

Methaemoglobinaemia following ingestion of a commonly available food additive

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Five cases of methaemoglobinaemia after ingestion of sodium nitrite occurred in two clusters in Sydney in 2006. All cases were unintentional poisonings following use in cooking of an imported compound sold as a food additive. In all cases, methaemoglobinaemia was recognised early and treated promptly, with all patients making a full recovery. These cases highlight the importance of accurate food labelling and surveillance of imported goods. (MJA 2008; 188: 156-158)

Clinical record

In 2006, at Liverpool Hospital in Sydney, two separate clusters of patients presented to the emergency department with cyanosis after consuming home-prepared food to which sodium nitrite had been added.

In the first cluster, a husband and wife of Vietnamese–Chinese origin developed cyanosis and dyspnoea after consuming homemade rice cakes containing “Nutre Powder” and “Borax Powder”, which were commonly available from local Asian food stores in the area. Both patients arrived by ambulance and, despite oxygen therapy, remained cyanotic. Their blood samples had a distinctive chocolate brown appearance, and laboratory testing confirmed methaemoglobinaemia. The husband, who was the more unwell, had a measured methaemoglobin level of 57%. After treatment with intravenous methylene blue, his condition rapidly improved. The wife, who had a methaemoglobin level of 21%, was treated supportively with oxygen and monitored closely. Both patients were admitted to the intensive care unit for a brief period of observation before being transferred to the haematology unit. Their subsequent progress was uneventful, and both patients were discharged from hospital 2 days later.

On request from medical staff, the couple brought into the hospital the two packets used, both containing whitish powder. The first was labelled “Goldfish” brand “Borax” and the second, “Goldfish” brand “Nutre Powder” (Box). No further information about the contents was printed on the packaging. The packets were imported through a specialty Asian food distributor based in Melbourne, and the wife claimed they were commonly available food additives. She had used both ingredients in the meal she prepared that evening from a recipe given to her by her mother. She also claimed her mother had previously used the products in China without incident. Neither patient knew the composition of the products, and questioning of the product's importer by the medical team yielded no further information.

Two weeks later, a second cluster of three new cases, involving a Vietnamese family unrelated to the index cases, presented to Liverpool

A packet of “Goldfish” brand “Nutre Powder”



Hospital emergency department with identical symptoms after eating a pork dish prepared using an unidentified white powder. Laboratory testing again confirmed methaemoglobinaemia, with levels ranging from 39% to 51%. Intravenous methylene blue was administered, leading to rapid clinical improvement. All three patients made uneventful recoveries after being observed in the emergency department overnight and were released from hospital the next day.

In both clusters, the onset of initial symptoms, such as vomiting, shortness of breath and dizziness, was dramatic, within minutes of consuming the contaminated food preparations. In the second cluster, two family members who had eaten the contaminated pork dish noticed the symptoms just after leaving home. They called back to warn the others that the food might be contaminated, but the others had already consumed the dish as well. A fourth person in that cluster also became ill, but had much less severe symptoms, having eaten only a small amount. She was seen by paramedics but not transported to hospital with the others. On review by her local doctor the next day, she had made a full recovery.

Investigation by the New South Wales Food Authority and staff of the Public Health Unit of Sydney South West Area Health Service found that identical Goldfish brand Nutre Powder had been used in food consumed by the patients in the second cluster, reportedly as a flavour enhancer. The packages were purchased from separate local retailers. Importantly, this group was found not to have been exposed to any other known causes of methaemoglobinaemia. Residual Nutre Powder from both clusters and Borax Powder from the first cluster were submitted to the Division of Analytical Laboratories in Lidcombe, Sydney, for testing. Those labelled Nutre Powder contained 100% sodium nitrite, while the packet labelled Borax contained 100% sodium tetraborate.

On the day that laboratory results on the additives used by the first cluster patients became available, NSW Health alerted hospital emergency departments and the public to the risk of methaemoglobinaemia associated with ingestion of Nutre Powder. As Goldfish brand Nutre Powder was imported via Victoria, the Victorian Department of

Human Services initiated a national recall after the discovery of nutritional information on some packets of the products, implying that they were intended for human consumption. The Borax packets and two other packets labelled “Natural Powder” and “Natural Baking Powder”, which were also found to contain sodium nitrite, were recalled as well.

Nevertheless, packets labelled Nutre Powder were found for sale in Asian grocery stores in NSW several months after the national recall, and the proprietors denied any knowledge about the product being potentially harmful or illegal for sale as a food additive. They were directed to the NSW Food Authority and have since stopped selling these products.

