A young woman who drank Strep test reagents

A woman in her 20s was brought to the casualty clinic due to symptoms of psychosis, and it was deemed necessary to section her. While she was there, she drank two small bottles of reagents that she found in a Strep test kit. She then became somnolent and her oxygen saturation decreased. Guidance from the Poisons Information Centre was required for rapid clarification and correct treatment.

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A woman in her 20s arrived at the casualty clinic by ambulance after having jumped into the sea. Her clothes were wet, she was in a miserable state and was behaving oddly with symptoms that raised suspicion of psychosis. She stated that she had jumped into the sea on impulse, and denied suicidal intent. She explained that she had made the decision to jump just seconds in advance. She stated that she was glad to have been rescued from the sea and to be receiving help. Upon conferring with a psychiatrist, it emerged that she had previously had weekly sessions with a psychologist. She was not on any medication. The day before she had drunk alcohol and smoked marijuana, but her use of intoxicants was not explored further at this time.

On examination, she had a regular pulse of 79 beats per minute, tympanic temperature 36.4 °C, peripheral capillary oxygen saturation 100 % in room air and blood glucose level of 6.2 mmol/l (4.0–8.0 mmol/l). Her skin was dry and warm, and her breathing normal. Her pupils were equal, of normal size with normal reactions to light. She had no outward signs of head injury or injury elsewhere, normal strength in her arms and legs, and symmetrical movements of the extremities.

Following the clinical examination and psychiatric assessment, a decision was made to admit her to the psychiatric department for compulsory observation on suspicion of substance-induced psychosis. There was a wait for the ambulance, and in the meantime she was checked frequently by both a nurse and a doctor. During the wait she was restless and dismantled medical equipment in the examination room.

The patient was regarded as psychotic, but not suicidal. She was, however, considered a danger to herself due to her dramatic impulsive act and continued restlessness, and admission to the psychiatric ward was deemed necessary. An attempt to get the patient to consent to voluntary admission failed, and a decision was therefore made to admit the patient for compulsory observation (Section 3–2 of the Mental Health Care Act).

Immediately prior to departure from the casualty clinic, members of staff found empty bottles of Strep test reagents on the floor on the examination room, and the patient confirmed that she had drunk their contents. How much had been left in the bottles beforehand was unknown, thus it was unclear how much she had consumed.

The Strep test reagents, which are used to detect streptococcal pharyngitis (Fig. 1), were on a trolley in the examination room, as part of the standard equipment in most examination rooms in the casualty clinic. The patient had drunk bottles containing 2 M sodium nitrite and 0.2 M acetic acid.

The patient had been checked frequently, but was not under continuous observation. It is difficult to predict which patients will harm themselves. Personnel are a scarce resource, and in the casualty clinic there are often many competing demands. Although this patient was to be sectioned, frequent checks were seen as a sufficient degree of observation, which unfortunately turned out not to be the case.

The Poisons Information Centre was contacted immediately and, based on information on the reagents' toxicity, it was decided to admit the patient to the local hospital for observation. Upon departure from the casualty clinic, she was awake with stable respiration and circulation.

The journey time to the hospital was short, and she arrived at Acute Admissions about 45 minutes after ingesting the reagents. Upon arrival, information from the casualty clinic was not available, and the receiving doctor therefore did not know what type of reagent the patient had drunk. During the clinical examination her Glasgow Coma Scale (GCS) score was 15 and she was cooperative. She had cyanosis of the lips, but an otherwise normal skin colour. Her extremities were cold peripherally but without signs of cyano-

sis. Mild facial oedema was observed. Blood pressure was 112/56, she had a regular pulse of 90/min, respiratory rate 18/min and SaO_2 was 82 % without supplemental oxygen. Clinical status, ECG and preliminary blood tests were otherwise normal. Arterial blood gas showed pO_2 11.1 kPa (10.0–14.0 kPa), pCO_2 4.6 kPa (4.7–6.0 kPa) and bicarbonate 25 mmol/l (22–26 mmol/l). Due to unexplained cyanosis, restlessness, signs of psychosis and poisoning by a substance of unknown identity there and then, the patient was transferred to the Intensive Care Unit for further observation. Prior to the transfer, she was given olanzapine 10 mg orally. Olanzapine was chosen as a sedative due to its antipsychotic efficacy.

