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TWO CASES OF EXTREME METHAEMOGLOBINAEMIA DUE TO INHALATION OF NITROUS OXIDES

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ABSTRACT

During the production of 5-nitro-hydroxiethyl isophtalamic acid (NHI) two healthy workers were accidentally exposed to a mixture of gases and turned dark cyanotic. One of them, a 40 year old man, had a 65% methaemoglobinaemia without any severe complications until one year after the accident, when an atrial fibrillation was diagnosed. The other, aged 24, was found to have 50% methaemoglobinaemia and, subsequently, a moderate increase of SALAT (GPT)-transaminase and triglycerides.

The only possible cause of the poisoning must have been nitric oxide (NO).

In April 1977 two engineers working in an experimental plant of the Bofors, Nobel Kemi division suddenly became dark cyanotic within a few minutes. Several years ago we had some cases of a moderate cyanosis in connection with methaemoglobinaemia due to contact with metadinitrobensene. Thus the older and more experienced man of the two assumed that it could be methaemoglobinaemia and immediately took his colleague to hospital, where both were kept for treatment. The older man (40) a head engineer, had an extremely deep blue colour. About 65% of the haemoglobin (Hb) was transferred into methaemoglobin (MetHb) – 88 g MetHb out of a total of 135 g Hb/l blood. In spite of this he himself did not experience any symptoms, but was mainly concerned about his colleague, a 24 year old man, who had 68 g MetHb of 140 g Hb/l blood, i.e. a 50% methaemoglobinaemia. Both were given oxygen while resting and each an injection of 8 ml 1% solution of methylene blue, i.e. methylthionin chloride, intravenously. Twenty-four hours later both had a MetHb value of less than 2 g/l blood and their general condition appeared unaffected.

The other standard laboratory tests were without remarks. The acid/base balance showed a satisfactory O_2 (oxygen) saturation and pO_2 was above normal during O_2 ventilation. The day after the intoxication the O_2 saturation was slightly decreased in the older patient (8.3 – 9.8 aB-pO_2) who had a most severe methaemoglobinaemia. Both had a normal ECG and they could leave hospital within 48 hours.

After returning home the younger man had no symptoms while the older one felt very tired and had a pronounced moving dyspnoea. At a thorough examination one week after the intoxication both were found free from symptoms both subjectively and objectively. The liver function was checked for a long time. Repeated blood tests did not reveal any abnormality in the older man (Fig. 1). The younger man (Fig. 2) had slightly increased S-alanine--aminotransferase [S-ALAT (GPT)] and triglycerides after one month, and normal values not until 7 months later. Sixteen months after the accident the transaminases were moderately increased without any obvious reason, neither due to alcohol consumption nor to any new exposure to chemicals. Otherwise the younger man was quite healthy.

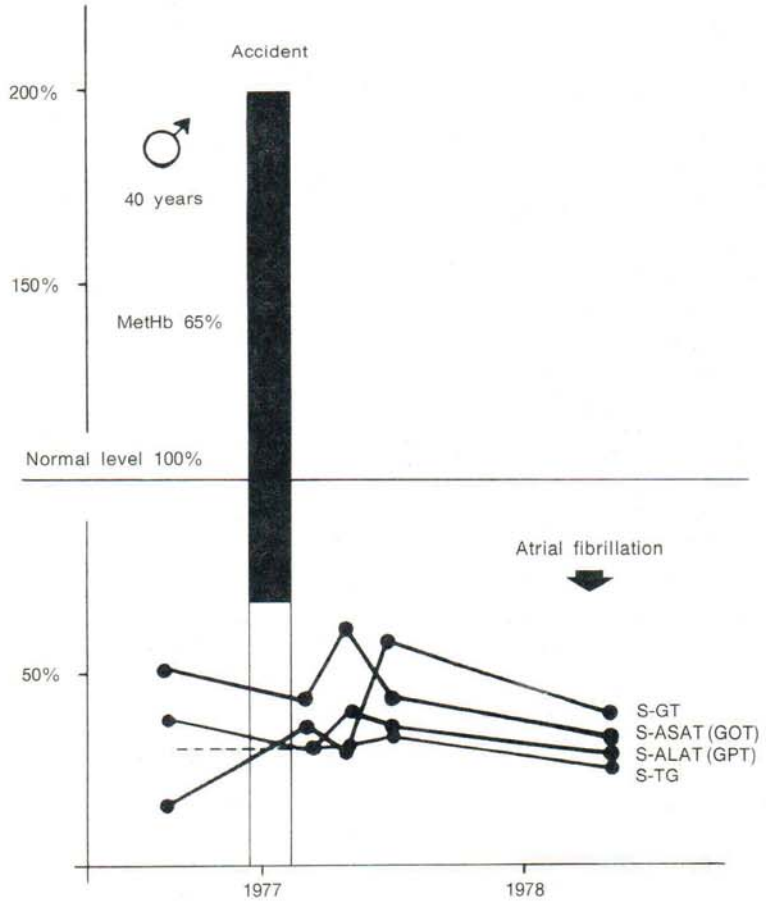

FIG. 1 – A 40 year old man with 65% methaemoglobinaemia had subsequently normal S--aspartate-aminotransferase [S-ASAT (GOT)]. S-Alanin-amino-transferase [S-ALAT (GPT)], S-glutamyl-transferase (S-GT) and S-triglycerides (S-TG) but atrial fibrillation.

