A fatal suicidal sodium nitrite ingestion determined six days after death

Stefania Zerbo, Mario Spanò, Giuseppe Davide Albano, Roberto Buscemi, Ginevra Malta, Antonina Argo

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Authors information:

Stefania Zerbo [1]<stefania.zerbo@unipa.it>

Mario Spanò [1]<spano.mario94@gmail.com>
Giuseppe Davide Albano[1]<giuseppedavide.albano@unipa.it>,

RobertoBuscemi [1]<rbuscem@hotmail.com>
Ginevra Malta[1] <ginevra.malta@unipa.it>

Antonina Argo[1]<antonella.argo@unipa.it>

[1] Institute of Legal Medicine, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Section of Legal Medicine, University of Palermo, Palermo, Italy

Corresponding author:

Giuseppe Davide Albano giuseppedavide.albano@unipa.it

Institute of Legal Medicine, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, Section of Legal Medicine, University of Palermo, Palermo, Italy, Via del Vespro 129, 90100 Palermo, Italy

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Abstract:

Sodium nitrite (SN) is an inorganic salt that appears as a slightly yellowish crystalline solid, odorless, and highly soluble in water at room temperature. It is highly toxic to humans at specific doses because it can oxidize hemoglobin to methemoglobin, causing severe tissue hypoxia. A 20-year-old woman was unconscious in her bedroom and died shortly after that. Two days later, following the discovery of a jar of SN and a paper in which were written instructions on how to take it (and the website from which the procedure was learned) in the same room were death occurred, the Judicial Authority ordered the execution of the autopsy on the exhumed body of the young woman. The autopsy procedure was performed ~ 2h after exhumation. It showed greyish-purple hypostasis, labial cyanosis, stomach distension and greenish color but empty, subpleural petechiae, brownish fluid in the pleural cavities (~300 ml), congested and edematous lungs and diffuse visceral congestion. At autopsy, foamy liquid was observed at the lung section and subsequent squeezing. In addition, the autopsy showed edema and hemorrhagic petechiae of the laryngeal, glottal, and tracheal submucosa and green-brownish foamy liquid in the tracheal lumen. The cause of death was attributed tocardiac arrest induced by anoxia resulting from acute methemoglobinemia caused by sodium nitrite poisoning, intensified by severe malnutrition.. Manner of death was suicidal.

Keywords:
Forensic pathology; Sodium Nitrite; Methemoglobin; Suicide; Autopsy

1. Introduction

Sodium nitrite (SN, $NaNO_2$) is an odorless inorganic salt that appears as a slightly yellowish or white powder. $NaNO_2$ is very soluble in water, much more than sodium chloride ($NaNO_2$ solubility 820 g/L vs NaCl 358 g/L). It has multiple uses, but its best-known application is as a food additive. Nitrite additives are essential to prevent the growth of dangerous pathogenic microorganisms, such as *Clostridium botulinum*. They are widely used to fix and maintain the color of meat and its derivatives. In the human body, nitrites can also oxidize iron (Fe) in the hemoglobin haem group from ferrous (Fe +2) to ferric (Fe +3) state, producing methemoglobin (MetHb) [1, 2]. A certain physiological MetHb is constantly formed in normal subjects, but several endogenous systems keep the MetHb level at about 1%.[2] European Parliament has set the maximum concentration of nitrite in meat products at 150 mg/kg. [3] Therefore, dietary exposure to such small amount is considered harmless. However, if $NaNO_2$ is ingested in larger quantities, it causes a condition known as acute methemoglobinemia. In fact, iron oxidation from Fe + 2 to Fe + 3 renders MetHb unable to bind and transport oxygen, reducing the amount of O_2 that reaches the tissues, resulting in cellular hypoxia. In addition, since nitrite in the body is reduced to nitric oxide (NO), it acts as a potent vasodilator, leading to severe hypotension, further reducing oxygen supply to tissue, and exacerbating MetHb toxicity [1, 4]. Tissue damages are related to severity and persistence of oxygen deficiency and range from reduced ATP synthesis to cell death, causing organ damage up to death. The specific antidote is methylene blue [2]. The estimated lethal dose for humans is approximately 2.6 grams, although a fatal case after ingestion of 1 g [5] and a survival case after ingestion of 6 g [6] have been reported. In this case, the authors documented a distinctive case of fatal anoxia resulting from the ingestion of sodium nitrite six days after death, emphasizing the significance of conducting a thorough death scene investigation and adopting a multidisciplinary approach in cases involving suspected sodium nitrite poisoning within the field of forensic practice.

