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CASE REPORT

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# Clinical and morphological aspects of death due to liquid nitrogen

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**Abstract** A 24-year-old student died while filling flasks with liquid nitrogen. The arms, legs and back were frozen and the face, ears and neck showed a dark red and livid colour with horizontal lines of demarcation. In the electrocardiogram, the heart showed asystolia followed by wide ventricular complexes. The patient was intubated orally as the situs of the larynx and pharynx showed no pathology findings. Cardiopulmonary resuscitation was carried out and terminated after 90 min. Unfortunately, the body temperature was not measured. The gas analysis of venous blood showed metabolic acidosis and oxygen deficiency. The student had worked alone with nitrogen, without opening the windows and without a working ventilation system. While filling the third flask he lost consciousness. As nitrogen does not cause characteristic prodromal signs he laid on the floor and was unable to help himself. The liquid nitrogen which was still escaping spread over the floor and vaporized. The student died from asphyxia due to oxygen deficiency in an atmosphere of nitrogen.

**Key words** Liquid nitrogen · Cold · Frostbite · Asphyxia · Pathomorphological findings · Mechanism of death

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## Introduction

Liquid nitrogen ($N_2$) is an inert gas which is liquefied on cooling down. The gas is colourless and odourless, it is slow to react and does not burn. It is used in laboratories in large quantities especially for freezing purposes and is widespread in industry and science, but there are only a few case reports about accidents caused by the use of $N_2$.

## Case report

A student was found in a laboratory lying in a face-up position with the arms bent (18.00 p.m.) and the body was frozen to the floor. During cardiopulmonary resuscitation the patient was transported to the University Hospital, Göttingen. He was declared dead at 19.30 p.m. At 19.45 and 22.50 p.m. the corpse was still frozen with white frost at the ankles. The last time he was seen alive was at 17.30 p.m. and 30 min later another person entered the cold room. A Dewar-flask (10 l) had overflown and the floor was completely covered with ice (Fig. 1). The person immediately closed the valve on the cylinder but for the time period afterwards he had a loss of memory and could not say how he came out of the room. Other persons had brought him outside and had opened the windows and the door [9, 12].

The time interval between the accident and the beginning of resuscitation was about 15–30 min (17.30–18.00 p.m.). During the first examination, the extremities and the back were frozen and the patient had complete iridoplegia. The electrocardiogram showed sporadic and broadenend QRS complexes. On the face, the neck and the thorax livid-red coloured areas of the skin were found, which partly showed horizontal lines of demarcation. Unfortunately, the core temperature of the body was not measured. During the transport to the hospital, artificial respiration was continued, but total iridoplegia continued followed by asystolia. Furthermore, hemorrhagic pulmonary edema and severe metabolic acidosis with hyperkalaemia developed. Resuscitation attempts were terminated after approximately 90 min. The back and the extremities remained frozen for 210 min after resuscitation attempts. The frozen state of the face and of the neck disappeared 120 min later and after 240 min on the arms. The back and the thighs thawed after 9 h and after 11 h the frozen state had disappeared from the lower legs and from the feet [12].

### Pathomorphological findings

The autopsy was carried out 3 days later so that the core body temperature was influenced by storage in the refrigerator. Reddened

