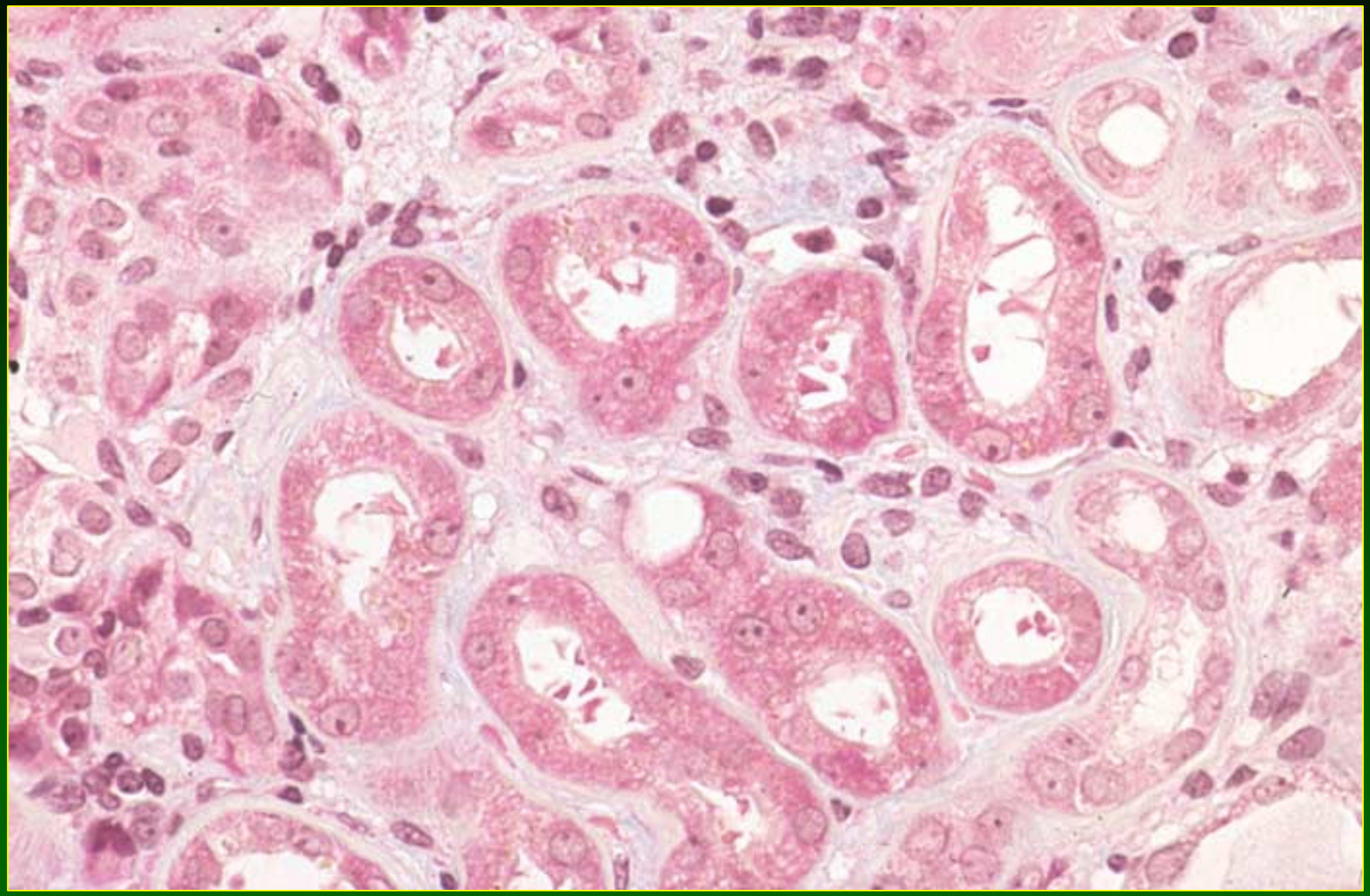
TOXIC METALS IN PEDIATRICS
LEAD-FETUS

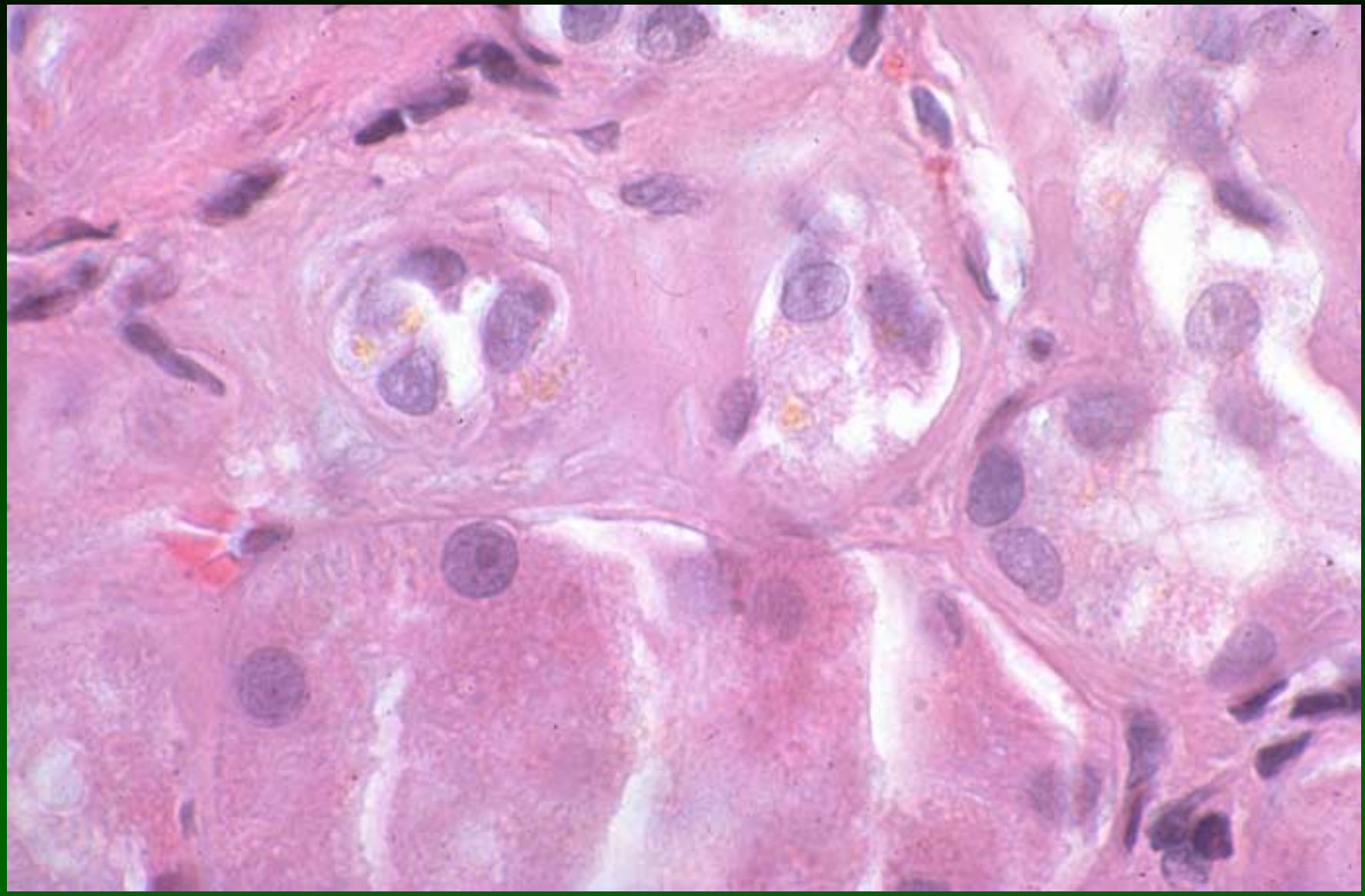
- Concentration in pregnant women and children should not exceed 20ug/100ml of blood
- Decreased growth and neurobehavioral deficits with levels as low as 10-15ug/100ml

