

SEVEN CASES OF POISONING BY SODIUM NITRITE*

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With the ready availability of sodium nitrite, it is surprising that cases of poisoning caused by the ingestion of this salt in food are uncommon occurrences. Sodium nitrite is manufactured chiefly for its use in the dye industry. It is also employed as an anti-corrosive in anti-freeze mixtures and used as a counter against rust when surgical instruments are sterilized. It is used either alone or mixed with saltpetre (sodium nitrate) in the curing of meat, to bring out the red colour and as a preservative. In South Africa, the Food, Drugs and Disinfectants Act No. 13 of 1929, as amended, permits the use of nitrites in the curing of meat provided the end product contains not more than 200 parts per million (ppm) calculated as sodium nitrite. The same 'maximum permissible amount' is laid down in the USA by the Bureau of Animal Industry of the Department of Agriculture. Heat used in cooking destroys nitrites, but this cannot be depended on since the amount destroyed varies with the degree of heat and the length of cooking. Sodium nitrate is more commonly used in curing than is sodium nitrite. While saltpetre (*US Pharmacopeia*) is 99.5% pure, commercial saltpetre frequently has a large admixture of sodium nitrate.

Meat curing was a process originally aimed at the preservation of meat without refrigeration. Its primary feature was the addition of salt to the meat, but through the centuries variations have been introduced and combinations have been made with other processes so that today a cured-meat product may not only be salted, but also smoked and/or dried; sugar-cured; treated with sodium nitrite and/or sodium nitrate in order to 'fix' the colour, i.e. render the colour heat-stable; or spiced and aged to improve flavour. The ready availability of refrigeration today has reduced the need for meat preservation with salt.

Basically there are two types of curing processes. The first involves the addition of the curing agents in the dry state and the second in the form of a brine. The curing agents customarily used are: salt, sugar, sodium nitrate, sodium nitrite, and vinegar. Salt is primarily a flavouring agent, but is also a preservative. Sugar is largely added for its flavour, though not exclusively. As already stated, the nitrite and nitrate of sodium are colour-fixation agents, though the nitrate is also bacteriostatic. This colour-fixation enables cured meats to retain their redness after cooking.

Sodium and potassium nitrate were the first colour-fixation agents used. Later, when it was realized that the nitrates were merely sources of nitrites, the direct use

of nitrites was permitted. Many contend that the best results in curing meat are achieved by a combination of the two curing agents.

CASE REPORTS

At 1.30 p.m. on Sunday 21 May 1961, a White family, consisting of the father aged 31, the mother aged 29, a male child aged 14 months and a female child aged 5 years, together with 2 adult females and 1 adult male who were visiting their household, partook of a meal consisting of cocktail sausages, cheese pancakes, potatoes in their jackets, bread and butter, and tea with milk. The only item which was consumed by all 7 was the sausages.

Case 1—G.F., female child aged 5 years. Within 30 minutes of her meal, which consisted of 4 sausages and potato, the child complained of severe headache and palpitations. Examination revealed an alert child who was well orientated and lucid. She was, however, rather unsteady on her feet and wanted to lie down. There was no vomiting or diarrhoea, but she had some nausea. As the examination proceeded, however, she became drowsy and tended to fall asleep. A striking feature was the marked tachycardia, the heart rate being 170 a minute, while the pulse was of good volume and the blood pressure was 100/60 mm. Hg. While she was being transferred to a nursing home, cyanosis of the lips and mucous membranes became evident, but there was no respiratory distress. No adventitious lung sounds were detected. Drowsiness increased, but a good response to supra-orbital pressure remained. Gastric lavage yielded large quantities of undigested and partially digested sausage. Treatment was continued in an oxygen tent. Thereafter the child's condition improved considerably—drowsiness disappeared fairly soon and the cyanosis vanished after about 2 hours' stay in the oxygen tent. The heart rate returned to normal more slowly; 12 hours later it was 100 a minute and the blood pressure was 110/65 mm. Hg. Thereafter she remained well and suffered no after-effects.

Case 2—G.F., male child aged 14 months. This child had eaten only 1 or 2 sausages. He was irritable, but had no vomiting or diarrhoea. Examination showed that the child's condition was good. There was no cyanosis or respiratory distress. The temperature was 99°F., but the heart rate was 180 a minute. Some cyanosis of the lips and tongue became evident about 1 hour later, that is about 1½ hours after the meal. No other abnormal physical signs were detected. Gastric lavage yielded a good quantity of sausage. The child was placed in an oxygen tent where the cyanosis soon disappeared. The heart rate of 180 a minute persisted for 2 hours and then gradually slowed down, being 110 a minute the following day. There was no recurrence of the cyanosis and the child remained well.