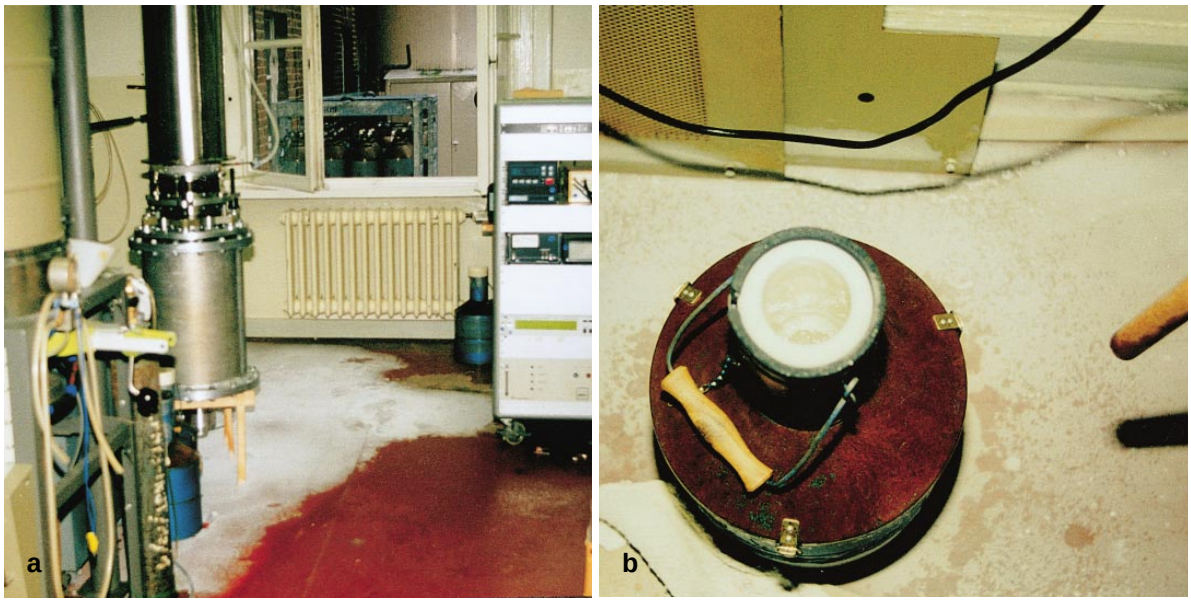


**Fig. 1** The scene of the accident showing **a**) the cold experimental room with the liquid nitrogen apparatus and the tank for $N_2$ and **b**) the Dewar flask which flowed over and the valves for liquid nitrogen