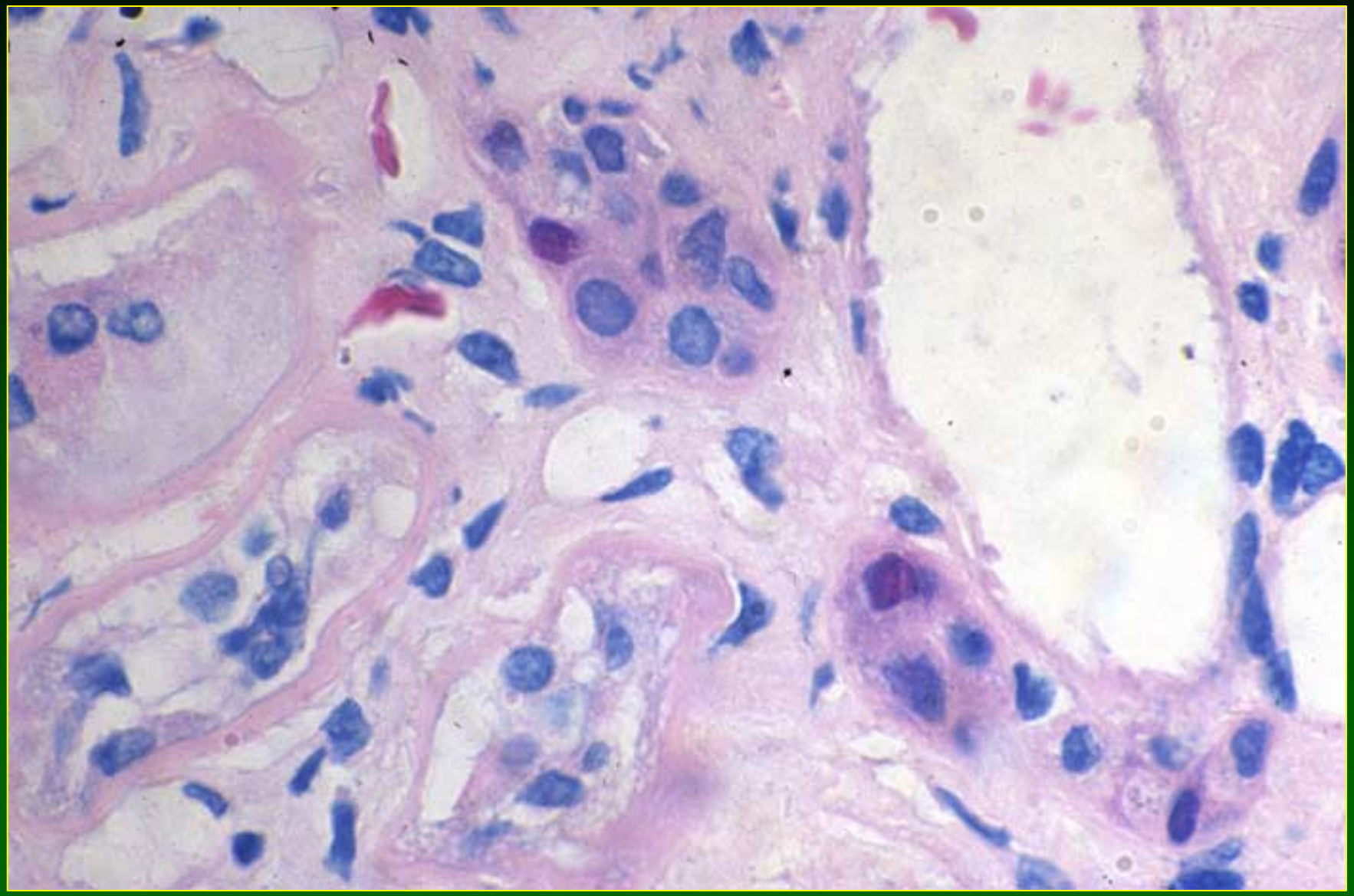
LEAD NEPHROPATHY

- Aminoaciduria
- Hypophosphatemia
- Glucosuria





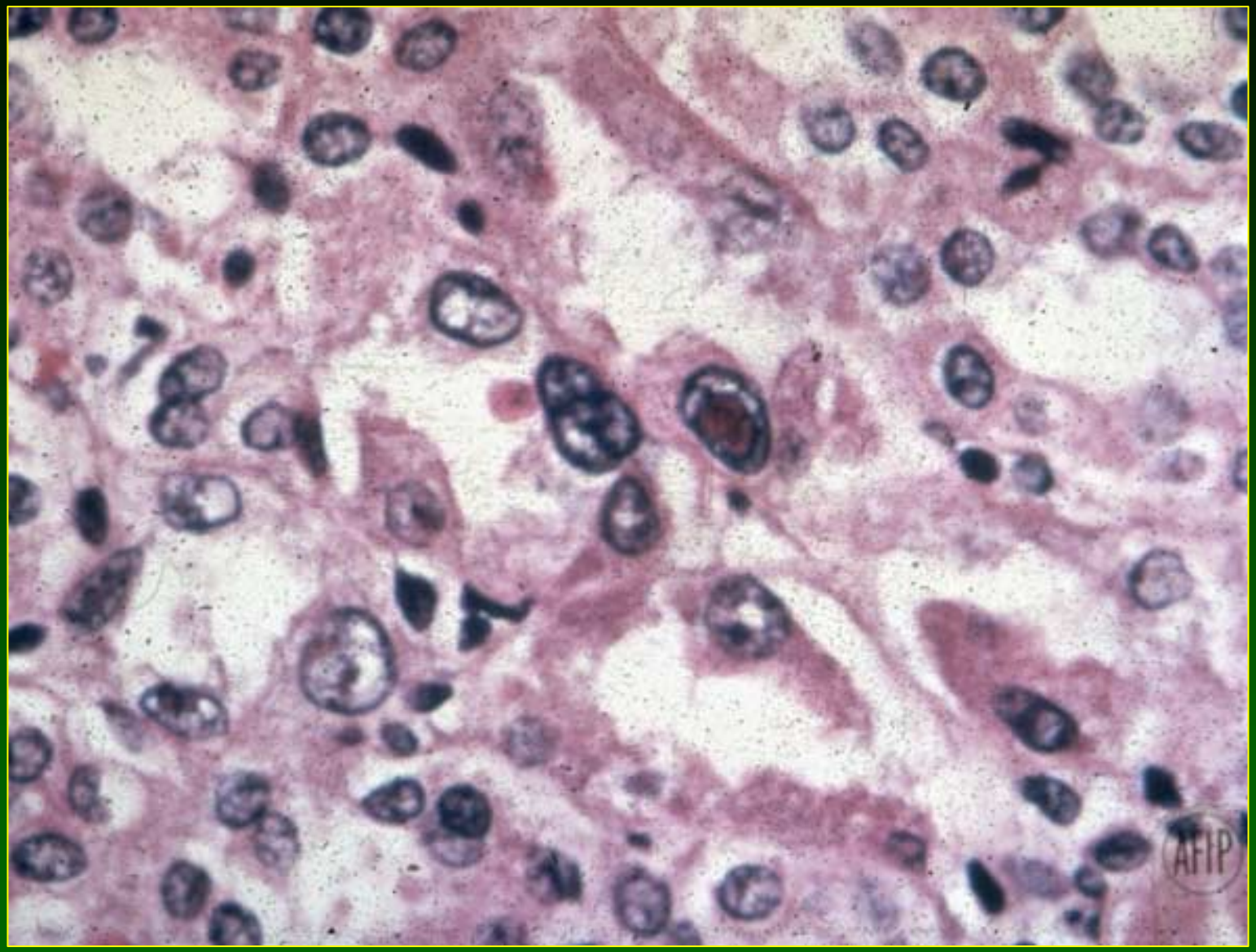




- A 17 month old girl was admitted to the hospital because of convulsions that were localized to the right side. She became comatose and died. Toxic granulations were noted in the neutrophils. A diagnosis of lead poisoning due to pica was made.

LEAD POISONING

- Intranuclear inclusions in renal tubular epithelium


AFIP

TOXIC METALS IN PEDIATRICS
LEAD MONITORING

- Inhibits Fe incorporation into porphyrin ring
- ZP and EP rise (zinc protoporphyrin and erythocyte porphyrin)
- Blood Lead quant