2. Case report

2.1 History

A severely underweight 20-year-old woman (height 157 cm, body weight ~35 kg; BMI ~14.20) was discovered unconscious in her bed at 8 pm by family members. Emergency services were immediately contacted, and upon their arrival at the scene at 8:11 pm, they found the young woman in cardiopulmonary arrest and displaying cyanosis. Despite their attempts to resuscitate her, they were unsuccessful, and her death was pronounced at 8:46 pm.

During the post-mortem inspection conducted at 11.45 pm, no traumatic injuries were identified, except for an acupuncture mark on the woman's left arm, which was the result of the administration of catecholamines during the resuscitation attempts.. External examination of the body at the scene revealed labial and subungual cyanosis, greyish-purple hypostasis distributed among suprascapular region, lumbar region and posterior surface of the lower limbs. Additionally, around nasal and oral orifices there was dried brownish-green liquid and from nasal cavities it was also visible in liquid form (fig. 1 A-B-C). Furthermore, the woman’s pants were wet in the genital area. She was found

lying on a tiled floor and wore thin t-shirt, sweatpants, and underpants. Rigor mortis was present in the jaw and absent in the remaining parts of the body that were examined. At 12:51 am ambient and rectal temperatures were respectively 22.7°C and 32.4°C. The evidence at the scene suggested a short post-mortem interval and it was estimated to be 3h 30 min ± 2h 30 min. From circumstantial data it emerged that the last time she was seen alive was at 7pm the same day in the house kitchen by her sister. The 20-year-old woman had been suffeering from anorexia, in fact she refused to take food or took it reluctantly for months, replacing meals with multivitamin supplements. She had also expressed suicidal thoughts to her family members about six months before her death. However, in this period there were no suicidal attempts on her part. In addition, on the same day she died, she formatted her cellphone.

Four plastic cups were discovered on the nightstand next to the bed where the body was found.Two of the cups were empty, while the other two contained a yellowish liquid (fig. 2 A). These liquid samples were collected for toxicological analysis. Nevertheless, at first the Judicial Authority decided not to proceed further with the investigations and gave the authorization to bury the deceased woman. Two days later, after the discovery of a jar of SN and a handwritten note containing instructions on how to consume it(along with the website from which the procedure was learned) (fig. 2 B) in the same room where the death occurred, the Judicial Authority ordered an autopsy to be performed on the exhumed body of the young woman.

2.2 Autopsy findings

Th exhumation took place on the sixth day after death (approximately 132-133 hourspostmortem). The autopsy procedure was conducted approximately2 hours after exhumation. The findings revealed greyish-purple hypostasis, labial cyanosis, stomach distension and greenish color but empty, subpleural petechiae, brownish fluid in the pleural cavities (~300 ml), congested and edematous lungs and diffuse visceral congestion. The right lung weighed 498 grams while left lung 371 grams. Furthermore, foamy liquid was observed at lung section and subsequent squeezing. In addition, autopsy showed edema and hemorrhagic petechiae of the laryngeal, glottal, and tracheal submucosa and green-brownish foamy liquid in the tracheal lumen (fig. 3 A-B-C). The heart was cone-shaped and weighed 217 grams. The longitudinal diameter from the apex to the crux cordis was 7.8 cm, and the transverse diameter at the atrioventricular sulcus was 9 cm. The myocardium of the right ventricle was 3 mm thick at the outflow tract, and the myocardium of the left ventricle was 10 mm wide. The coronary arteries showed no were free pathological changes, including stenosis. The liver weighed 800 grams and had slight putrefactive greenish tinges on the posterior surface. The kidneys weighed 207 grams and were pale in color; when cut, they showed normal cortico-medullary differentiation and poor representation of hilar fat. The spleen weighed 80 grams, was 9 x 5.5 x 2.2 cm, and had a smooth surface; the lower pole showed putrefactive greenish discoloration. When cut, the pulp was shiny and pinkish-red in color and partly affected by putrefactive phenomena. The bladder was empty. No other significant macroscopic or microscopic findings were identified, apart from post-mortem alterations (fig. 4).

2.4 Toxicological findings

Chemical analyses were conducted to detect nitrite on aqueous samples found at the scene. The initial analysis utilized the LCK341 kit (blue package) for the determination of nitrite in water

having a concentration between 0.05-2.00 mg/L NO2 of nitrite with the bench spectrophotometer DR 3900 from the company HACH.