In Intensive Care, a nurse took a further arterial blood gas sample and noted that the blood had a dark brownish colour prior to the analysis (Fig. 2). The patient was by then lying down receiving 4 litres of oxygen via nasal catheter, pO_2 was 22.4 kPa, pCO_2 5.4 kPa, bicarbonate 27.5 mmol/l, lactate 0.8 mmol/l (0.5–1.4 mmol/l), and electrolytes were normal (Table 1). There was a discrepancy between peripheral oxygen saturation (SaO_2) of 79–83 % and arterial pO_2 of 22.4 kPa. By the next assessment an hour later, information from the casualty clinic had been obtained, and methaemoglobinaemia was suspected due to «chocolate-coloured» blood and nitrite ingestion. Methaemoglobin level was 22 % (reference range < 1.0 %), and the patient was becoming increasingly somnolent. The Poisons Information Centre was contacted again to clarify the indication for treatment and level of monitoring required, and on the advice of the duty medical officer there, it was agreed to transfer the patient to the regional hospital to consider antidote therapy.

Nitrite poisoning is rare but can lead to methaemoglobinaemia with subsequent cyanosis and failure of oxygen transport. SaO_2 is usually low, while arterial blood gas analysis shows almost normal pO_2; at the same time, the blood has a brownish-blue colour («chocolate cyanosis») which is most apparent in the lips and mucous membranes (1, 2). Some of the pO_2 levels measured in our patient were above the reference value, but this was due to supplemental oxygen.

Upon arrival at the hospital, she was somnolent, had a steady pulse of 64, blood pressure 99/58 mm Hg, respiratory rate of 18 and SaO_2 of 94 % with 15 litres of O_2 via a mask. The patient was admitted to the Intensive Care Unit. Arterial blood gases now showed pO_2 63.8, SaO_2 99.8 % and methaemoglobin 17 %. Haemoglobin was 12.0 g/dl (11.7–15.3 g/dl), electrolytes were normal and glucose was 9.3 (Table 1). Blood tests otherwise showed white blood cells 6.0 (3.5–10.0), neutrophil granulocytes 2.5 (1.5–7.3), normal creatinine, normal liver function and negative CRP. ECG was normal.

Figure 1 *Bottles of Strep test reagents. The bottle on the left, with the poison symbol, contains sodium nitrite*

As the methaemoglobin level was no higher than 17 %, antidote therapy was not initiated right away. The recommended threshold for treatment is 25–30 % (1, 2). The patient was monitored, arterial blood gases were analysed repeatedly, and she received supplemental oxygen.

Three hours after admission her methaemoglobin level had fallen to 8 %, and by the next day it had normalised. She was then assessed by a psychiatrist and admitted to the psychiatric ward.

Discussion

Haemoglobin consists of four polypeptide chains, each with its own haem molecule. Each haem molecule contains a central iron atom which binds oxygen. In normal haemoglobin, the iron is thought to exist in its divalent form, Fe^{2+}. Methaemoglobin is an oxidised form of haemoglobin in which the iron is oxidised from Fe^{2+} to Fe^{3+} (Fig. 3). Methaemoglobin cannot transport oxygen and is dark brown in colour (1, 2).

Methaemoglobinaemia involves a reduction in the ability of erythrocytes to transport oxygen, giving rise to tissue hypoxia and cyanosis that is refractory to oxygen therapy. The normal level of methaemoglobin in human blood is less than 1 %, and a clinically significant reduction in oxygen transport occurs at levels of 10 % or above. Symptoms of methaemoglobinaemia are cyanosis, drowsiness, lethargy, muscular weakness, ataxia, dyspnoea, tachycardia, nausea and vomiting. The blood turns brownish-blue, giving rise to so-called chocolate