TOXIC METALS IN PEDIATRICS

IRON POISONING IN PEDIATRICS

ACCIDENTAL IRON OVERDOSE:
US REGULATIONS

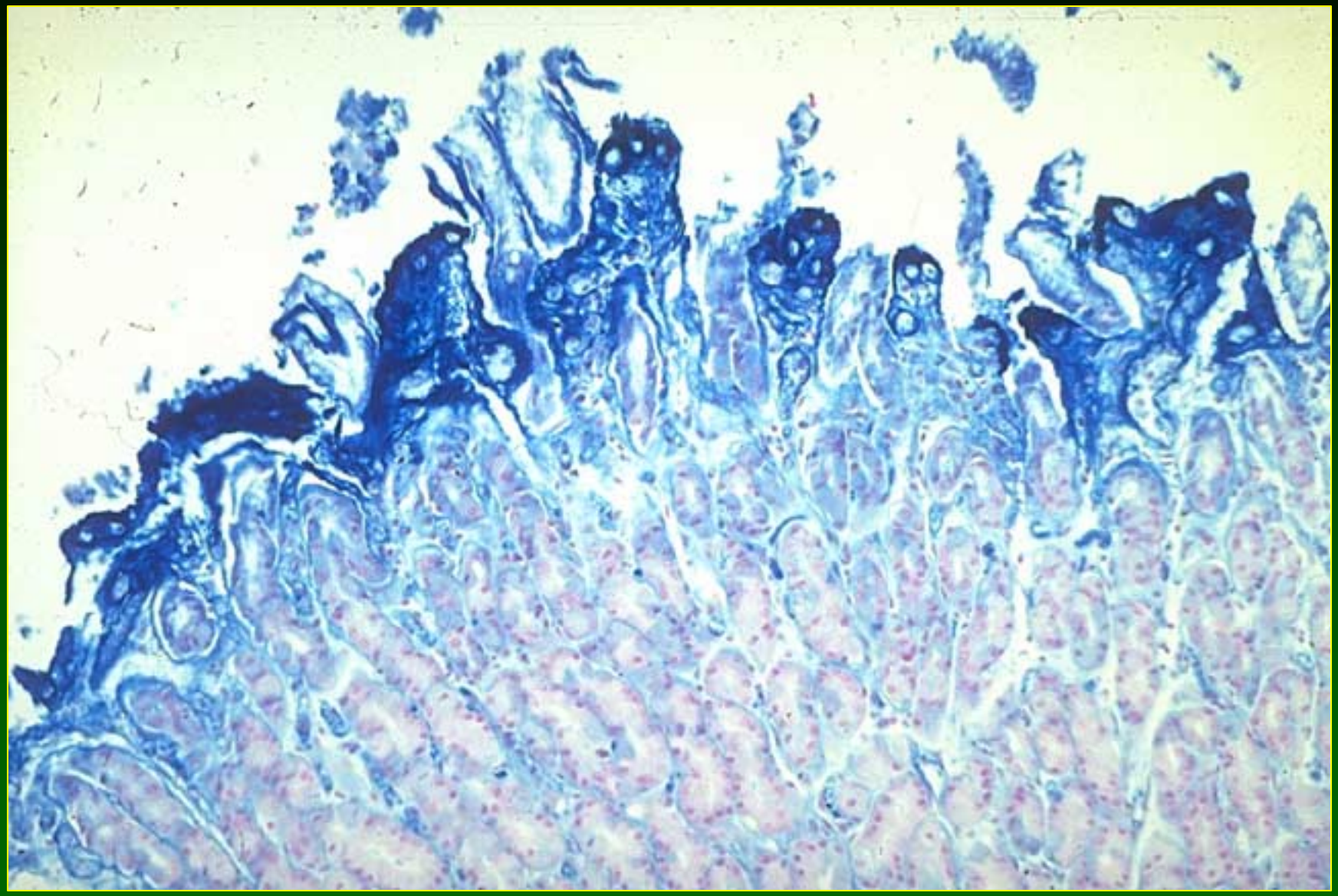
- 1987: Child resistant packaging for most drugs and food supplements with more than 250 mg of iron per container.
- 1997: FDA issues additional packaging regulations in response to 3 citizen petitions submitted to FDA