Case 3—Mr. R.M.H.F., male aged 31 years.

Case 4—Mrs. J.R.F., female aged 29 years.

Case 5—Mr. B.H.U., male aged 64 years.

Case 6—Mrs. M.U., female aged 63 years.

Case 7—Mrs. L.T., female aged 50 years.

Within 30 minutes of their meal, all the adults experienced palpitations and a sensation of constriction in the throat, followed by headache, dizziness and numbness of the fingers. There was epigastric discomfort and some nausea, but no diarrhoea, vomiting or colic. They all became somewhat drowsy. The headache was disturbing and was described as throbbing and bounding. Examination of all the adults revealed a tachycardia of 120-140 a minute; blood pressures

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varied from 100/60 to 135/95 mm. Hg; all were afebrile. Cyanosis of the lips and buccal mucosa became evident 1 hour after the meal, but there was no respiratory distress. There were no other abnormal physical signs.

All the adults were encouraged to vomit and, with the assistance of an emetic, 3 succeeded. Mr. R.F. and Mrs. L.T. had gastric lavages which yielded undigested sausage and partially digested remnants of the recent meal. None of the adults was detained in hospital. They complained of some headache for 2-3 days. A mild diarrhoea developed the following day and, with general lassitude, remained for 2-3 days, by which time all had recovered completely.

ACTION BY JOHANNESBURG CITY HEALTH DEPARTMENT

The sources of the sale and the manufacture of the sausages were immediately traced. Samples of uncooked as well as the original cooked sausages, together with samples of the stomach contents of the 2 children, were submitted to the South African Institute for Medical Research for bacteriological analysis, and subsequently to the City Health Department's chemical division. Careful inspection at the home of the victims revealed no insecticide, detergent or other poison which might have been added inadvertently in cooking the sausages, nor was any clue apparent at the delicatessen store which sold the product.

At one (A) of the 2 butcheries which manufactured the sausages there were grounds for suspecting that saltpetre and borax might well have been added to the sausage meat in excessive quantities. Samples of the saltpetre, borax and the cornflour used in the processing were submitted for chemical analysis, together with samples of the sausages.

The borax and the cornflour were chemically pure, but the saltpetre, which should be practically 100% sodium nitrate, was found to be 100% sodium nitrite. Meanwhile, bacteriological reports from the South African Institute for Medical Research on the sausages and the gastric contents showed no pathogenic organisms. The following further chemical analyses then became available:

Description	Sodium nitrite (parts per million)
Uncooked sausage from butchery A	4,700
Cooked sausage from butchery A	7,400
Stomach contents of each affected child	48
Cornflour from butchery A	nil
Borax from butchery A	nil
Uncooked sausage from second butchery (B)	178

From these analyses it was clear that the poisoning was due to excess sodium nitrite in the sausages caused by faulty supplies of 'saltpetre' to butchery A.

The supplier of the contaminated saltpetre was immediately traced and a stop-order placed on all his stocks of this product. The names and addresses of all butchers and suppliers of meat and meat products throughout the country who had bought saltpetre from this firm during the previous 2 months were obtained, and each one was contacted by telephone. An appeal to return suspected stocks was also made through the press. No fewer than 43 firms had to be contacted, many from as far afield as Bethal, Zeerust, Swaziland, Sabie, Pietersburg, Letaba,

Tzaneen, Ermelo, etc. Health departments at these places were also informed.

The supplier's stocks of saltpetre consisted of: 101 × 50 kg. hessian bags, 48 × 100 lb. paper packets, 47 × 8 lb. bags (dispensed), and 27 × 20 lb. boxes (dispensed).

Each container was tested and found to be in order, the average sodium nitrite content being no more than 10 ppm.

A bin containing 280 lb. of 'saltpetre', from which cash orders for small quantities were dispensed, was found to contain a mixture of saltpetre and sodium nitrite.

Stocks of saltpetre from the 43 firms mentioned above were returned to the supplier and all were tested by the City Health Department. Six of the 43 consisted of a mixture of saltpetre and sodium nitrite and were confiscated. Of these, 4 were from the Johannesburg area, 1 from the Orange Free State, and 1 from the East Rand. Stocks of the remaining 37 were satisfactory.