In this case, an abnormal result was obtained, due to the high concentration of nitrite; hence, the analytical determination was carried out diluting the sample and by using the LCK342 kit (red pack) 2-20 mg / L NO2; a value of 555 g/L (below the solubility value of nitrite in water, but in any case, particularly high) was obtained.

Unfortunately, obtaining a reliable assessment of nitrite or nitrate levels in the blood was not possible due to the extended interval between death and autopsy, as well as the storage conditions of the body. In whole blood, nitrites rapidly convert into nitrates, resulting in a loss of approximately 95% of their original concentration within one hour at room temperature [7]. Determination of MetHb percentage, a reliable indicator of toxic effect of sodium nitrite, was performed using an AVOXimeter 4000 ITC oximeter, on a specimen of central blood collected during the autopsy. The MetHb concentration was 12.8%, about 10 times higher than reported normal values (1-1.5%); this value is comparable to that recorded in cases of fatal intoxication; in fact, a fatal case of accidental sodium nitrite poisoning with an MetHb level of 9.87% has been reported [8], although it was a case where death was attributed to the exacerbation of hypertensive and ischemic heart disease resulting from accidental sodium nitrite poisoning However, it is possible that the long post-mortem interval resulted in a reduction in MetHb levels due to both residual MetHb-reductase activity and post-mortem microbial activity as well it should be noted that a blood sample of poor quality due to delays and/or sample heating or putrefaction can cause optical artifacts for measurements such as CO-oximetry or spectrophotometry, leading to MetHb misestimations [9].

Further toxicological investigations targeting common drugs of abuse (opioids, benzodiazepines, cannabinoids, cocaine, and amphetamines) using immunoenzymatic techniques, yielded negative results.

In conclusion, the cause of death was determined as cardiac arrest induced by anoxia resulting from acute methemoglobinemia caused by sodium nitrite poisoning, intensified by severe malnutrition.. Manner of death was suicidal.

3. Discussion

Sodium nitrite is a potent oxidizing agent that induces hypotension and restricts oxygen transport and delivery in the body by forming methemoglobin. The complete oxidation of hemoglobin to MetHb results in a 4-electron loss because it is a tetrameric molecule. As hemoglobin has four subunits (alfa2beta2) and two iron valences (Fe 2+ and Fe 3+), there can be up to 8 distinct dimers, so eight different states can exist. Under conditions of oxidative stress, partial oxidation of individual subunits prevails. These hybrid valence forms have a stronger affinity for oxygen and shift the oxygen dissociation curve to the left. So, in addition to functional anemia, produced by MetHb's inability to bind oxygen, as described in the introduction, methemoglobinemia causes the remaining oxygen-binding sites on the hemoglobin tetramer to have an increased affinity for oxygen, further reducing oxygen delivery to tissues and exacerbating cellular hypoxia[10]. Clinical symptoms of sodium nitrite poisoning include cyanosis, hypoxia, altered consciousness, dysrhythmias, and death.

The manifestation of cyanosis becomes evident when methemoglobinemia affects about 10% of the blood cells reds. If it affects more than 20%, others appear symptoms: headache, dizziness, polypnea, tachycardia and general asthenia. With close values at 60% serious disorders can occur as a loss of consciousness and, with values higher than 70%, if the intoxication is not treated quickly becomes deadly. All these symptoms are likely more severe in patients with comorbidities such as anemia, heart disease, or G6PD deficiency [10]. Subjects with anemia may experience more severe symptoms for a given percentage of MetHb as anemia may further limit O2 delivery exacerbating signs of methemoglobinemia. Furthermore,considering that sodium nitrite poisoning is characterized by significant vasodilation leading to severe hypotension, the presence of anemia may exacerbate cellular hypoxia. In our case, MetHb concentration was 12.8%, which alone may not be fatal. Additionally, many works and textbooks describe post-mortem hypostases in cases of methemoglobinemia (including sodium nitrite poisoning) as brownish or chocolate-brown. However, in our case, hypostases were regular greyish-purple. Therefore, we can excludepure acute methemoglobinemia as the cause of death due to anoxia. .