by American Association of Poison Control Centers, the attorneys general of 34 states and the Nonprescription Drug Manufactures Association.

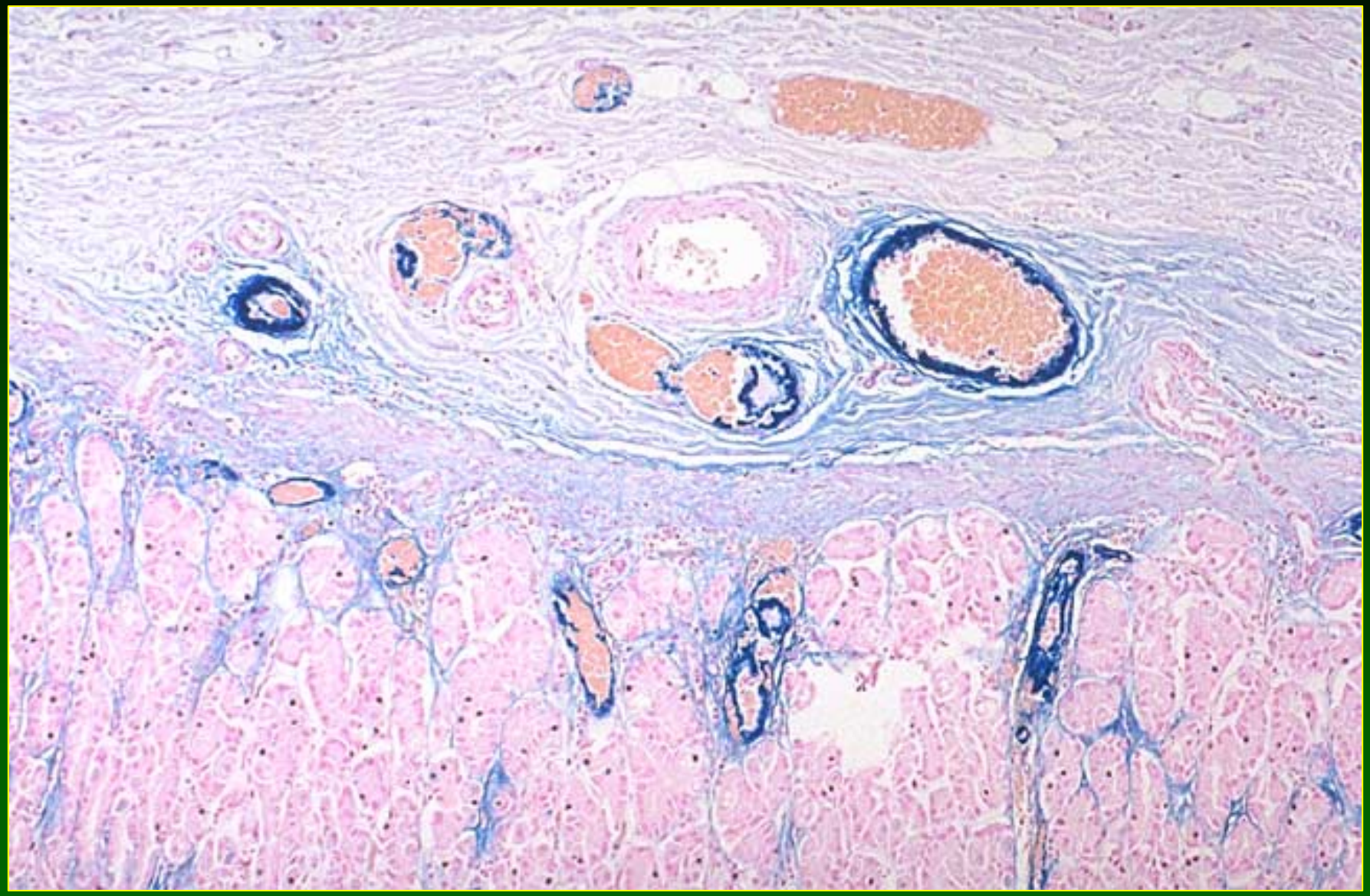
IRON LETHAL INGESTIONS

- Lethal amounts of elemental iron range from 220 mg/kg to 900 mg/kg.
- Death may result from 220 mg.
- Mitochondrial injury may be underlying mechanism.