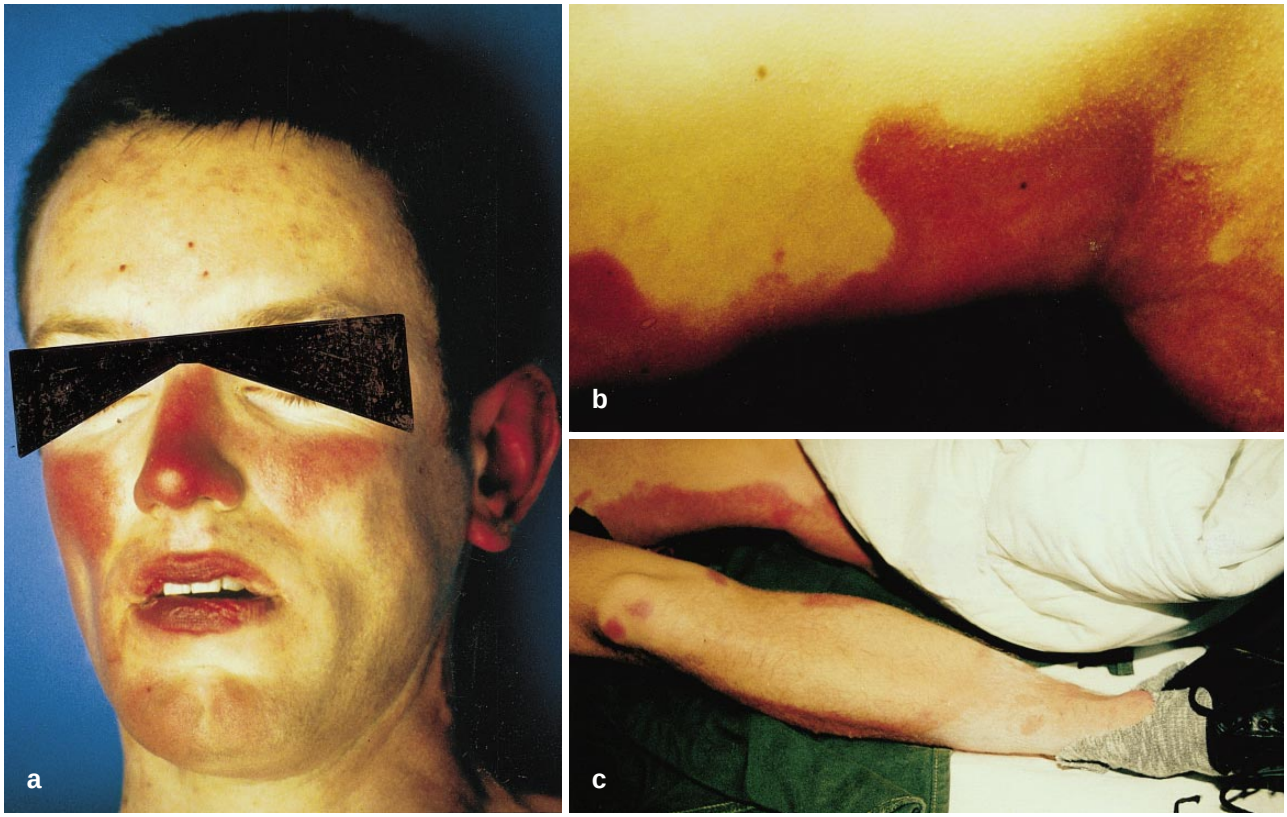


**Fig. 2** The autopsy showing **a**) sharply defined, dark red discoloured frostbite injuries with the exception of the eye region, **b**) a sharply defined demarcation line as boundary line of coldness influence on the right side of the trunk and **c**) mainly horizontal demarcation lines on the legs and covering of the right lower leg with frost (4 h after unsuccessful resuscitation)

areas of the skin without lesions of the epithelium were seen in the face, at the backs of the arms and legs and also on the fingers the neck and the rump (Fig. 2). Multiple petechiae were located in the conjunctivae and in the skin of the eyelids. The histological investigations revealed acute pulmonary emphysema and hemorrhagic edema, cerebral edema, hyperemia and cyanosis of the abdominal viscera as well as liquid blood. The pulmonary emphysema may have been due to resuscitation. None of the organs showed other pathomorphological alterations.

**Table 1** Post mortem biochemistry in liquor cerebrospinalis, corpus vitreum, blood and urine (samples were taken during the autopsy three days post mortem)

| Parameter | Liquor c. | C. vitreum | Serum (Blood) | Urine |
|---|---|---|---|---|
| Alk. phosphatase | 148 U/L | 4 U/L | 486 U/L | 54 U/L |
| Amylase | 7 | 0 | 119 | 92 |
| Creatine kinase | 1590 | 931 | 20310 | 830 |
| GOT | 112 | 78 | 2320 | 17 |
| GPT | 27 | 12 | 2440 | 23 |
| Gamma GT | 10 | 5 | 25 | 575 |
| LDH | 2300 | 296 | 8930 | 931 |
| Bilirubin | 0.03 mg/dl | 0.03 mg/dl | 0.4 mg/dl | 0.21 mg/dl |
| Cholesterol | 9.0 | 1.0 | 203 | 2 |
| Creatinine | 1.5 | 0.34 | 1.52 | 111.5 |
| Glucose | 0 | 0 | 294 | 0 |
| Uric acid | 3.91 | 5.22 | 18.17 | 26.59 |
| Blood-urea $N_2$ | 24.7 | 14.4 | 22.0 | 18.7 |
| Triglycerides | 5.0 | 2.0 | 482 | 0 |
| Phosphate | 30.0 | 3.7 | 35.2 | 74 |
| Total protein | 0.46 g/dl | 0 | 8.75 g/dl | 0.75 g/dl |
| Sodium | 115 mm0l/l | 143 mmol/l | 114 mmol/l | 137 mmol/l |
| Potassium | 42 | 16 | 46.8 | 60.3 |
| Calcium | 5.8 | 6.7 | 12.6 | 14.7 |
| Lactate | 26.8 | 7.72 | 41.0 | 10.23 |
| $HbA_1$ | – | – | 5.4% | – |
| HbA1c | – | – | 4.7% | – |
| Insulin | 0.9 µU/ml | 0.3 µU/ml | 5.8 µU/ml | – |

Special histological examinations of the skin and of the heart

Specimens were taken from the discoloured skin of the left chest wall fixed in 4% formalin, embedded in paraffin and stained with hematoxilin and eosin and by the EvG method (5 µm sections). Inflammatory changes were not found in the skin, but in the upper half of the discoloured skin karyopyknosis and perinuclear vacuolation of keratinocytes could be seen. Oedematous changes were present in the basal layer, the blood vessels were dilated and the surrounding tissue was loosened as a sign of hyperemia. None of these alterations were seen in the pale region of the adjacent skin.

The histological examination of the heart was performed on six different regions of both ventricles and of the septum. Staining was done by hematoxilin and eosin and by the EvG method.

Subepicardially there were thinly scattered infiltrates of round cells, especially at the margin of the myocardium. These infiltrates were sometimes diffuse, sometimes focal. Vast extravasates of erythrocytes were sometimes seen in the oedematous interstitial tissue which were smaller and mostly circumscript in the septal region. Throughout the myocardium, in the adjacent connective tissue and in some intramural arteries a diffuse marginality of round cells could be observed. These were mostly lymphocytes and macrophages. Sometimes these accumulations of round cells showed a beginning emigration such as diffuse infiltrates.

