

# **AROMATIC HYDROCARBONS: DEFINITION, CLASSIFICATION, ETIOLOGY, DIAGNOSIS, TREATMENT AND PROPHYLAXIS**

## **Definition of arenas:**

- arenas are substances composed of carbon and hydrogen in the structure of which one or more benzene nuclei appear.
- are also called aromatic hydrocarbons, containing in their molecule one or more rings of 6 carbon atoms.
- when the arena molecule consists of a single ring they are called mononuclear arenas, and when the molecule comprises two or more cycles they are called polynuclear arenas.

## **The structure after Friedrich August Kekule:**

- the 6 C atoms in the molecule are joined in a ring by 3 double bonds that alternate with 3 single bonds.
- As a gasoline additive, benzene increases its octane number and reduces detonation.
- Consequently, it often contained significant amounts of benzene before the 1950s, when lead tetraethyl was introduced as an antidetonator.
- In recent years, as a result of declining lead gasoline production, benzene has been reintroduced as an additive.
- In the USA, due to the negative effect on health and to reduce the risk of groundwater pollution with this substance, a maximum permissible emission of approximately 1% of benzene was imposed.
- A large number of chemical compounds of high industrial importance obtained by replacing one or more benzene hydrogen atoms with other functional groups

## Compounds obtained by substitution with an alkyl group:

- $C_6H_5-CH_3$  toluene
- $C_6H_5-CH_2CH_3$  ethylbenzene
- xylene  $C_6H_4(-CH_3)_2$
- mesitylene  $C_6H_3(-CH_3)_3$

## Compounds obtained by substitution with other groups:

- phenol  $C_6H_5-OH$
- $C_6H_5-NH_2$  aniline
- chlorobenzene  $C_6H_5-Cl$
- nitrobenzene  $C_6H_5-NO_2$
- picric acid  $C_6H_2(-OH)(-NO_2)_3$
- trinitrotoluene  $C_6H_2(-CH_3)(-NO_2)_3$
- $C_6H_5-COOH$  benzoic acid
- salicylic acid  $C_6H_4(-OH)(-COOH)$
- acetylsalicylic acid  $C_6H_4(-O-C(=O)-CH_3)(-COOH)$
- paracetamol  $C_6H_4(-NH-C(=O)-CH_3)(-OH)$

- phenacetin  $C_6H_4(-NH-C(=O)-CH_3)(-O-CH_2-CH_3)$

Compounds with two or more benzene rings:

- mothballs
- anthracene
- indol
- benzofuran.

Benzene:

- The simplest combination of aromatic hydrocarbons is 2,7 times heavier than air.
- Colorless liquid
- Boiling point 80 C
- Easily soluble in water
- Very fat soluble.

Occupations at risk of exposure:

- Dry distillation of coal
- Oil refineries
- Synthetic chemical industry
- Pharmaceutical industry
- Dye industry
- Explosives industry
- Rubber industry (solvent)
- Solvent for paints, varnishes
- Plastic industry (solvent)
- Fat extraction
- Degreasing in metallurgy, leather, textile, footwear industry
- Printing houses
- Wood industry
- Manufacture and use of soldering solutions
- Leather processing (solvent for paints, gluing).

Pathways to the body:

- Respiratory
- Digestive
- skin.

Benzene is obtained:

- Benzene is obtained from carbon-rich compounds that suffer from incomplete combustion.
- It is obtained naturally from volcanoes and forest fires, being present in many other combustion products including cigarette smoke.
- Until World War II, significant amounts of benzene were a by-product in the production of coke used in the iron industry.
- In the 1950, the demand for benzene increased substantially, especially in the plastics industry, thus necessitating its much more productive extraction from oil.
- Currently, benzene is obtained mainly in the petrochemical industry, the production of the coal compound being very little used.

Chemical processes in industrial benzene production:

- catalytic reforming
- hydrodalkylation of toluene

- disproportionation of toluene
- steam cracking.
- In 1996, it was 33 million tons, of which 7 million came from the United States
- 6.5 million from the European Union
- 4.2 from Japan
- 1.4 million from South Korea
- one million from China.
- Romania is a country that produces, consumes and exports benzene, the most important refineries where benzene is manufactured are Rafo Onești, Oltchim S.A. and Rompetrol.
  - Before the 1920s, benzene was frequently used as an industrial solvent, especially for degreasing metals but due to its high toxicity it was replaced with other solvents.
  - Its main use is as an intermediate reagent for the synthesis of other chemical compounds.
  - Benzene derivatives that are produced in significant quantities are styrene, used in the manufacture of polymers and plastics, phenol, from which resins and adhesives are prepared, cyclohexane, used for the preparation of nylon.
  - Smaller amounts of benzene are used in the manufacture of tires, lubricants, dyes, detergents, medicines, explosives or pesticides.

In the 1980, the main compounds obtained from benzene:

- ethylbenzene, in the process using 48% benzene
- cumen 18%
- 15% cyclohexane
- 7% nitrobenzene.
- As a gasoline additive, benzene increases its octane number and reduces detonation.
- Consequently, it often contained significant amounts of benzene before the 1950s, when lead tetraethyl was introduced as an anti-knock.
  - In recent years, as a result of declining lead gasoline production, benzene has been reintroduced as an additive.
  - In the United States, due to the negative effect on health and the reduction of the risk of groundwater pollution with this substance, a maximum permissible emission of approximately 1% benzene has been imposed.
  - The same figure is found in European Union standards.

Role in the human body:

- in the blood it is transported by lipoproteins and accumulates in high-fat tissues, especially in the hematopoietic marrow and CNS, adrenal glands.
- In the body undergoes metabolic changes and turns into phenols, pyrocatechins, hydroquinone (Nomyama) and degrades even to carbon dioxide. By opening the benzene nucleus, muconic acid is also produced, it can be condensed with cysteine, by acetylating its NH<sub>2</sub> radical and 1-phenyl-mercapturic acid is formed.
- Phenols are conjugated with glucuronic acid and sulfates, appear in the urine as ether sulfates and glucuroconjugates.

The elimination:

- Through the respiratory tract (30-75%) on average 50% of the inhaled, through urine in the form of phenols and diphenols; pyrocatechol, hydroquinone and phenyl-mercapturic acid. Lim. fiz. sup. for total phenols: 130mg / l.