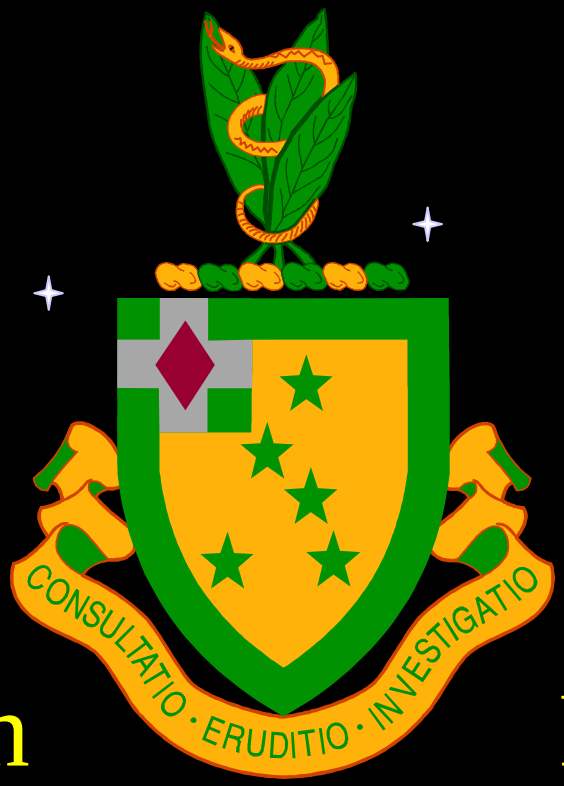
PATHOLOGY OF IRON POISONING

- Mucosal erosions in gastrointestinal tract associated with hemorrhage. (Predominantly gastric and small intestinal mucosa)
- Metabolic acidosis
- Periportal (zone 1) hepatic necrosis
- Gastric scarring