Clinical and post mortem biochemistry

*Important data of nitrogen*

Molar mass 28.013; specific gravity (1013 mbar; O/25° C) 1.25/1.145 kg/m$^3$, melting point –210° C, boiling point –196° C. Temperature of liquid nitrogen approx. –220° C, during flask filling approx. –180° C [13].

*Blood gas analysis*

Hemoglobin 13.8 g/dl, hematocrit 43%, sodium 152 mmol/l, potassium 7.4 mmol/l, oxygen saturation 15%, pH 6.64, partial pressure $CO_2$ 137 mmHg, partial pressure $O_2$ 29.3 mmHg, base excess –24.4 mmol/l, SBC 7.9 mmol/l.

The results of post mortem biochemical investigations are given in Table 1.

Toxicological analyses

The left lung was tied off and air samples were taken using a sterile syringe directly next to a mass spectrometer. The injection was done immediately (mass spectrometer MAT 95, determination of the relationship between $N_2$ and $O_2$). The measured proportion of $O_2/N_2$ was the same as in breathing air.

Furthermore, systematic and specific toxicological investigations were carried out (ADH/GC for ethanol/screening by Emitdau for cannabinoides, opiates, amphetamines, benzodiazepines and barbiturates). Further analyses (Valov) were done for drugs, organic poisons, cyanides and other psychoactive drugs. An electron-capture-detector was used for the analyses on benzodiazepines. None of these investigations showed exogenous or other psychoactive substances.

## Discussion

Nitrogen is liquefied by cooling down under high pressure. The gas is colourless, odourless and very cold (–220° C). The conversion from liquid to gas develops quickly and as the cold vapour is heavier than air, the vapours spread out along the floor pushing away the breathing air from the

bottom at the same time [7]. The laboratory must be ventilated sufficiently and when the proportion of nitrogen in the air exceeds 78% breathing equipment must be used. Protective clothing, safety goggles, protective shields and protective leather gloves must be worn [4, 9]. Liquid nitrogen is usually stored in isolated (Dewar-) containers.

Nitrogen does not cause irritant or warning symptoms. When the proportion of nitrogen in the air exceeds 88%, the respiration process is blocked resulting in asphyxia [7]. The symptoms depend on the duration of inhalation and on the remaining concentration of oxygen. There may be somnolence, indisposition, rise in blood pressure and dyspnoea. Furthermore, liquid nitrogen may cause severe frostbite lesions similar to burns especially to the eyes and on the skin.

The analysis of gas from the intrapulmonary bronchi showed a relationship between $N_2$ and $O_2$ as found in environmental air. But it must be taken into account that this result is not representative for the early stage because of the long duration of resuscitation attempts. Before intubation a trismus had to be overcome. The larynx and pharynx did not show any alterations due to the effect of coldness. In case of nitrogen exposition, intubation should be carried out quickly, although there is a risk of ventricular fibrillation [1].

Blood-gas analysis during the resuscitation showed metabolic acidosis in combination with a massive electrolyte disturbance and a very low pH. In addition, there was a considerable increase of the partial pressure of $CO_2$, whereas the partial pressure of oxygen decreased to a very low level. As a result of a counter-regulation, the base excess was –24.4 mmol/l ! The post mortem biochemical values were mostly within the normal range (Table 1), but some parameters were massively increased e.g. potassium and especially cell-linked enzymes such as creatine kinase, GOT, GPT and LDH. Special attention should be paid to the high value of glucose in serum but in contrast glucose was not found in any of the other body fluids analysed. The reason for this may be that there was a retroactive inhibition because of ante mortem hyperglycemia and nearly complete metabolisation of glucose to lactic acid. So the results of clinical and post mortem biochemical investigations were characteristic of a massive oxygen deficiency. These findings were the same as reported by Britt et al. [1] who found acidosis and hyperkalaemia in cases of hypothermia [2]. The pathophysiological mechanism may result from reactions of capillaries in the lungs which are similar to those in the peripheral vessels. A causal relationship is postulated between a sudden effect of cold and its consequences as disturbed circulation and hypoxia/acidosis [3, 5, 6].

Morphological equivalents of asphyxia due to oxygen deficiency were seen as many petechiae in the conjunctivae as well as distinct pulmonary emphysema. Nevertheless, emphysema with multiple interalveolar ruptures could also have been caused by intensive artifical respiration and may also have caused multiple extravasates of erythrocytes in the myocardium. Contrary to this, petechiae in the conjunctiva seen during the autopsy 3 days post mortem rarely appear as a result of resuscitation. Additionally, the heart showed a slight or beginning myocarditis which was presumed to be pre-existing.

