

# Intoxication with methemoglobinizing substances

## Aromatic amines

- Aniline, toluidine - liquids.
- Benzidine , 2-naphthylamine - pinkish powder substance.

## Professional exposure

- Production of dyes (textiles, paper, leather), plastics, rubber, pesticides.

## Etiopathogenesis

- Fat-soluble substances - they are well absorbed by the skin ,
- They are metabolized into hydroxylamines, which change hemoglobin into methemoglobin , create VR in erythrocytes and give rise to so-called Heinz bodies in erythrocytes (precipitated hemoglobin with cytoskeletal proteins),
- Erythrocytes are more fragile, hemolysis , hemoglobinuria and subsequent kidney damage may occur .
- They are removed by acetylation (people we refer to as so-called slow acetylators are at risk of bladder cancer ).

Aniline (its metabolite phenylhydroxylamine) has the strongest methemoglobinizing effect → functional anemia occurs , the curve shifts to the left, and tissue hypoxia increases . Therapy uses alternative ways of reducing methemoglobin by the enzyme NADPH methemoglobin reductase - it needs methylene blue (a redox substance) as a cofactor.

## Clinical picture

**Acute - lower exposure** - CNS excitation (so-called aniline spike);

- *Then the manifestations depend on the degree of methHbemia ,*
  - 10-30% cyanosis , tachycardia , fatigue,
  - 30-50% weakness, shortness of breath, headache,
  - 50-70% impaired consciousness and death,
- The blood taken is dark brown to black in color (striking plum-blue cyanosis).

**Chronic** - polyglobulia due to chronic hypoxia.

## Therapy

Antidote - *methylene blue* .

## Indication

- Symptoms of hypoxemia ( dyspnea , confusion, chest pain),
- Methemoglobinemia at 25%,
- Initial dose - 1-2 mg/kg iv,
- Risks - people with a defect of G6P-dehydrogenase (they do not create NADPH) - it does not work and, moreover, it accumulates and can aggravate methemoglobinemia and cause hemolysis.

*Toluidine blue* - works by the same mechanism, paradoxically, cyanosis deepens after administration (given by the color of the antidote) *ascorbic acid* - works weaker and slower.

## Aromatic nitro compounds

- They have the NO<sub>2</sub> group , e.g. nitrobenzene, TNT, trinitrophenol (picric acid),
- Professional exposure - production of aniline, dyes, explosives,
- Etiopathogenesis - they are well absorbed by the skin, by a similar mechanism to the previous ones, they cause methemoglobinemia. In addition, TNT causes massive necrosis and yellow atrophy of the liver with a lethal end, or cataract.

## Nitroglycerin

- Oily liquid, easily explosive,
- Application - manufacture of explosives, pharmacology,
- They are easily absorbed through the skin, after absorption they are hydrolyzed into inorganic compounds and cause vasodilation,
- After 2-4 days of professional exposure, tolerance develops (thanks to compensatory sympathetic mechanisms) → angina pectoris may occur after exposure is interrupted ,

- After high doses, methemoglobinemia, of mild degree, without Heinz bodies, may occur.
- **Acute intoxication** - headaches (caused by vasodilatation of CNS vessels), "powder headache" in the occiput, restlessness, depression, sleep disorders, paleness of sweating, drop in pressure, shock,
- High doses - methemoglobinemia, shortness of breath, unconsciousness,
- Professional exposure - typically the so-called "Monday sickness" - always after a weekend break, compensation sets in during the week, symptoms disappear...,
- **Chronic intoxication** - angina pectoris and sudden death, paradoxically on days off from work (after interruption of exposure), pseudoneurasthenic symptoms are also described.

## Therapy

- Angina from habit - we will remove nitrates,
- Acute hypotension is difficult to influence therapeutically - anti-shock position, IV fluids, possibly dopamine, norepinephrine.

## Nitrites

*Synonym:* nitrites, -NO<sub>2</sub>,

- Sodium nitrite - a yellowish solid substance soluble in water,
- It was also used as a methemoglobinizing substance in cyanide poisoning,
- Additive for smoking meat, for cigarette papers, for fuel,
- Lethal dose after - **4g**.

## Nitrates

*Synonym:* nitrates, -NO<sub>3</sub>,

- In order to cause methHbemia, they must be reduced to nitrites by flora in the intestine,
- They are dangerous for infants (they have bacteria in the GIT higher - due to less acidic stomach contents),
- As little as 10 mg/l can be dangerous for infants,
- Others, chlorates, drugs - primaquine (antimalarial), phenacetin (analgesic).

## Links

### related articles

- Intoxication by mercury and its compounds
- Intoxication by lead and its compounds

### Source

- BENEŠ, Jiří. *Studijní materiály* [online]. [cit. 24.02.2010]. <<http://jirben.wz.cz>>.

## References

- PELCLOVÁ, Daniela. *Nemoci z povolání a intoxikace*. 2. vydání. Praha : Karolinum, 2006. 207 s. ISBN 80-246-1183-X