Education



Consultation

Research

ALUMINUM ACCUMULATION

- Chronic renal failure/dialysis
- Immature or impaired kidneys

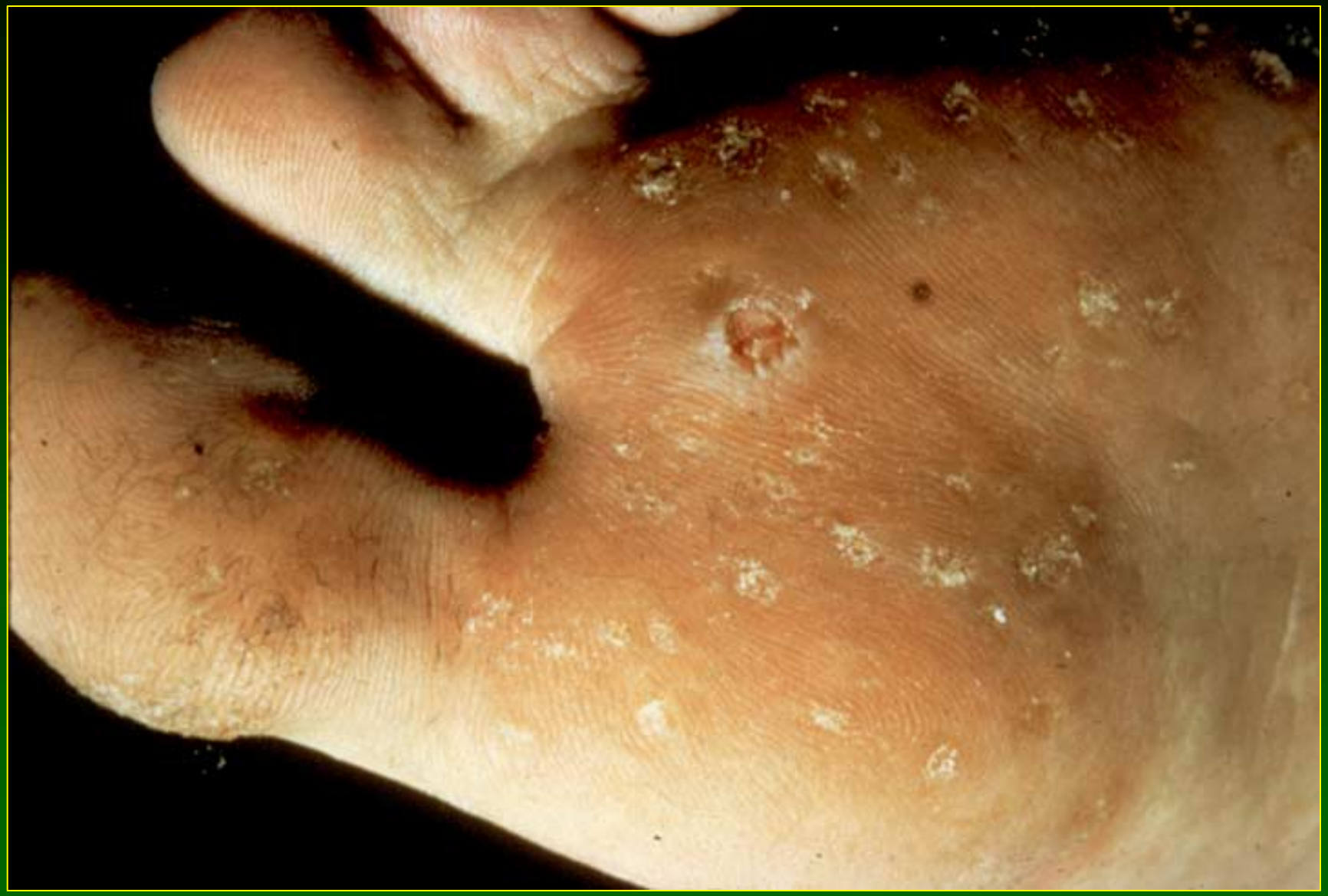
ALUMINUM ACCUMULATION

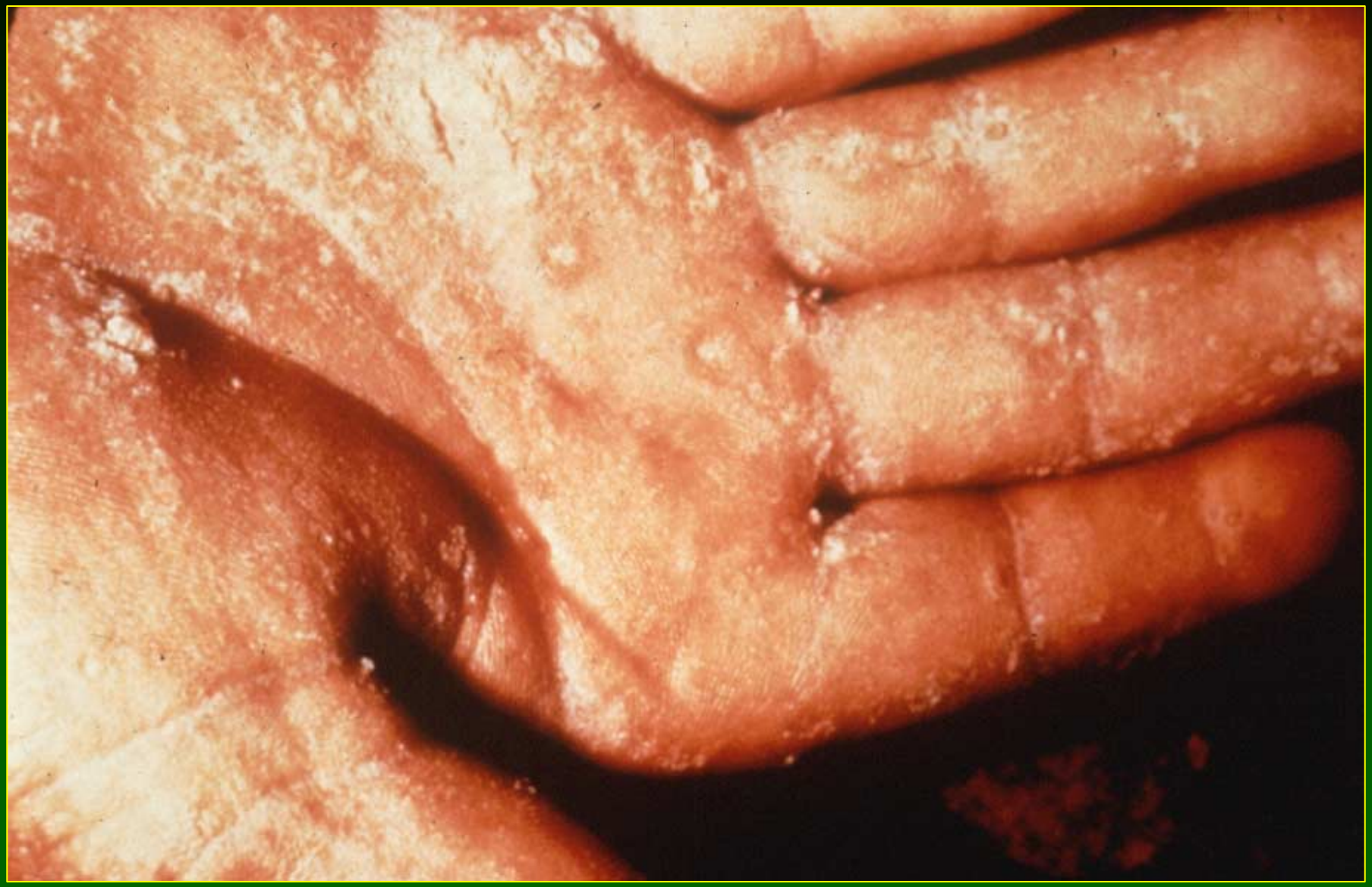
- Neurologic syndrome
- Osteomalacic osteodystrophy