The main macroscopical pathomorphological alterations were vast dark-red discolourations of the skin which had sharply defined margins and were not in a hypostatic region (Fig. 2). The zones of discolouration were in direct contact to liquid nitrogen (face, arms, trunk) and covered approximately 70–80% of the total skin. Horizontal demarcation lines were also found and similar findings have been reported for frostbite injuries of the hands [7, 12, 16]. Histologically the epidermis of these reddened regions showed karyopyknosis and vacuolation. According to Tabata et al. [15] these findings can indicate that the skin damage was caused by cold, possibly due to liquid nitrogen. However, such changes may appear not only ante mortem but sometimes also post mortem.

Tabata et al. [15] recently reported a case of exposition to large quantities of liquid nitrogen. Gaseous nitrogen had accumulated in a room which caused death by asphyxia to two men. At the scene of death there was frost on the floor and white fog in the air as shown in Fig. 1. Resuscitation attempts lasted more than 1.5 h. The authors described alterations to the skin quite similar to those seen in the present case. The colour was comparable to that of post mortem lividity.

Santoni [11] also ascribed such dark red discolourations of the skin to a direct influence of liquid nitrogen, but proposed that such alterations are not specific for nitrogen as they may also occur during contact with liquid propane (–43° C). The acute reaction may be massive bullae, sometimes combined with hypesthesia and myokinetic disturbances lasting half a year. Residual symptoms may be patchy red discolouration of the skin and a deformation of the fingernails. When the frostbite injuries are extensive, the prognosis is usually unfavourable.

Severe residual symptoms after exposition to liquid nitrogen may be infections and gangrene. Leu et al. [8] reported the case of an engineer who had 4th degree frostbite injuries to the foot and lower leg. The skin was in direct contact to 2–3 l of overflowing liquid nitrogen. In the early phase, the foot had been hard as ice and intensively red and 7–8 h after the accident bullae and pain appeared. The 4th degree frostbite injuries had caused severe ischemic necroses of the skin, the subcutis and the muscles. Contrary to this, small splashes of liquid nitrogen on the skin do not normally cause any lesions because there is a form of isolating bubble around the splash (the so-called Leydenfrost phenomenon). Special danger arises when liquid nitrogen flows over the skin, soaks into clothes or when it infiltrates into boots or gloves. There may be abrupt freezing of the tissues and an intensive refrigeration anesthesia [8].

When death occurs during hypothermia, certain postmortem phenomena may be lacking and sometimes, the signs of death are only moderately present. In the case presented, livor mortis did not appear before 12 h after death. A differential diagnosis may be difficult concerning marking the limits of lividity due to the effect of cold.

In principle, the prognosis of resuscitation is relatively good in cases of hypothermia, but there are only reports about body temperatures down to 18° C and no data exist about temperatures of tissues down to freezing point [1, 10, 14].

When pure nitrogen is inhaled loss of consciousness may occur suddenly. Furthermore, during the inhalation of nitrogen carbon dioxide can still be exhaled at the same time. So an increase of the process of respiration can only be caused in relation to oxygen deficiency. Because of this, there is no dyspnoea which may be an important warning sign.

All members of the institute involved had been informed about the dangers and protection measures when working with liquid nitrogen. The filling of flasks should be done only in the presence of two persons. The window should be opened before beginning to work and the ventilation system should be switched on. A contact-switch at the door should have switched on the ventilation, but unfortunately the ventilation could be switched off by a separate switch. Important facts for the diagnosis were given by the anamnesis and the scene of death as the exposition to $N_2$. During resuscitation hemorrhagic pulmonary edema developed and blood gas analysis showed massive oxygen deficiency. Toxicological and further morphological investigations showed no other pathology alterations. The main findings for the diagnosis of asphyxia could be derived from the anamnesis, from the scene of death, the autopsy and the blood gas analysis with a low partial pressure of $O_2$ and a base exess of –24.4 mmol/l. As a result, the biochemical findings can be classified as vital effects and perhaps also the morphological alterations of the skin. Nevertheless, these and other morphological findings could not be clearly classified as vital effects.

According to the circumstances of death, the autopsy findings and the results of clinical and post mortem biochemistry the cause of death of the student was asphyxia or oxygen deficiency. The body froze after death by asphyxia had occurred.

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