Mechanism of action:

- Toxic to mitosis; inhibitory action on medullary cells, enzymatic disorders of mitosis, on young forms - on granulocyte, erythrocyte, platelet series.
- Causes disorders in the synthesis of corticosteroids, hypovitaminosis B<sub>2</sub>, C, B<sub>6</sub>, PP, toxic endothelial damage, enzymatic disorders: catalase, peroxidase, phosphatase; decreases the phagocytic reaction. It is hepatotoxic. It has a narcotic effect.

Symptoms of acute intoxication:

- begins with dizziness
- walking unsafe
- state of euphoria
- drowsiness
- headache
- vomiting
- anesthesia
- areflexion
- **vasomotor** paralysis
- heart attack
- convulsions
- the death

### **Complications in acute intoxications:**

- in the first phase, serious complications are cerebral and parenchymal hemorrhages, followed by neuropsychiatric disorders, toxic hepatitis, kidney damage and hematological changes.

- Prognosis - reserved, serious.

- The disease begins slowly, insidiously, in the first phase, in latent benzeneism, usually without characteristic, obvious symptoms. In the first phase of the disease there is macrocytosis, hyperchromia, (Manu P.) a transient leukocytosis, (Timar M.) a net hyperplasia of the reticulo-histiocytic system (Hilt, Manu) and chromosomal abnormalities (Manu, Popescu).

In this phase a transient increase of the phagocytic reaction and a transient catalase hyperactivity is observed.

(Dienes).

### **Chronic intoxication:**

- The leukopenicizing action of benzene, alteration of the white series, erythrocytes and platelets, occur gradually, successively, simultaneously or in isolation.

- At this stage, astheno-vegetative symptoms are observed and anemia becomes more and more obvious.

- Bleeding occurs, is associated with hepatosplenomegaly, signs of toxic hepatitis.

- In untreated cases there are intercurrent infections, superinfected ulcers. Acute or chronic leukemias have been described in chronic benzene poisoning.

- Toxic encephalopathies occurred only in very severe cases.

### **Prognosis of the disease:**

- in all cases it is reserved

- serious

- the toxicant going in severe cases until the complete destruction of the bone marrow.

### **Diagnosis:**

- It is based on exposure, characteristic clinical and laboratory symptoms (leukopenia, myelocytes, promyelocytes) and phenols (over 130mg / l);

- decrease in urine ratio = inorganic sulfur / total sulfur below 0.8;

- hematological changes

- Roetter test 1 (delayed skin discoloration more than 10-15 minutes after intradermal injection of 2mg dichlorophenol-indophenol solution in 4.9 cm water, 0.1 ml)

- Rumpel-Leede test.

**Differential diagnosis:**

- organic solvents with narcotic action
- diseases of the hematopoietic system.

**Treatment:**

- in acute intoxication: ADRENALINE is CONTRAINDICATED,
- analeptics
- glucose infusions
- procainamide (in case of extrasystole)
- gluconic calcium
- corticosteroids
- antibiotics
- oxygen therapy
- combating hemorrhages.
- Chronic intoxication - glucose infusions
- C vitamin
- B vitamins
- sodium hyposulphite
- transfusions
- corticosteroids
- antibiotics
- bone marrow transplant
- symptomatic treatment.

**Prophylaxis:**

- of early importance is the early diagnosis of the disease, in the phase of latent benzeneism.
  - technical
  - individually - in protective clothing, masks, shower, technical training.
  - medical - urine examination (for haematuria), reactive test with dichlorophenol solution, alcohol test, alkaline leukocyte phosphatase (F.A.L.), red blood cell count, hemoglobin, leukocyte count, leukocyte formula, reticulocytes, platelets, before and after medullary excitation, bleeding time, coagulation time, dysproteinemia tests, Rumpel-Leede test, Sulfate-index, phenols in the urine, myelogram (in the presence of quasi-specific changes in the peripheral blood), clot retraction.
- Contraindications:

- Congenital or acquired haematological diseases, involving red series, leukocyte, platelet, hemorrhagic syndromes, liver diseases affecting the parenchyma, small and repeated bleeding (hemorrhoids, menometrorrhagia, etc.), operated stomach (resection), significant exposure to medullary toxins ionizing in the background (in the last 5 years).
- C.M.A. 50mg / m<sup>3</sup>.

**Benzene derivatives:**

- Toluene (methylbenzene) C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub>)
- Xylene (dimethylbenzene) C<sub>6</sub>H<sub>4</sub> (CH<sub>3</sub>)<sub>2</sub>)
- Styrene (vinylbenzene) C<sub>6</sub>H<sub>5</sub>CH = CH<sub>2</sub>)
- Ethylbenzene C<sub>6</sub>H<sub>5</sub>C<sub>2</sub>H<sub>5</sub>)
- Cumene (isopropylbenzene) C<sub>6</sub>H<sub>5</sub>CH (CH<sub>3</sub>)<sub>2</sub>)
- Naphthalene C<sub>10</sub>H<sub>8</sub>)
  1. Benzene nitrodivatives are:
  - Nitrobenzene C<sub>6</sub>H<sub>5</sub>NO
  2. Aminoderivatives of benzene?

- Aniline (phenylamine, aminobenzene)
- Benzidine
- 3. Aliphatic halogenated hydrocarbons ...?
- Dichloroethane (ethylene chloride)
- Trichlorethylene (CHCl = CCl<sub>2</sub>)

### **Toluene (methylbenzene C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub>):**

- Higher volatility than benzene
- Professions: benzene + aviation fuel.
- Mechanism of action: does not produce hematological changes.
- Role in the body: in the body it is converted into benzoic acid which is conjugated with glycochol and is eliminated as hippuric acid.
- Elimination: upper physiological limit of hippuric acid: 0.7g / urine of 24; by expired air 18-20%
- Acute intoxication: begins with euphoria, followed by drowsiness and narcosis.
- Chronic intoxication: is characterized by astheno-vegetative symptoms and irritation of the respiratory tract and conjunctiva, toxic hepatitis, minor-moderate kidney damage.
- Diagnosis:
- symptoms
- exposure
- hippuric acid 1 g / l of urine
- Differential diagnosis: intoxications with other organic solvents.
- Treatment: similar with benzene.