The 20-year-old woman suffered from anorexia, which was associated with numerous disorders and dysfunctions directly related to weight loss and caloric restriction. These disorders include cardiovascular system diseases like hypotension, bradycardia, and arrhythmias; hematological system diseases like anemia; hydro-electrolyte alterations and acid-base balance impairment; there may also be alterations of endocrine, gastrointestinal, renal, nervous, and immune systems [11, 12]. The deceased 20-year-old woman had a BMI of ~14.20, and she refused to take food or took it reluctantly for months replacing meals with multivitamin supplements. In this setting, it is highly probably that at least anemia developed. In conclusion, the cause of death was attributed to cardiac arrest induced by anoxia resulting from acute methemoglobinemia caused by sodium nitrite poisoning, intensified by severe malnutrition.

Deaths by ingestion of sodium nitrite are not common. However, accidental sodium nitrite poisoning has been reported, particularly among infants who consume well water with high nitrate levels [13]. A few persons experienced weakness, nausea, numbness, shortness of breath, tachycardia, and cyanosis after accidentally ingesting sodium nitrite; 32-78% methemoglobin levels were noted in 9 adults [14-17].

Recently, the incidence of intentional $NaNO_2$ poisoning has increased, especially among young adults, and this phenomenon is a major cause of concern. This practice has substantially increased in the USA [18, 19, 20], Canada [21], South Korea [22, 23], Australia [24], and Europe [25 – 28], where several cases have been recorded in recent years.

In June 2021, the Rome prosecutor's office blocked access from Italy to the website from which some young Italians learned information about suicide with$NaNO_2$ [29]. It seems that this suicide method is growing in popularity thanks to websites and online forums that encourage it, also offering real "consultations" via private chats and providing very precise information on how and how much SN to take, as well as information on anti-emetic drugs to prevent vomiting, which is a side effect of $NaNO_2$ ingestion. In addition, SN is readily available on internet from many e-commerce where it can be bought in the order of kilos.

It is challenging to predict whether the incidence of this suicidal method will continue to increase in the future. However, it is crucial for forensic experts to recognize warning signs during post-mortem examinations, such as the absence of traumatic injuries associated with general signs of asphyxiated death, the color of hypostasis, and other circumstantial evidence. Furthermore, it is

essential to promptly collect blood samples for determining nitrite, nitrate, and methemoglobin levels to prevent the rapid conversion of nitrites to nitrates, which may alter the results.

In our case the autopsy revealed generic signs of asphyxiated death. The cause of death was attributed to cardiac arrest induced by anoxia due to acute methemoglobinemia caused by sodium nitrite poisoning, potentiated by severe malnutrition, based on crime scene data, histological and toxicological findings. In this case the MetHb concentration was 12.8%. Although it was not possible to obtain reliable assessments of nitrite levels in the blood due to the extended interval between death and autopsy, recent knowledge suggests the use of alternative biological samples, such as costal cartilage and vitreous humor, for toxicological analysis when blood is unavailable or in cases of exhumation [30].

4. Conclusion

The cause of death was attributed to cardiac arrest induced by anoxia resulting from acute methemoglobinemia caused by sodium nitrite poisoning, intensified by severe malnutrition. Manner of death was suicidal. The case report underlines that data and evidence deriving from death scene investigation, autopsy findings, and laboratory examinations are needed to obtain a plausible diagnosis of cause of death, even after body exhumation.

Figure legends (color should be used for all figures in print):

Fig. 1. External examination findings at the death scene. Labial cyanosis (1A); subungueal cyanosis (1 B); greyish-purple hypostasis (1 C).