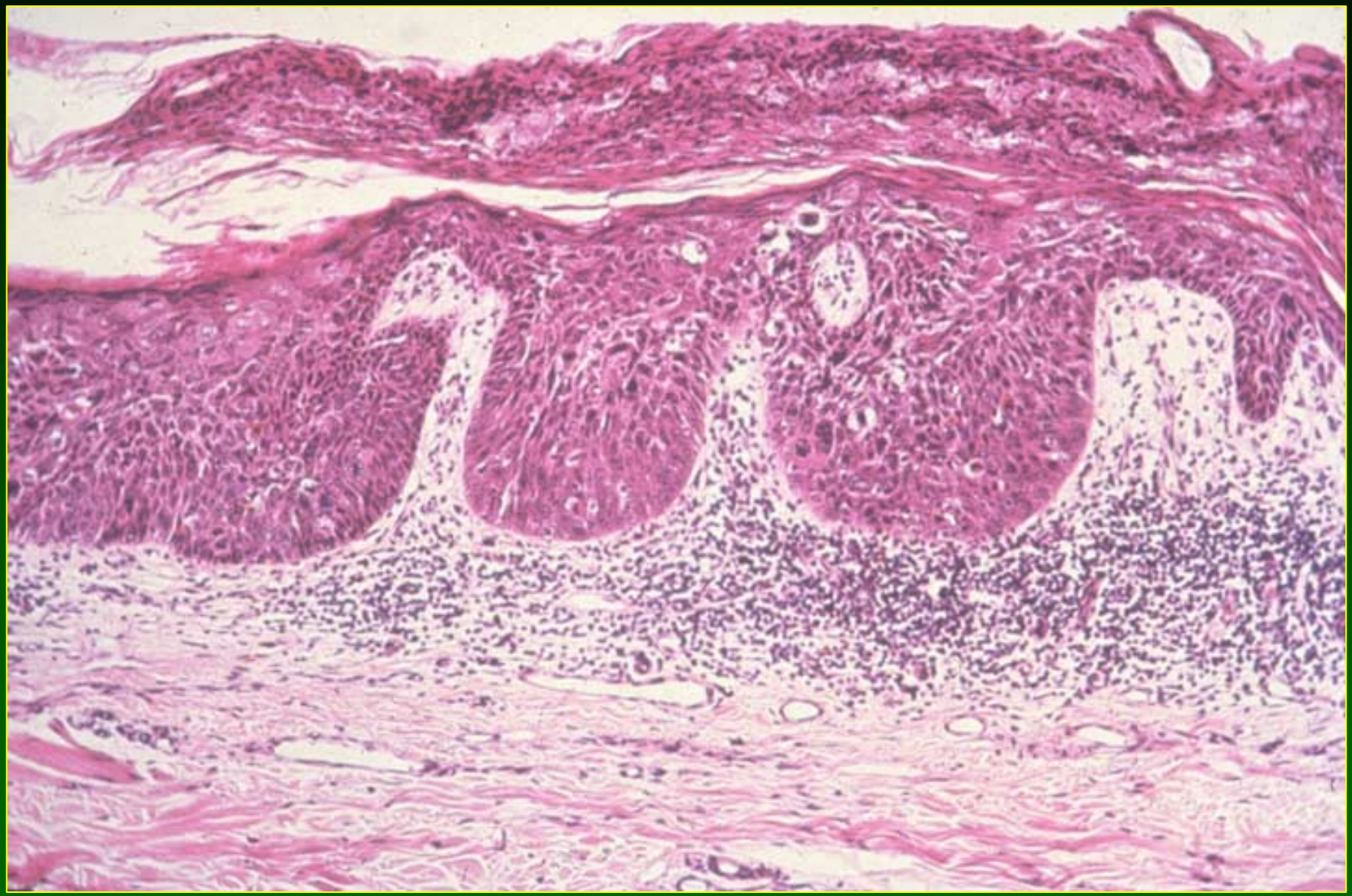
ARSENIC-2 TO 4 WEEKS

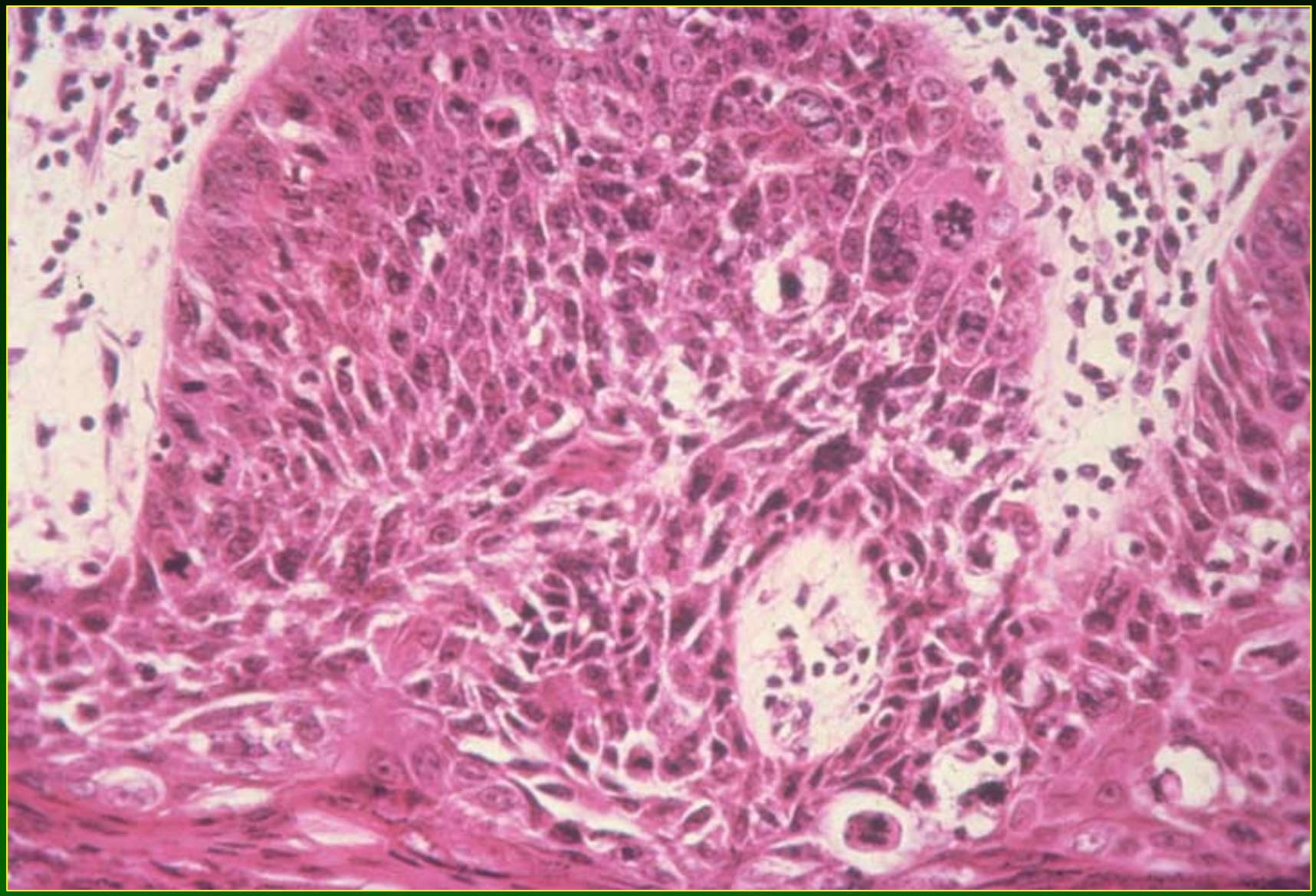
- HAIR
- NAILS
- SKIN
- BY 4 WEEKS IN BONE
- CAN CROSS PLACENTA

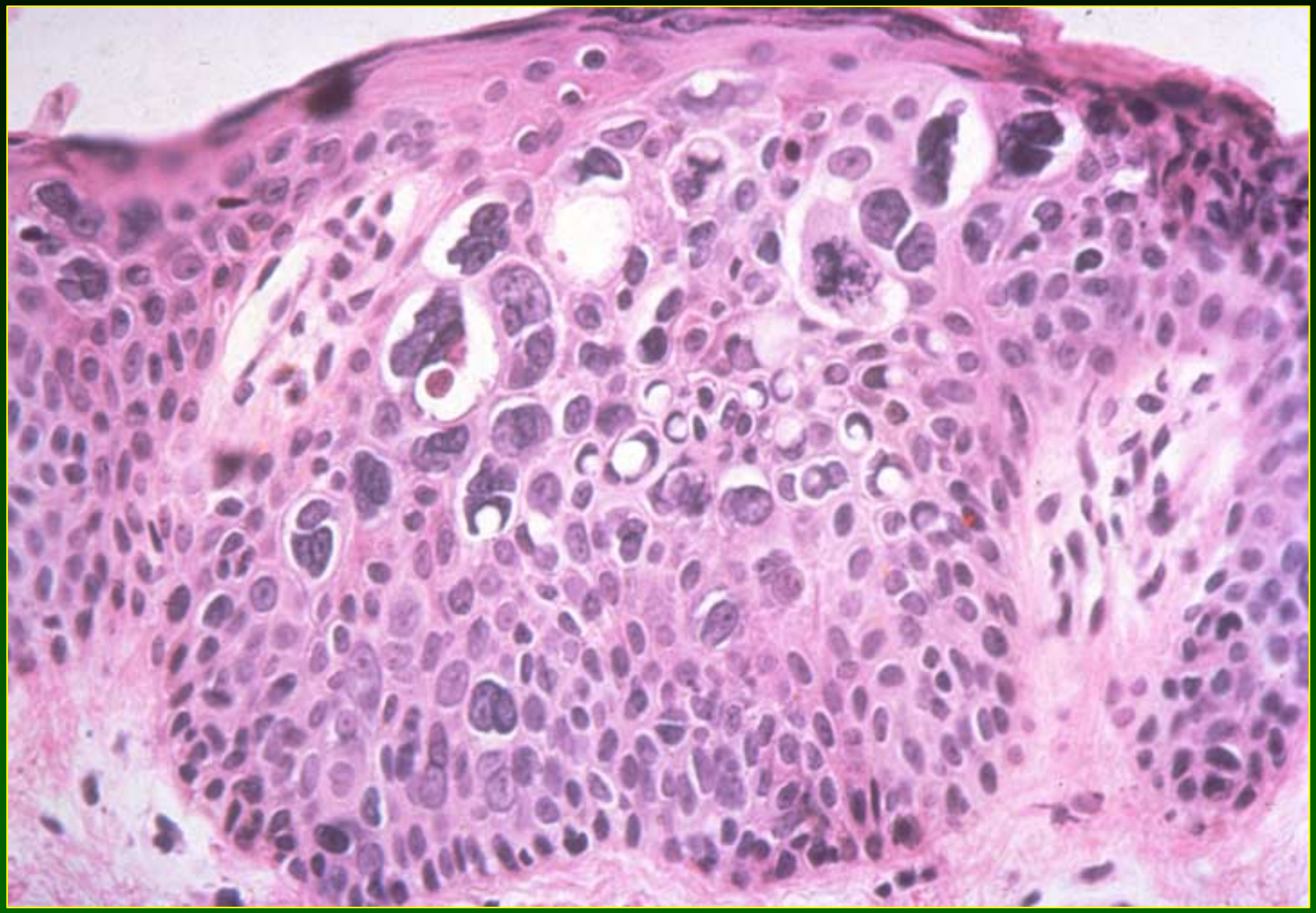
- A 52 year old Caucasian man with a 20 year history of