### **Xylene (dimethylbenzene) C<sub>6</sub>H<sub>4</sub> (CH<sub>3</sub>)<sub>2</sub>:**

- Professions: see benzene.
- Role in the body: it turns into toluic acid.
- Mechanism of action: inhibits the function of the hematofforming marrow, effect on erythrocyte, platelet and leukocyte series.
- Acute intoxication: euphoria, drowsiness, anesthesia.
- Chronic intoxication: dermatitis, eczema, conjunctivitis, respiratory tract irritation, anemia, leukopenia, thrombocytopenia, dyspepsia, neuro-vegetative dysfunction.
- Diagnosis:
- symptoms
- exposure
- Treatment: (similar with benzene).
- C.M.A. 100mg / m<sup>3</sup>.

### **Styrene (vinylbenzene) C<sub>6</sub>H<sub>5</sub>CH = CH<sub>2</sub>:**

- Professions: synthetic chemical industry, monomer for polystyrene, solvent for polyesters, synthesis of synthetic rubber, manufacture of emulsifying substances.
- Penetration route: respiratory, gastrointestinal, through the skin.
- Accumulation: in the liver, kidneys, adrenal glands, small intestine and blood.
- Role in the body: turns into mandelic acid and benzoic acid.
- Elimination: through expired air and unchanged in the urine in the form of metabolites.
- Acute intoxication: with various symptoms: conjunctival irritation, respiratory tract, tremor, balance disorders, dizziness, drowsiness, anesthesia.
- Chronic intoxication: with conjunctivitis, dermatitis, depressive states, pseudo-neurosis with EEG changes, astheno-vegetative signs, dysmenorrhea.
- C.M.A. : 350 mg / m<sup>3</sup>.

### **Ethylbenzene C<sub>6</sub>H<sub>5</sub>C<sub>2</sub>H<sub>5</sub>:**

- Occupations at risk of exposure: production of styrene, solvent for paints and varnishes, motor fuel in aviation.
- Role in the body: it turns into hippuric acid (70%), mandelic acid and phenaceturic acid.
- Elimination: through exhaled air and urine.
- Acute intoxication: begins with drowsiness, narcosis, in severe cases causes pulmonary edema, pulmonary hemorrhage. Causes conjunctival irritation, tearing.
- Chronic intoxication: conjunctivitis, dermatitis.
- C.M.A. : 1400 mg / m<sup>3</sup>.

### **Cumene (isopropylbenzene) C<sub>6</sub>H<sub>5</sub>CH (CH<sub>3</sub>)<sub>2</sub>:**

- Professions: solvent for nitrocellulose, motor fuel, synthetic chemical industry.
- Role in the body: turns into phenylpropanol and phenylpropionic acid.
- Elimination: through unchanged exhaled air and in the form of phenols in the urine.
- Mechanism of action: has a higher narcotic effect than toluene and benzene.
- Accumulation: in the liver, CNS, endocrine glands.
- Acute intoxication: in high concentrations causes acute intoxication with narcosis that installs slowly and has a long duration. Liver damage is possible after acute intoxications.
- Chronic intoxication: can cause dermatitis, hepatitis, kidney damage.
- Since 2014 it has been included in the list of carcinogens.

### **Naphthalene C<sub>10</sub>H<sub>8</sub>:**

- Water-insoluble, colorless crystals with a characteristic odor.
- Professions: it is used in the chemical industry, in wood preservation and as an insecticide against moths.
- Naphthalene is mainly used in the synthesis of thinners, dyes or adhesives in the plastics industry such as PVC, in the development of insecticides from the carbamate group, as well as in the manufacture of soaps.
- It has an irritating effect on the mucous membranes and skin. Inhalation of vapors or accidental consumption of crystals causes nausea, vomiting, tenesmus, diarrhea, chills, fever, tachycardia and hypotension, hematuria. In severe cases, coma and death. Kidney damage is possible, even causing uremia.
- Differential diagnosis: compared to intoxications with nitro- or aminoderivatives of benzene.
- Treatment: gastric lavage with paraffin oil, transfusions, in case of artificial renal-renal lesions.
- Contraindicated: foods containing fats, milk and castor oil in the first aid.
- C.M.A. : 40 mg / m<sup>3</sup>.

### **Benzene Nitroderivatives - Nitrobenzene C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub>:**

- It is an oily, yellowish liquid with an almond smell.
- Occupations at risk of exposure: intermediate in the synthesis of aniline and benzidine, cosmetic industry, constituent of boot cream, synthetic chemical industry. To a lesser extent it is used as a diluent in obtaining ointments, fuels, photographic films or explosives. In the past it was used as a flavoring in soaps, today it is forbidden to use it in the manufacture of cosmetics.
- Pathways: respiratory, through the skin.
- Role in the body: it turns into phenols.
- Elimination: through phenols in the urine. Mechanism of action: methemoglobinizing, causes redox disorders, is toxic to the SN, hepatotoxic and nephropathic.

- Acute intoxication: cyanosis and dipnea. After high-dose exposure, circulatory failure, collapse.
- Chronic intoxication: the characteristic signs are cyanosis, anemia (methemoglobinemia) and toxic hepatitis with splenomegaly, kidney damage. It is also associated with gastrointestinal symptoms: nausea, vomiting, rarely causes toxic pneumonia. Dermatitis occurs frequently.
- Diagnosis: exposure, symptoms, is confirmed with methemoglobinemia present and phenols in the urine.
- Prognosis: favorable.
- Treatment: in acute intoxication: oxygen, glucose infusions, vitamin C, methylene blue i.v., 1% nicotinic acid.
- C.M.A. : 6 mg / m<sup>3</sup>.

#### **Aminoderivatives of benzene: Aniline (phenylamine, aminobenzene):**

- Oily liquid widely used in chemical synthesis industry, pharmaceutical industry, paint industry, varnishes. It oxidizes in the air and becomes closed.
- Route of penetration: skin, gastrointestinal and respiratory.
- Mechanism of action: it is a strong methemoglobinizer.
- Acute intoxications: latency 2-3 hours, there is a cyanosis, fatigue, dyspnea, so phenomena caused by methemoglobin.
- Prognosis: favorable.
- Treatment: see nitrobenzene.

#### **Benzidine:**

- Used in: organic synthesis; manufacture of paints, especially Congo red, detection of blood stains (Gregersen reaction), dye in microscopy, analytical reagent for Pb, Ce, Pt, W, hardening agent in the preparation of rubber, Used in chemical and medical laboratories, enters body, primarily through the skin.
- After prolonged exposure, it may cause bladder and uterine cancer. Naphthylamine - used in the manufacture of dyes, Aminophenol - used in the manufacture of rubber, Auramine - made of dimethylaniline and formaldehyde, used in the coloring of paper and as an antiseptic, have a similar carcinogenic effect.