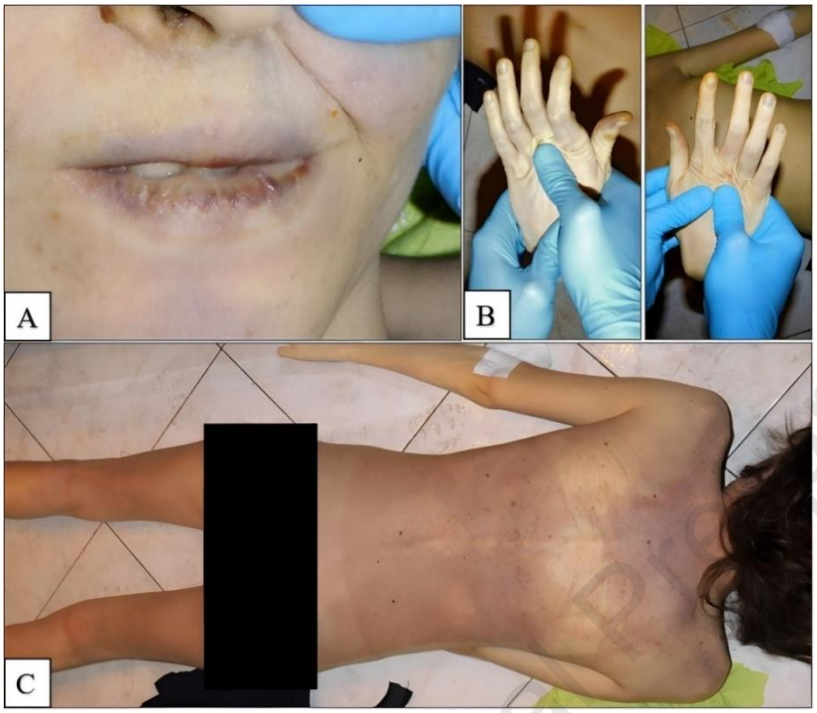


Fig. 2. Plastic cups in the nightstand next to the bed at the death scene (2 A); handwritten paper with instructions (2 B): "*SN = sanctioned.suicide.org FORUM / SN + 50 ml (1/4 of a plastic cup of water) / Sodium Nitrite = 20 grams (kitchen scale) / Metoclopramide (plasil) = 35 mg (45 minutes before drinking SN) / If you understand that you are vomiting too much SN, take the second dose of SN + prepare + doses of SN 3 cups) / (the substance must be completely dissolved) / If you fail there is an antidote*".

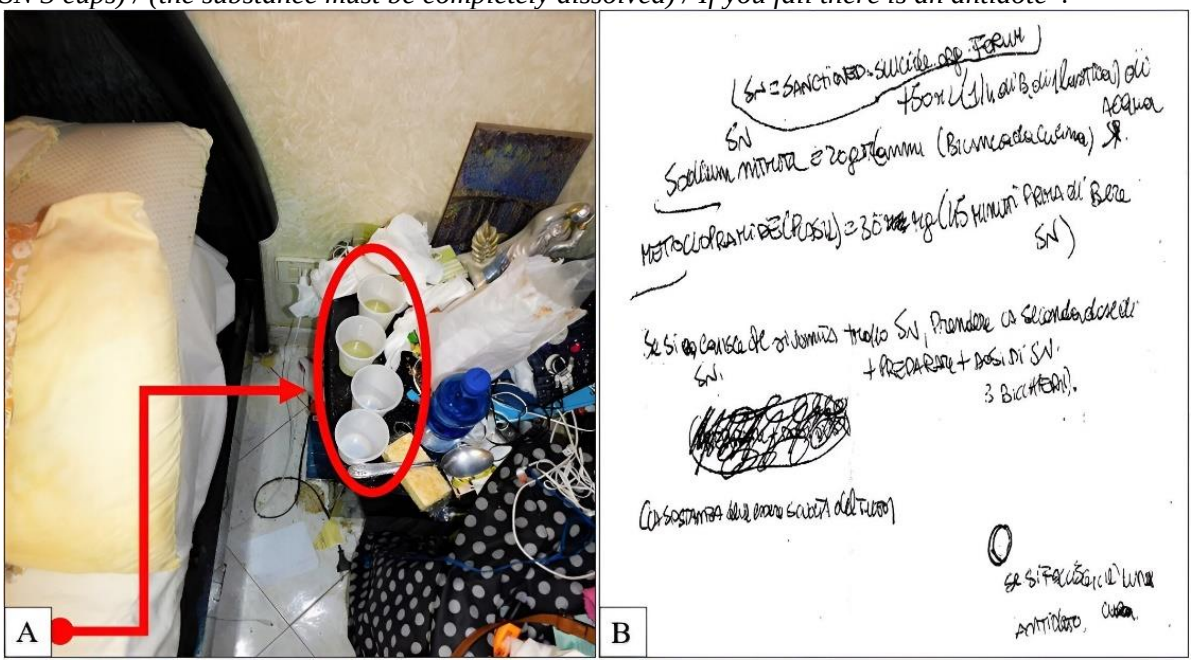


Fig. 3. Autopsy findings. Subpleural petechiae (3 A); hemorrhagic petechiae of the laryngeal, glottal, and tracheal submucosa, with foam and green liquid (3 B). Stasis, red liquid and foam coming out after lung compression (C).