having had many skin cancers caused by arsenic. History of treatment with inorganic arsenic as a child. History of treatment with Fowler's solution for several years starting at age 36.



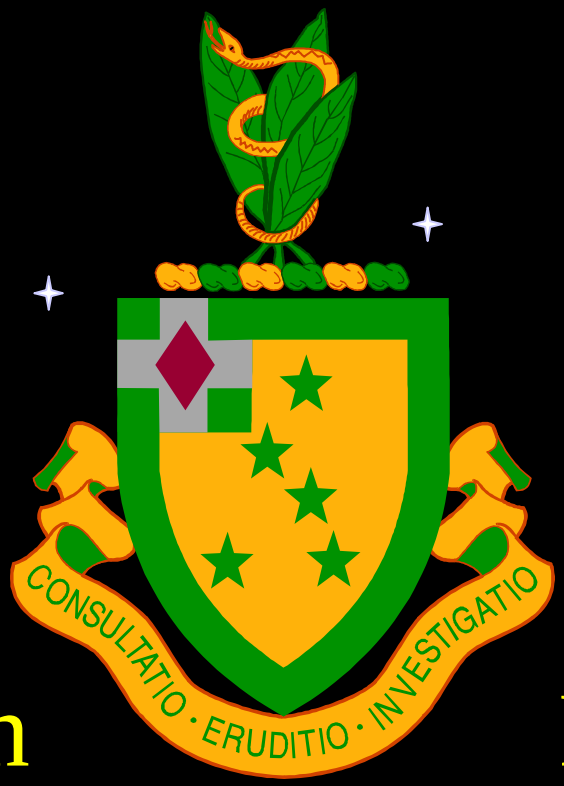








Education



Consultation

Research