#### **Aliphatic halogenated hydrocarbons - Dichloroethane (ethylene chloride):**

- Colorless, chloroform-like liquid.
- Professions: solvent for greases, resins, paraffins, cellulose, rubber, disinfectant, insecticide.
- Route of penetration: respiratory and through the skin.
- Role in the body: turns into glycol and oxalic acid.
- Elimination: through exhaled air and urine.
- Mechanism of action: irritant effect on the respiratory tract and nephrotoxic due to oxalic acid metabolites.
- Acute intoxication occurs in three phases:
  - I- preanesthesia, nausea, vomiting, abdominal pain, anesthesia
  - II- latency time- oligosymptomatic lasting several hours
  - III- signs of toxic hepatitis, signs of toxic nephrosis with proteinuria, oliguria and rarely pulmonary edema.
- Chronic intoxication: is characterized by digestive disorders, polyneuritis, astheno-vegetative symptoms, in severe cases - toxic encephalopathy.
- Complications: anuria, uremia.
- Diagnosis: 1) exposure and 2) symptoms.
- Treatment: D.M.P., symptomatic, in case of artificial kidney-kidney lesions.



- Prophylaxis: C.M.A. 150mg / m<sup>3</sup>, periodic medical check-up.

### **Trichlorethylene (CHCl = CCl<sub>2</sub>):**

- Colorless liquid, with aromatic odor, insoluble in water. It evaporates at room temperature and decomposes under intense light, producing hydrochloric acid and phosphogen.
- It is non-flammable.
- It is used in countless industries, among which we can mention: the rubber industry, in the footwear industry, in the vulcanization process, in the cleaning of clothing, in the chemical industry.

### **Role in the body:**

- It enters the body in the form of vapors, through the respiratory tract, accidentally through the digestive tract.
- By contact with the skin it has an irritating effect, transcutaneous absorption is also possible.
- $\frac{3}{4}$  of the inhaled amount is retained in the body, the rest is eliminated by respiration.
- In the body it turns into hydrochloric acid, followed by trichloroacetic acid and trichloroethanol.
- Both metabolites are slowly excreted in the urine.

### **Mechanism of action:**

- Locally acts as an irritant on the skin and mucous membranes of the airways. By drying the skin leads to microtrauma and secondary infection.
- It has a narcotic and euphoric effect; in long-term exposed workers have been described neurological and psychological changes (Grandjean), is hepatotoxic and nephrotoxic.

### **Acute intoxication:**

- It begins with phenomena of anesthesia, respectively prenaresis, rarely with euphoria, more frequently with nausea, vomiting, dizziness and symptoms of irritation of the upper respiratory tract.
- In case of high doses it can lead to loss of consciousness: death can occur due to paralysis of the bulbar respiratory center or due to heart failure (ventricular fibrillation).

### **Chronic intoxication:**

- It is installed after a longer exposure with neurovegetative disorders: sleep disorders, headache, asthenia, irascibility, paresthesias, alcohol intolerance, decreased sexual potency; with lesions of the nervous system: materialized by gait disorders, altered reflexes, characteristic of TRIGEMINE NEURITIS, less often optic neuritis, with signs of toxic encephalopathy.
- Prolonged exposure can lead to addiction; drug addiction leading to a series of serious morphofunctional changes. Ventricular fibrillation is thought to occur due to the hypersympathototonic action of the toxicant. Euphoria in drug addicts can lead to serious accidents.

### **Diagnosis:**

- It is based on occupational or accidental exposure, on characteristic clinical signs and is confirmed by the presence of toxic metabolites in urine, trichloroacetic acid above a limit of 200mg / l in urine.

### **Prognosis:**

- In general, it is favorable in acute intoxications if a quality first aid is ensured in time.
- Complications are related to trigeminal nerve damage. In chronic intoxications the prognosis is also good in the case of appropriate treatment.

### **Treatment:**

- In acute intoxications: with oxygen, artificial respiration, if necessary, corticosteroids, vitamin infusions. Adrenaline, noradrenaline, ephedrine are contraindicated.
- In chronic intoxications - treatment with corticosteroids, vitamins (B<sub>1</sub>, B<sub>6</sub>, infusions) and

symptomatic treatment. Adequate diet in case of liver or kidney damage.

Prophylaxis:

- It is recommended to seal the technological processes where the trichlorethylene evaporates, ensuring a local suction ventilation.
- Workers will be monitored during the regular check on toxic addiction.

Contraindications:

- Obesity, alcoholism, lung disease, hypertension, gastric and duodenal ulcers, liver, skin, kidney, peripheral nerve and people who are sensitive to the toxic.
- C.M.A. 300mg / m<sup>3</sup>.

## **QUESTIONS FOR KNOWLEDGE VERIFICATION:**

### **1. What are the places where lead is spread?**

- Sea water
- Aer
- Sol
- Plant
- Animal body
- Food
- The earth's crust
- Metal ores

### **2. What are the commercial and industrial applications of lead?**

- varnishes and paints
- battery
- pigments
- insecticides
- plastics and ceramics
- Medical equipment
- armament
- petrol
- welding industry

### **3. List jobs at risk of lead exposure.**

- extraction of ores containing Pb
- melting of Pb and Pb alloys
- collecting and melting old materials containing Pb
- welding of Pb plates
- battery industry, graphics, chemistry
- lining and repairing acid tanks with Pb plates
- light and food industry
- making Pb tubes
- mower with Pb alloy
- manufacture of Pb piston rods
- preparation and use of Pb paints
- manufacture of explosives, fuels, plastics industry, etc.

### **4. The main etiological factor of intoxications is lead, give the characteristic of this metal:**

Lead is not found as such in its natural state, but only in ores. The most important lead ore is galena (lead sulfide), from which metallic lead is extracted. It melts lead at 327°C and emits vapors at 450°C.

### **5. What are the predisposing (secondary) etiological factors that belong to the body?**

- Intense physical exertion
- overworked
  - malnutrition

- alcoholism
- virus
- the appearance of metabolic acidosis

6. What are the predisposing (secondary) etiological factors that belong to the workplace?

- Unventilated enclosed spaces
- Poor ventilation
- Failure to observe individual hygiene
- Failure to comply with labor protection rules
- Failure to use specific personal protective equipment.