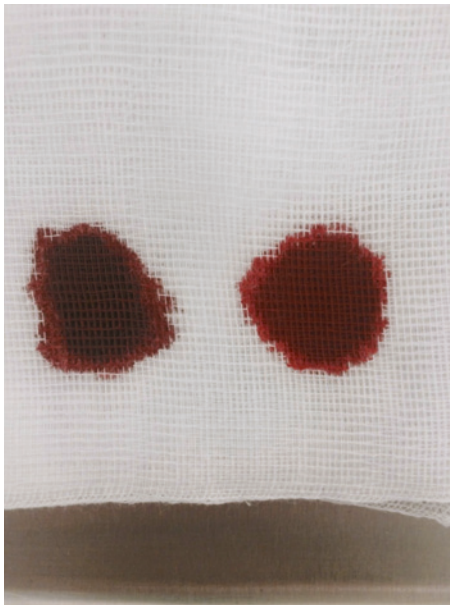

Figure 2 *Brown blood. Patient's arterial blood on the left. Treating doctor's arterial blood on the right*

cyanosis. The urine may become brownish-black and proteinuria is common. If levels increase to over 30–40 %, more serious phenomena such as CNS depression, unconsciousness and cardiac arrhythmias occur. Methaemoglobin levels above about 70 % are assumed to be fatal (1, 2).

In methaemoglobinaemia there is often a discrepancy between pO_2 and SaO_2. Arterial blood gas analysis shows approximately normal pO_2, whereas peripheral capillary oxygen saturation (SaO_2) falls. The pO_2 value reveals the amount of oxygen dissolved in the plasma component of the blood, i.e. the partial pressure of oxygen in the plasma. It is influenced by several factors: the oxygen content of inhaled air, the diffusion of oxygen from the alveoli to the capillary blood, and the shunt fraction, i.e. the proportion of the cardiac output that is not oxygenated upon passage through the lungs. SaO_2, or oxygen saturation, is expressed as a percentage and is the proportion of haemoglobin available for oxygen transport that actually binds oxygen. Measurement of SaO_2 with pulse oximetry is spectrophotometric and is based on the ratio of oxyhaemoglobin to deoxyhaemoglobin in the blood. The extent to which methaemoglobin influences this measurement varies between different models of pulse oximeter, but in general SaO_2 falls as the methaemoglobin level rises (2, 3).

Methaemoglobinaemia may be congenital, as a consequence of enzyme defects, or caused by ingestion of toxic agents, such as nitrates, nitrites, methanol, aniline, dapsone and some local anaesthetics (1, 2).

Nitrites are powerful oxidising agents and are among the most common causes of methaemoglobin formation. Exposure to nitrite occurs mainly via endogenous conversion of nitrate. Nitrate itself is relatively non-toxic, but concerns have been raised over the nitrate metabolites nitrite, nitrogen monoxide (NO) and N-nitroso compounds. Human exposure to nitrate is mainly through ingestion via vegetables or contaminated well water, and a certain amount is also produced by the body itself (2). The few human studies of nitrate exposure that exist have not shown methaemoglobinaemia after ingestion of nitrate alone (4). The nitrate concentrations normally found in food and water are considered unlikely to induce methaemoglobinaemia (5, 6).

A number of volatile nitrites are used as intoxicants and aphrodisiacs, often under the name «poppers». There have been several reported cases of severe methaemoglobinaemia following ingestion of volatile nitrites (7).

Most methaemoglobinaemias are mild and do not require specific treatment once the triggering agent has been removed. Supplemental oxygen is recommended, even though the ability of erythrocytes to make use of this is reduced. Methylene blue is used as an antidote and is recommended with methaemoglobin levels above 25–30 % or severe symptoms. The recommended dosage is 1–2 mg/kg (1, 2). Methylene blue has a rapid onset of action, but a short half-life, and repeated dosing may be necessary. Methylene blue works by acting as a cofactor that increases the rate of reaction of enzyme systems responsible for reducing the methaemoglobin formed inside cells (1, 2). In our patient the maximum methaemoglobin level detected was 22 %. She recovered well with no treatment other than supplemental oxygen.

The reagent in the Strep test kit contained sodium nitrite. The label states that the reagent is toxic if swallowed, highly corrosive and should be kept locked away and out of reach of children. This case report shows that the Strep test reagent contains enough sodium nitrite to cause significant methaemoglobinaemia. In the wake of this incident, the casualty clinic in question has reviewed its procedures for storing the Strep test kit.