Discussion

Methaemoglobinaemia is a potentially fatal condition in which native haemoglobin loses its ability to carry oxygen due to oxidation of the ferrous iron component of the haem molecule to the ferric state. Ferric forms of the haem molecule are unable to bind oxygen, and the oxygen affinity of accompanying ferrous haems in the haemoglobin tetramer is increased. As a result, the oxygen dissociation curve is “left shifted”, and oxygen delivery to the tissues is impaired.¹ Ferric forms of the haem molecule are generated physiologically by deoxygenation, but are kept at low levels by endogenous haemoglobin reduction mechanisms, so that blood concentrations of methaemoglobin do not normally exceed 1%–2%.²

Hereditary causes of methaemoglobinaemia are well described but rare.³ Most reported cases arise from exposure to an oxidising agent, including those containing nitrites. Symptoms include nausea, vomiting, lethargy, shortness of breath, obtundation and coma. Patients typically present with profound cyanosis and have a deeply greyish-blue appearance. Blood samples from affected individuals often have a characteristic chocolate brown colour. The degree of oxygen desaturation varies with the degree of methaemoglobinaemia, but may not correlate well clinically and therefore is not necessarily a reliable predictor of outcome. Pulse oximetry readings of oxygen saturation are generally inaccurate, and arterial blood gas measurements frequently show normal dissolved oxygen and carbon dioxide tensions with falsely elevated oxygen saturations.⁴ The observed cyanosis is refractory to standard oxygen therapy.

Despite this, management of methaemoglobinaemia comprises both supportive measures, such as oxygen therapy, and intravenous methylene blue administration in moderate to severe cases. Methylene blue is reduced by the action of a normally minor enzyme pathway involving reduced nicotinamide adenine dinucleotide phosphate (NADPH) — methaemoglobin reductase. The reduced form of methylene blue, leukomethylene blue, can then go on to reduce methaemoglobin to haemoglobin.^{5,6} Methylene blue (2 mg/kg body-weight as a 1% solution) is administered to patients with methaemoglobin levels exceeding 25%–30% and to patients with underlying anaemia or cardiac or respiratory disease, in whom tissue oxygen delivery might already be impaired. While methylene blue is generally well tolerated, it must be administered with caution to people with severe renal impairment and is relatively contraindicated in those with glucose-6-phosphate dehydrogenase (G6PD) deficiency, as it may lead to profound oxidative haemolysis in these individuals without lowering methaemoglobin levels, and, indeed, has been reported to cause methaemoglobinaemia itself.⁷

Of interest, follow-up of one of the patients who was given methylene blue demonstrated G6PD deficiency, although no adverse effects were seen clinically. G6PD deficiency is more common in

South-East Asian populations, where it is believed to offer some protection against malaria.⁸ Thus, although an effective antidote for nitrite-induced methaemoglobinaemia exists, it is not without risk, which can present a management dilemma in an emergency setting where rapid assessment for G6PD deficiency is not available. Rapid administration of methylene blue has also been associated with local pain and tissue necrosis.⁹

While sodium tetraborate is used as a food additive in some countries — particularly in noodles, where it is believed to improve colour, texture and flavour — this use is prohibited in Australia. Though potentially fatal in large doses, it is not known to cause methaemoglobinaemia.^{10,11} Nitrites, on the other hand, are a well known cause of methaemoglobinaemia, although the mechanism underlying this process has recently been disputed.¹² Numerous cases have been reported worldwide, most commonly associated with drinking contaminated water^{6,13} or ingestion of meat products in which nitrite compounds have been used as a preservative.^{14,15} Both sodium and potassium nitrite are permitted for use in Australia in the preparation of processed meat, poultry and game products, where they are used both as a preservative and to improve appearance. However, their sale is prohibited for use in home cooking.¹⁶ Fortunately, in the cases reported here, all patients promptly sought medical attention, and there were no deaths or persistent adverse outcomes.

The cases we report here highlight the need for accurate labelling of all potential food products and surveillance of these products to ensure that imported goods meet local standards. Overall, the recall delivered an effective and rapid response, with national media coverage (including community media in local spoken languages) and the alerting of hospital emergency departments. However, the cases also highlight potential problems in putting these measures into practice. Unlabelled or inappropriately labelled goods are able to slip into Australia undetected if they are not specifically imported as food additives. The Australian Quarantine and Inspection Service works with Food Standards Australia New Zealand on a national level, and the responsibility for products released into the marketplace passes to state and territory authorities. If improperly labelled goods have entered the country undetected and been locally distributed, coordination of their recall is complex, requiring cooperation of numerous parties across levels of government as well as bridging communication and cultural barriers.

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Competing interests

None identified.

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