7. How long does it take for lead poisoning to develop?

• From 2-3 months to 2 3 years (depending on the amount of lead absorbed and individual characteristics: the presence of favorable factors).

**8. What are the ways that lead enters the human body?**

- cutaneous
- digestive
- Respiratory system

**9. What is specific to the airway of lead poisoning?**

• It is the major route of penetration, the deposition rate ranges between 30-85%, half of the exposed rate is found in the blood over 50 hours, the rest is deposited in the tissues or is eliminated

**10. What is specific to the digestive tract of lead poisoning?**

• Non-compliance with hygienic measures at work - unwashed hands, keeping food at work, smoking during work

**11. What is specific to the skin route of lead poisoning?**

• It is a specific path of intoxication only in the case of fat-soluble organic compounds - stearate, naphthenate, tetraethyl and tetramethyl of lead. Metallic lead is not absorbed through the skin.

**12. What is the mechanism of action of lead in the human body?**

- Lead enters the body through the respiratory tract in the form of vapors and dusts and through the digestive tract, but absorption is limited to 2% of the amount ingested.
- A large part is transformed in the digestive tract, into insoluble lead sulfide, black in color. Lead produces a caustic effect on the digestive tract.
- Lead is not absorbed through intact skin (except for lead tetraethyl - it can pass through intact skin).
- Circulation takes place in the colloidal form of basic lead triphosphate, bound to erythrocytes.
- Storage is done in bones in a non-toxic form, its metabolism being similar to calcium.
- lead deposition in bone trabeculae is a mechanism of inactivation by sequestering  $\alpha$  in a biological compartment with a low sensitivity to its toxic action.

13. What are the mechanisms by which excess lead in the blood causes phenomena?

- direct aggression on the hematopoietic tissue followed by inhibition of hemoglobinosynthesis
- direct action on the erythrocyte membrane followed by weakening of the erythrocytes, reducing their lifespan and early intravascular hemolysis
- action on chromosomes followed by alteration of genetic material, which in young women causes sterility, abortions or stillbirths with birth defects
- direct nephrotoxic action as well as damage to the mitochondria of renal tubule cells, which is the

morphophysiological substrate of saturnine nephropathy

- neurotoxic action on the central and peripheral nervous system
- harmful action on the cardiovascular system

**14. Excess lead ions in the peripheral blood inhibit at least three enzymes in the heme synthesis chain, what are these enzymes?**

- aminolevulinic acid dehydrase that presides over the conversion of aminolevulinic acid to porphobilinogen
- coproporphyrinogenase that allows the conversion of coproporphyrin III to protoporphyrinogen
- hemsynthetase that favors the integration of activated iron ( $\text{Fe}^{2+}$ ) in the tetrapyrrole structure of protoporphyrin IX to result in heme

**15. What is the effect of lead on erythropoiesis?**

- Affects erythropoiesis
- Inhibits heme synthesis from marrow erythroblasts
- lead blocks the activity of some of the enzymes in the heme biosynthesis chain (ALA dehydrase, coproporphyrinogen oxidase, hemsynthetase, PBG deaminase)

**16. List the consequences of enzymatic damage in lead poisoning:**

- Increased ALA levels in the blood and excreted in the urine
- Increased levels of coproporphyrinogen III in red blood cells and coproporphyrin in urine
- Increased levels of protoporphyrin IX in red blood cells
- Increased urine porphobilinogen and uroporphyrin
- Increased total serum iron levels

**17. What morphological changes in sternal puncture are attested in lead poisoning?**

- Increasing the number of megaloblasts
- Occurrence of polypoid erythroblasts and erythroblasts with basophilic granulations
- Fixation of Pb on the erythrocyte membrane producing inhibition of membrane glucose-6-phosphate dehydrogenase
- This increases the mechanical fragility of erythrocytes by decreasing their lifespan

**18. What is characterized by acute nephrotoxicity in lead poisoning?**

- Morphological and functional changes occur in the proximal renal tubules
- As a consequence decreases transtubular ion transport with hyperaminoaciduria, glucosuria
- These changes are the consequence of altered respiratory function of mitochondria

**19. What is characterized by chronic nephrotoxicity in lead poisoning?**

- It is the consequence of the chronicity of acute nephropathy or the progressive development of chronic nephropathy
- With the advancement of nephropathy, tubular atrophy and interstitial fibrosis appear, then there is a decrease in the rate of glomerular filtration and an increase in serum nitrogen.
- In addition to tubular damage, the glomerular vessels also change
- Pb produces effects on DNA and RNA metabolism with increasing urinary excretion of N-aminoisobutyric acid (ABA which is a product of thymidine degradation, a constituent of DNA and RNA)

**20. What is characterized by the development of hypertension in lead poisoning?**

- Disorder of eicosanoid synthesis in renal tissue

- Increased thromboxane production (vasoconstriction) with decreased production of PG E and G, ketoprostaglandin F (vasodilation)
- Prostaglandin depletion increases sodium retention and intensifies the pressor response to angiotensin II and vasopressin - essential hypertension is installed
- Decreased urinary kallikrein
  - lead acts on the renin-angiotensin-aldosterone chain by increasing the activity of plasma renin, angiotensin and conversion enzyme
  - The relationship with BP depends on the dose. At low exposures, affected individuals may have elevated plasma renin activity. In severe exposures - its activity may be normal or even low

### **21. What is characterized by impaired vitamin D metabolism in lead poisoning?**

- Physiological synthesis of vit. D requires a present hydrolysis in the kidneys which converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D which facilitates the absorption of Ca in the intestine
- Lead produces an inhibitory effect on the hydroxylase that presides over the formation of vit. D
- lead reduces urinary uric acid excretion with consequent increase in blood uric acid concentration (the level of lead caused is higher in patients with gout who have nephropathy)
- lead alters the receptivity of the smooth muscle of the vessels to vasoactive stimuli with the consequent increase in the response to alpha 2-adrenoreceptor stimulation of cardiac and vascular cholinergic and dopaminergic receptors
- lead can alter the Ca-related functions of vascular smooth muscle by lowering ATPase and stimulating the Na / Ca pump

### **22. What characterizes carcinogenesis and impairment of reproduction in lead poisoning?**

- Reduction of the number of births in the families of the members to whom they were exposed to the Pb action
- Increased number of premature births, premature rupture of the membrane, sperm changes (mobility, morphology, density)
- Improvement of sperm parameters has been demonstrated experimentally with a decrease in the blood concentration of Pb and protoporphyrin zinc
- There is a risk of congenital cardiovascular abnormalities in newborns whose parents have been exposed to significant amounts of Pb.
- Increases the incidence of renal tumors following the administration of proven carcinogenic substances (N-ethyl-N-hydroxyethylnitrosamine)
- This is due to the proliferation of renal tubular cells.