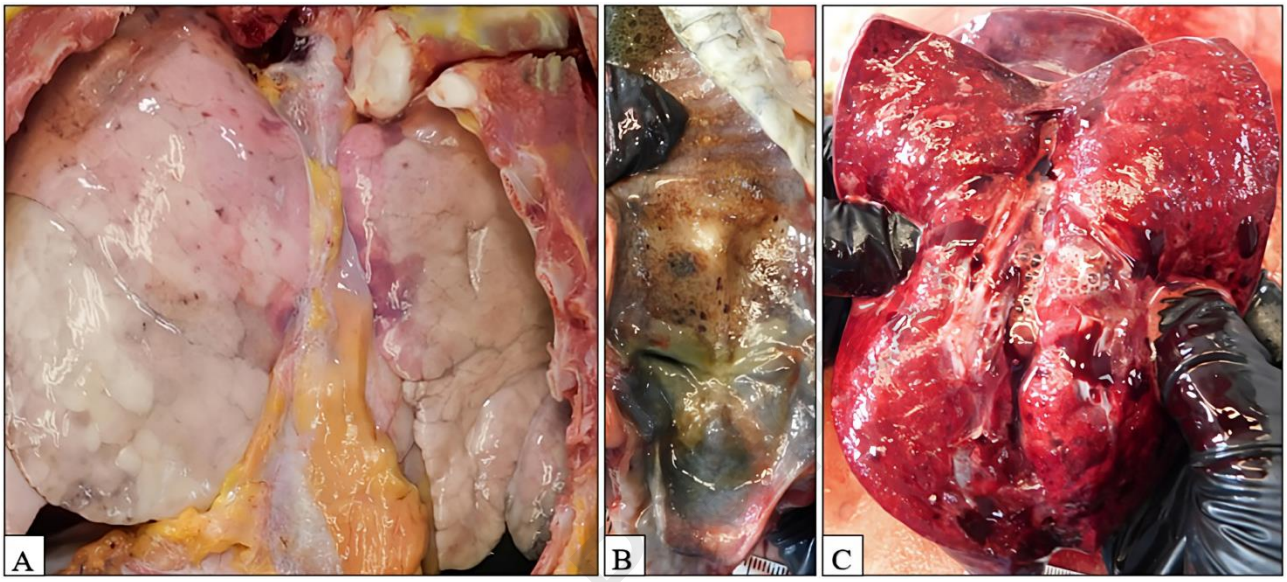
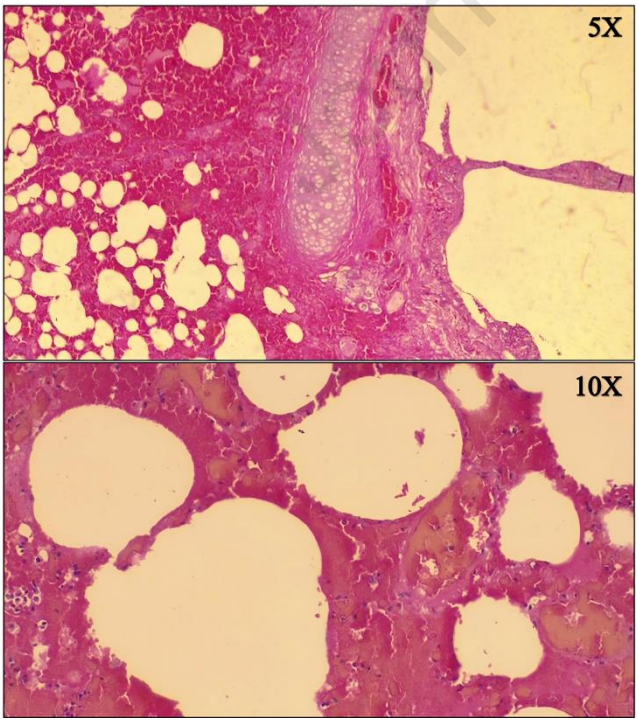


Fig. 4. Lung, 5x and 10x "Swiss cheese" appearance of lungs due to post-mortem changes.



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Highlights:

- Suicide with sodium nitrite is a growing phenomenon.
- Operating instructions for dilution of the toxicant were found at the scene.
- Autopsy investigations in these cases show general signs of asphyxiated death.
- Blood sample should be conducted in a timely manner to prevent alterations.

Conflict of interest statement:

The authors declare no conflict of interest as there's no financial/personal interest or belief that could affect their objectivity.