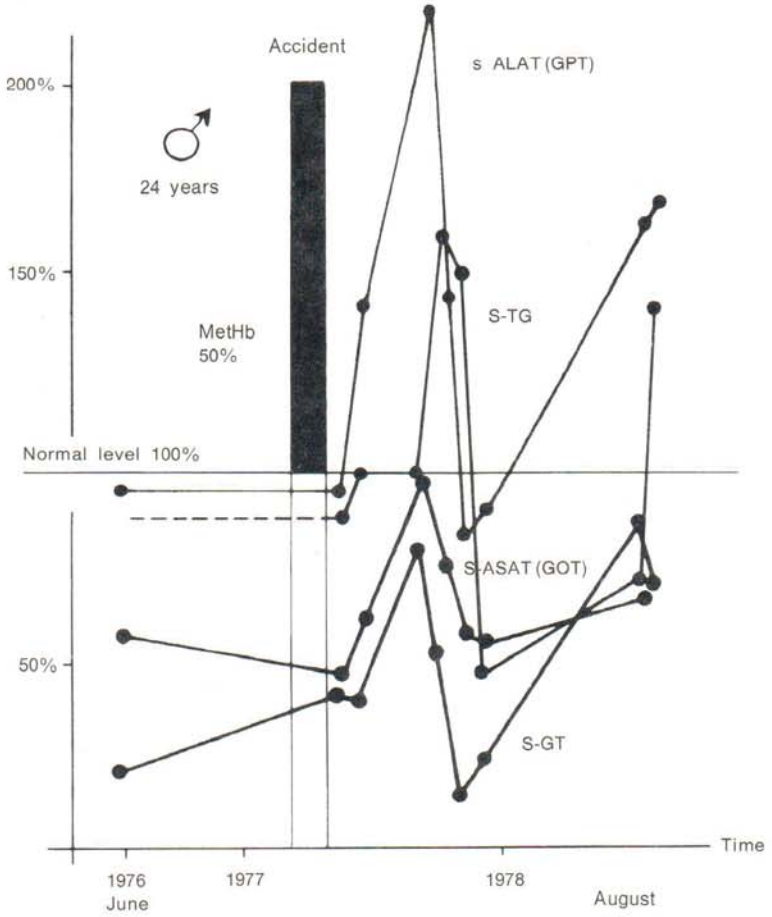

FIG. 2 – A 24 year old man with 50% methaemoglobinaemia had slightly increased S-ALAT (GPT) and S-TG after 5 months and again after 16 months.

Fourteen months later atrial fibrillation was found in the 40-year man when he was about to be operated for an injury. An attempt to normalize his state with digitalis proved unsuccessful, but after conversion with a pace-maker and supporting treatment with quinidine the heart function was good. Sixteen months after the accident, both men were back at work and felt healthy.

What was the cause of these two sudden intoxications? We thought it was dinitrobensene with which we had some bad experience before or that it was at least some aromatic nitro compound.

The accident occurred during the production of 5-nitro-hydroxiethyl--isophtalamic acid (NHI) (Fig. 3). A reactor was loaded with 5-nitro-isophtalic

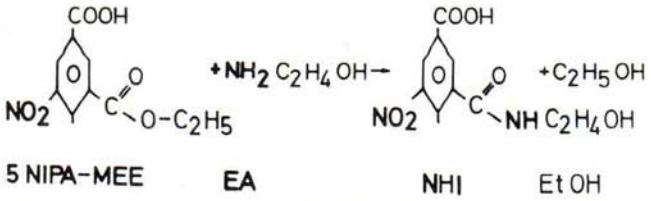

FIG. 3 – 5-Nitro-hydroxiethyl-isophtalamic acid (NHI) was produced from 5-nitro-isophtalic-acid-monoethylester (5-NIPA--MEE) and ethanolamine (EA).

acid-monoethyl ester (5-NIPA-MEE), ethanol-amine and ethanol as a solvent. After 20 hours 35% nitric acid was added to neutralize the excessive ethanolamine. The solution was purified with coal. The batch was warmed to 80-83 °C and 35% nitric acid was added again to lower the pH. At this moment a moderate foaming started with gas generation. The exhausting device failed to evacuate all the gas, and a white, possibly slightly reddish gas, smelling of ethanol spread in the factory. Trying to improve the evacuation the two workers became exposed to gas for 5–15 min and as a result turned dark cyanotic.

TABLE 1

Gaschromatographic and masspectrographic analysis of gas produced in the laboratory. The results are expressed as a relative percentage of the area.

Compound	%
N_2O	16
NO	17
CO_2	11
H_2O	1
C_2H_5OH	37
C_2H_4	0.5
CH_3CHO	3
N_2	14
Total	99.5

In order to reproduce the conditions at the time of the accident laboratory tests were performed. The produced gases were analyzed by gaschromatography and masspectrography. The results are shown in Table 1. The presence of metadinitrobensene can definitely be excluded. Thus, the only possible cause of the poisoning must have been nitric oxide (NO).