### **23. What is characterized by impaired thyroid and immune system in lead poisoning?**

- lead causes a decrease in iodine uptake in the thyroid with a decrease in serum thyroxine below 60 mcg%
- On the other hand, hyperthyroidism can cause the mobilization of Pb stored in the bones, inducing clinical phenomena of intoxication.
- Regarding the immune system, there was a decrease in the percentage of B lymphocytes and a decrease in the total number of lymphocytes, monocytes and granulocytes in workers exposed to Pb

### **24. What is characteristic of acute saturnine encephalopathy?**

- Prodromal period with intense headache, insomnia, agitation, generalized tremor
- Disorientation
- Stupor
- Visual disturbances
- Paresis of the cranial nerves
- Delirium with hallucinations and agitation

- Convulsions, coma and death may occur
- At the objective examination, tremor, osteotendinous hyperreflectivity are highlighted
- At the examination of the fundus - edema and papillary stasis, arterial spasm, retinal hemorrhages
- Blood Pb and urinary Pb values are much higher

## 25. Do chronic lead poisoning occur frequently?

- In industrial conditions it is common.

## 26. What are the main syndromes of chronic lead poisoning?

- Astheno-neurotic (headache, dizziness, asthenia, fatigue, insomnia, behavioral changes, daytime drowsiness, decreased memory, loss of appetite)
- Dyspeptic (epigastric embarrassment, constipation, bloating, early satiety, metallic taste, Burton lyser – lilac-gray gum and tooth staining, width 1-2-3 mm)
- CNS and peripheral impairment (impaired visual acuity, behavioral disorders, paresis and paralysis of the radial nerve, weakness in the hands and fingers, tingling, polyarticular pain in the joints of the lower limbs)
- Anemic - reticulocytosis, basophilic-granular erythrocytes in large quantities, oligochrome anemia.
- Cardinal symptom - Pb coloring - green-earth skin coloring

## 27. What is the positive diagnosis in the case of lead poisoning?

Establishing professional lead exposure

a. Subjective: -professional history.

b. Objective: -determination of lead in the air of the workplace, which shows exceeding the maximum allowed limits of lead.

Clinical picture: the presence of one, several, or all of the above-mentioned clinical syndromes

## 28. What are Laboratory Examinations and their Significance in Lead Poisoning?

- Exposure indicators: - Pb-S lead, over 70 mg / 100 ml □ - Pb-U lead, over 150 mg □
- Biological effect indicators: - ALA-U delta aminolevulinic acid in urine, over 20 mg / 1 □ - CP-U coproporphyrin in urine, over 300 mg / 1 □ - low Hb - less than 11g% - in women, - less than 12 g% - in men □ - Red blood cells with basophilic granulations - HGB □ - normal = less than 500 to 1 mil / h, □ - HGB between 500x10 - 5000x10 indicates increased lead absorption □ - safe lead poisoning = over 5000 to 1 mil / hem □ - Reticulocytosis over 13 □ - Sideremia = over 140 mg / 100 ml □
- EDTAMIN lead elimination test (total elimination over 5 days, corrected for normal diuresis): - normal = below 2 mg Pb-U □ - increased absorption = between 2-12 mg Pb-U □ - lead poisoning = over 12 mg Pb-U □

## 29. Saturnian colic must be differentiated from:

- kidney colic
- hepatic colic
- bowel obstruction
- perforated gastric or duodenal ulcer
- acute appendicitis

## 30. Anemia from lead poisoning should be differentiated from:

- other types of anemia

- viral hepatitis
- other hemolytic anemia with jaundice

### **31. Saturnine encephalopathy differentiated by:**

- hepatic encephalopathy
- hypertensive encephalopathy

### **32. Etiological treatment of Pb poisoning:**

- Interruption of professional contact with lead
- Gastric lavage with sodium or magnesium sulphate solution which precipitates Pb as insoluble sulphate
- EDTA chelating treatment (EDTAMIN) = (disodium monocalcium salt of ethylenediaminetetraacetic acid)
- Dimercaptosuccinic acid (DMSA) - mobilizes Pb from soft tissues, is used orally
- Penicillamine - 1-1.5 gr / day under the control of lead

### **33. Lead prophylaxis includes:**

- Technical-organizational measures:
  - Removal of lead from the technological process
  - Automation of technological processes
  - Isolation of equipment and / or technological processes generating vapors or lead dust, from the place where the worker works.
  - Preventing the penetration of vapors and lead dust into the workplace air through: local ventilation, use of wet processes, general ventilation.
  - Preventing or reducing lead on workers by:
    - reduction of physical effort;
    - endowing and obliging the use of personal protective equipment; its maintenance in good condition;
    - appropriate work regime (succession of work and rest periods), with appropriate rest conditions,
    - creation and good maintenance of social annexes
    - sanitary ware (locker rooms, showers, toilets);
    - reduction of the working day, in certain cases (to 6 hours / shift);
    - rational and protective power supply,
    - effective training for labor protection and observance of technological discipline
  - Medical measures
    - Recognition of the risk of lead poisoning in the territory of the enterprise or in the urban or rural constituency
      - Medical employment examination (according to H.G. 355/2007), which consists of: - blood count - blood creatinine - urinary uroporphyrins - EKG
    - Periodic medical examination
    - half-yearly clinic
    - annual creatinine
    - aminolevulinic delta acid or free erythrocyte protoporphyrin annually
    - annual lead
    - annual blood count
    - EMG



## **TESTS FOR KNOWLEDGE VERIFICATION:**

**1. C.S. Definition of lead in terms of interaction with the human body:**

- a. \* It is a metal toxic to the human body, the intoxication being called poisoning
- b. It is a light, non-toxic, low-density silver metal
- c. This metal is not toxic to the body
- d. At normal temperature lead is very unstable
- e. The density of lead is very low