Table 1 Summary of patient's blood gas values after ingestion of Strep test reagents

	Reference values[1]	1 hour	2 hours	5 hours	8 hours
Supplemental O_2 (l)		Unknown	4	15	Unknown
pH	7.35–7.45	Unknown	Unknown	7.46	7.40
SpO_2 (%)	94–99	82	79–83	99	99
PO_2 (kPa)	10–14	11.1	22.4	63.8	29.8
PCO_2 (kPa)	4.7–6.0	4.6	5.4	5.0	5.9
Bicarbonate (mmol/l)	22–26	25.0	27.5	26.2	26.6
Lactate (mmol/l)	0.5–1.4	Unknown	0.8	1.1	0.7
Base excess (mmol/l)	–3–3	Unknown	Unknown	2.4	1.7
Methaemoglobin (%)	<1.0	Unknown	22	17	8

[1] Reference values taken from the «Blue Book», *www.uus.no/labus/* (26.10. 2015).

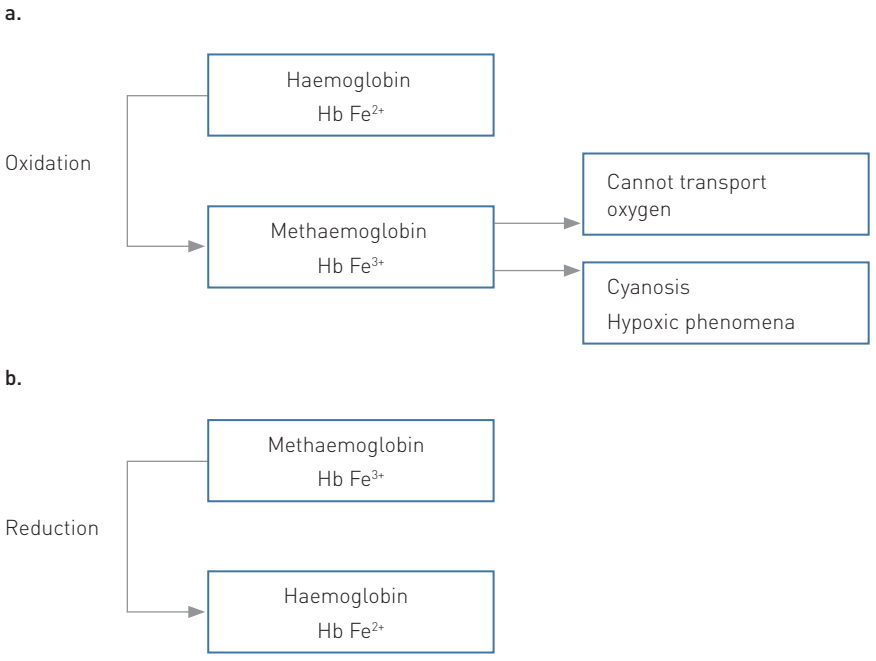

Figure 3 *a. In normal haemoglobin, iron is thought to be in its divalent form (Fe^{2+}). The oxidised form of haemoglobin is called methaemoglobin and cannot transport either O_2 or CO_2. Nitrites are powerful oxidising agents and are one of the most frequent causes of methaemoglobinaemia (1, 2). b. Enzyme systems inside cells reduce methaemoglobin as soon as it forms. Methylene blue can act as a cofactor (1, 2)*

When the patient first arrived at the Acute Admissions section of the local hospital, the receiving doctor had no information about what kind of substance the patient had ingested in the casualty clinic. The paramedics received an admission note from the casualty clinic, but this somehow disappeared during the patient transfer. The paramedics reported verbally that the patient had ingested a reagent in the casualty clinic which meant that she required observation in hospital. The doctor in the casualty clinic did inform the duty medical officer about the nature of the poison, but this information did not reach the receiving doctor straight away because of a busy Acute Admissions. Since the patient was stable, the casualty clinic was contacted and asked to send the admission note again, and it was eventually received by fax. There is always a risk that important information can disappear or become distorted when passed along many links in a chain, and our case report is an example of this. There were no consequences for the patient, but the situation could have been dangerous had the poisoning been more severe.

The patient has consented to the publication of this article.

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Received 12 February 2015, first revision submitted 29 June 2015, accepted 26 September 2015. Editor: Lise Mørkved Helsingen.