**2. C.S. What are the places where lead is spread?**

- a. Only in metalliferous ores
- b. \* Water, soil, air, plants, the earth's crust
- c. In the textile industry
- d. Food and plants
- e. No answer is correct

**3. C.S. What are the commercial and industrial branches where lead is found?**

- a. Welding industry
- b. Batteries
- c. Plastics and ceramics
- d. Gasoline
- e. \* All listed

**4. C.S. List jobs at risk of lead exposure:**

- a. In the furniture industry
- b. \* Battery industry, graphics, chemical
- c. Production and processing of crystal products
- d. Metallurgical industry
- e. In me

**5. C.S. The most important lead ore is:**

- a. Lead tetraethyl
- b) Asbestos
- c. Selenium
- d. \* Galena
- e. Diboran

**6. C.S. What are the predisposing (secondary) etiological factors that belong to the body in case of lead poisoning:**

- a. Obesity
- b) Diabetes mellitus
- c. \* Viruses

- d. Bronchial rallies
- e. Cardialgia

**7. C.S. What is the temperature of lead vapor emission:**

- 350 ° C
- b 400 ° C
- c. \* 450 ° C
- d 500 ° C
- e 550 ° C

**8. C.S. What are the predisposing (secondary) etiological factors that belong to the workplace in lead poisoning:**

- a. The microclimate
- b. Unfavorable working regime
- c. \* Poor ventilation
- d. High temperature
- e. No answer is correct.

**9. C.S. How long does it take for chronic lead poisoning to develop:**

- a. 3-4 years
- b. \* 2-3 years
- c. 1-2 weeks
- d) 2-3 hours
- e. 3-4 weeks

**10. C.S. What is one of the ways that lead enters the human body?**

- a. The placental tract
- b. The subcutaneous route
- c. The parenteral route
- d. \* The cutaneous route
- e. The intradermal route

**11. C.S. What is specific to the respiratory tract of lead poisoning?**

- a. It is the minor route of penetration,
- b. The deposit rate ranges between 20-35%
- c. Half of the exposed rate is found in the alveoli
- d. \* It is the major route of penetration
- e. The deposit rate ranges between 20-25%

**12. C.S. In which organs and tissue structures does lead storage take place?**

- a. Liver.
- b) Kidneys.
- c. Muscles.
- d. \* Bones.
- e. Store uniformly in all listed organs

**13. C.S. What organs and tissue structures are affected by lead poisoning?**

- a. Hematopoiesis system.
- b. The central and peripheral nervous system.
- c. Parenchymal organs.

- d. Skin, mucous membranes, bones.
- e. \* All listed

**14. C.S. Specify the pathogenesis of anemia in chronic lead poisoning:**

- a. Iron deficiency anemia
- b. Aplastic anemia
- c. Posthemorrhagic anemia
- d. B12 deficiency anemia
- e. \* Blocking heme formation

**15. C.S. What morphological changes in sternal puncture are attested in lead poisoning?**

- a. Decreasing the number of megaloblasts
- b. Increases the mechanical fragility of erythrocytes with increasing their lifespan
- c. \* Increasing the number of megaloblasts
- d. Morphological changes at the sternal puncture are not detected
- e. Morphological changes at the sternal puncture are detected

**16. C.S. Which acid is excreted in the urine in case of lead poisoning?**

- a. Arachidonic acid
- b. \* Aminolevulinic acid
- c. Ethacrynic acid
- d. Folic acid
- e. Uric acid

**17. C.S. What are the typical symptoms of saturnine colic?**

- a. \* Diffuse pain throughout the abdomen or paraumbilical, with lumbar irradiation
- b. Reduction of abdominal pain on palpation
- c. The abdomen is not tense
- d. Constipation
- e. Diarrhea.

**18. C.S. What syndromes are typical for chronic lead poisoning?**

- a. Astheno-neurotic
- b) Dyspeptic
- c. CNS and peripheral damage
- d. The cardinal symptom - the color of Pb
- e. \* All listed

**19. C.S. Which drug is the first-line treatment in Lead poisoning?**

- a. The succimer
- b. Unitiolul
- c. \* Edtamina
- d. Phenol
- e. Diproximum

**20. C.S. In what period of time is the general medical examination of patients previously subjected to the harmful action of lead carried out?**

- a. 1 time a month
- b. \* 1 time every 3 months
- c. 1 time in 6 months

- d. 1 time in 12 months
- e. 1 time in 18 months

**21. C.S. Is the employment medical examination performed according to which normative act?**

- a. \* HG 1025 of 07-09-2016
- b. HG 1282 of 29-11-2016
- c. GD 355 of 11-04-2007
- d. HG 775 of 02-10-2017
- e. HG 256 of 27-03-2018

**22. C.M The activity in which industries and which technological processes can lead to lead poisoning of employees?**

- a. \* Battery industry, graphics, chemical
- b. \* Lining and repair of acid tanks with Pb plates
- c. \* Light and food industry
- d. \* Preparation and use of Pb paints
- e. None is correct

**23. C.M. What are the main pathways for Pb to enter the body?**

- a. \* Respiratory
- b. \* Digestive
- c. \* Cutaneous
- d. \* Mucosa
- e. Hematogenous

**24. CM. Name the target organs of lead poisoning:**

- a. \* Brain
- b. \* Bones
- c. \* Liver
- d. Lungs
- e. Kidneys

**25. CM. Name the target organs of lead poisoning:**

- a. \* Brain
- b. \* Bones
- c) The eyes
- d. Lungs
- e. Kidneys

**26. CM. Name the body's systems that are predominantly affected by lead:**

- a. \* Nerves
- b. \* Pulmonary
- c. \* Hemapoietic
- d) Fermentative
- e. \* Cardio-vascular

**27. C.M. What pathological changes are typical for lead poisoning?**

- a. \* Inhibits heme synthesis in the bone marrow erythroblast

- b. Formation of methemoglobin in erythrocytes
- c. \* Blocks the activity of some of the enzymes in the heme biosynthesis chain
- d. \* Increased protoporphyrin IX levels in red blood cells
- e. All answers are correct

**28. C.M. Name the morphological changes at the sternal puncture:**

- a. \* Increasing the number of megaloblasts
- b. \* Increases the mechanical fragility of erythrocytes by decreasing their lifespan (hemolysis)
- c. \* Inhibition of membrane glucose-6-phosphate dehydrogenase
- d. The number of megaloblasts decreases
- e. \* Occurrence of polypoid erythroblasts and erythroblasts with basophilic granules

**29. C.M. The main forms of acute lead poisoning are:**

- a. Acute toxic hepatitis;
- b. \* Saturnine colic;
- c. \* Acute saturnine encephalopathy;
- d. Pseudo-rheumatic syndrome;
- e. Anemic syndrome.

**30. C.M. What are the typical symptoms of "saturnine colic"?**

- a. \* Astheno-neurotic or dyspeptic manifestations (nausea, vomiting, anorexia)
- b. \* Diffuse pain throughout the abdomen or paraumbilical, with lumbar irradiation
- c. \* The abdomen is normal or slightly excavated and has no muscle contracture
- d. \* The pain subsides at the deep pressure of the abdomen
- e. On palpation of the abdomen the pain is more pronounced

**31. C.M. For acute saturnine encephalopathy it is characteristic:**

- a. \* The paresis of the cranial nerves
- b. \* Tremor
- c. \* Urinary Pb is not detected
- d. Blood Pb does not change in comparison with another.
- e. \* Disorientation

**32. C.M. The clinical picture of chronic lead poisoning is characterized by the following syndromes:**

- a. \* Astheno-vegetative syndrome
- b. \* Digestive syndrome
- c. Cholestatic syndrome
- d. \* Anemic syndrome
- e. \* Syndrome of central nervous system disease

**33. C.M. Indicate the symptoms of chronic lead poisoning:**

- a. \* Abdominal pain attacks
- b. \* Tightening of the abdominal wall
- c. Reduction of abdominal pain on palpation
- d. Constipation
- e. Diarrhea

**34. C.M. What diagnostic criteria are NOT typical for chronic lead poisoning?**

- a. \* Saturnine colic
- b. \* Reticulocytosis

- c. Hyperchromic anemia
- d. Hemosiderin in urine
- e. \* Increased serum iron

**35. C.M. Diagnostic criteria for chronic lead poisoning are:**

- a. \* Professional route
- b. \* Astheno-vegetative syndrome
- c. Cholestatic syndrome
- d. \* The color of Pb
- e. \* Burton Lizard

**36. CM. What changes can be detected in the general analysis of blood in lead poisoning?**

- a. \* Anemia
- b. \* Leukocytosis
- c) Leukopenia
- d. Erythrocytosis
- e. \* Erythropenia

**37. CM. With which pathologies is the differentiated diagnosis of Saturnine colic made?**

- a. \* Renal colic
- b. \* Hepatic colic
- c. \* Intestinal occlusion
- d) Myocardial infarction
- e. \* Acute appendicitis

**38. C.M. Anemia from lead poisoning should be differentiated from:**

- a. Iron deficiency anemia
- b. \* Viral hepatitis
- c. Aplastic anemia
- d. \* Other hemolytic anemia with jaundice
- e. B12 deficiency anemia

**39. CM. Does the laboratory test show the levels of lead in the blood and urine, what are the permissible values?**

- Plumbemia below 50mg / 100ml
- b. \* Plumbemia below 70mg / 100ml
  - c. \* Lead below 150mg / l
  - d) Lead below 40mg / g
  - e. Plumbemia below 60mg / 100ml.

**40. C.M. The presence of which biochemical component is useful for the diagnosis of lead poisoning?**

- a. Arachidonic acid
- b. \* Aminolevulinic acid
- c. Ethacrynic acid
- d. \* Delta-aminolevulinic acid
- e. Deoxypholic acid

**41. C.M. Lead poisoning treatment includes:**

- a. \* Administration of penicillamine;
- b. \* Administration of EDTA;
- c. \* Administration of DMSA;
- d. Daily administration of BAL;
- e. \* Daily administration of vitamin C.

**42. CM. What are the personal hygiene measures that must be strictly followed by people exposed to Lead?**

- a. \* Bath or shower with hot water and soap
- b. \* Brush your teeth with a toothbrush and toothpaste
- c. \* Meal should be taken outside polluted areas
- d. High fat diet
- e. \* Avoid alcohol abuse

**43. C.M. In what period of time is the general medical control of the patients subjected to the harmful action of lead performed?**

- a. 1 time in 9 months
- b. \* 1 date in 3 months
- c. \* Medical examination for employment
- d. 1 time in 2 months
- e. \* Half-yearly

**44. C.M. What is the application of technical and organizational measures to prevent lead poisoning?**

- a. \* Removal of lead from the technological process
- b. \* Automation of technological processes
- c. Release from use of protective equipment
- d. \* Respecting the technological discipline
- e. \* Reduction of the working day, in certain cases (6 hours / shift)

**45. C.M. What includes the medical prophylactic measure applied to employment according to H.G. 1025 of 7/09/2016 to prevent the action lead?**

- a. \* neurologist
- b. \* blood count
- c. \* blood creatinine
- d. \* urinary uroporphyrins
- e. ECG

**46. C.M. What includes the medical prophylactic measure applied annually according to H.G. 1025 of 7/09/2016 to prevent the action lead?**

- a. \* general clinical examination, neurologist
- b. \* blood count
- c. \* blood creatinine
- d. \* EMG, at the doctor's indication in occupational pathologies
- e. TC

**47. C.M. What prophylactic measures are taken at the end of the worker's shift according to H.G. 1025 of 7/09/2016 to prevent the action lead ?**

- a. \* deltaaminolevulinic acid in urine
- b. \* free erythrocyte protoporphyrin in the blood
- c. \* lead
- d. blood count
- e. urinary uroporphyrins

**48. C.M What are the contraindications to employment with occupational exposure to lead poisoning according to H.G. 1025 din 7/09/2016?**

- a. \* chronic diseases of the cardiovascular system (hypertension, ischemic heart disease)
- b. \* chronic diseases of the nervous system
- c. \* anemia
- d) Gastric ulcer
- e. Asthma

**49. C.M What are the contraindications to employment with occupational exposure to lead poisoning according to H.G. 1025 din 7/09/2016?**

- a. \* Chronic nephropathy
- b. \* Women in the fertility period
- c. \* Minors under 18 years of age
- d) Pensioners
- e. Chronic tonsillitis

**50. What includes the medical prophylactic measure applied to employment according to H.G. 1025 of 7/09/2016 to prevent the action lead ?**

- a. ophthalmologist
- b. \* blood count
- c. \* blood creatinine
- d. \* urinary uroporphyrins
- e. ECG