By these means, save for 3 lb. of saltpetre supplied to 2 customers over the counter for cash, every pound sold or in stock was accounted for and tested.

Meanwhile, all the meat and meat products prepared at butchery A had been seized and subjected to analysis. This consisted of:

Description	Sodium nitrite (parts per million)
20 lb. of smoked stuffed turkey	986
32 lb. of smoked stuffed turkey	2,260
12 lb. of polony	2,730
8 lb. of polony	2,824
149 lb. of sausages	3,189

These products, together with other affected meat at the 6 establishments mentioned above, were confiscated. For example, 502 lb. of pickled tongue, pork and corned beef were condemned at the Orange Free State establishment, and 37 lb. of pickled meat from other premises.

Follow-up investigations at the premises of the supplier of the saltpetre revealed that 3 large Johannesburg firms acted as indent agents. One agent obtained saltpetre from the USA in paper packets, while the other 2 obtained it from West Germany packed in hessian bags. Incidentally it was established, after prolonged and careful enquiry, that the packing of these products is as follows:

Sodium nitrate:

Standard pack: Single jute or hessian bags.

Also available: Jute bags with polyethylene inner bag; iron and fibre drums.

Sodium nitrite:

Standard pack: Corrugated iron drums of about 200 kg. net weight.

Also available: Fibre drums, with polyethylene inner bag, of 50, 100 and 200 kg. net weight; drums of 112 lb. and 276 lb. net weight.

Special curing saltpetre:

Sodium nitrate, containing 1.8-2.0% sodium nitrite, packed in 100 lb. amounts in hessian bags with loose paper liners.

A telex message to Durban, the port of entry, showed that the suspected consignment of nitrate had been sent as 'fertilizer', according to the customs manifest and bill of lading. There are therefore valid grounds for sus-

pecting that this consignment might well have contained some sodium nitrite in addition to the saltpetre.

There is no doubt that consignments of this description should not be vaguely marked as 'fertilizer', but that the chemical nature of the product should be clearly stated and, where applicable, should state that it is 'for human consumption'. A responsibility should also be imposed on all importers to ensure that these precautions are adopted and that the products for human consumption are of adequate purity.

No further cases of sodium nitrite poisoning have occurred.

DISCUSSION

Earlier Reports of Sodium Nitrite Poisoning

Greenberg *et al.*¹ reported an outbreak of sodium nitrite poisoning affecting 11 men, which resulted from eating oatmeal in which sodium nitrite was used instead of table salt. One death occurred.

Padberg and Martin² reported poisoning which caused the death of 3 men who prepared a stew with sodium nitrite instead of salt, while McQuiston³ also reported the death of 3 persons under similar circumstances. Ruegg⁴ reported 3 deaths, while Huziter-Kramer⁵ reported 5 cases, of which 2 were fatal. Four patients described by Musso⁶ were given sodium nitrite in a drugstore in Algeria in a purgative lemonade. All 4 died. A similar error, in which a druggist gave 2 infants sodium nitrite instead of sodium citrate, resulting in 1 death, was described by Manicattide.⁷ Single cases of sodium nitrite poisoning, all terminating fatally, have also been described by Palmer,⁸ Arbuckle and Thies,⁹ Naidu and Rao,¹⁰ and Molitaris,¹¹ while a single fatal case of poisoning with potassium nitrite was reported by Farinand and Woltz.¹²

Oppe¹³ reported the case of an infant aged 2 months, with methaemoglobinaemia resulting from accidental sodium nitrite poisoning, who was successfully treated by an intravenous injection of 0.3 ml. of a 5% solution of methylene-blue. Kirby¹⁴ described the case of an 11-year-old girl, desperately ill with sodium nitrite poisoning resulting from the ingestion of machine oil containing 36.5% of sodium nitrite, who was successfully treated by exchange blood transfusion soon after admission.

Toxic Effects and Treatment

Sodium nitrite is absorbed rapidly, its effects starting 5-30 minutes after ingestion. Absorption starts sublingually, causing vasodilatation and, in large doses, syncope and methaemoglobinaemia. Methaemoglobin is the stable oxidized form of haemoglobin, with the iron in the trivalent ferric state. This form is of little value in supplying oxygen to the tissues.

Toxic methaemoglobinaemia in infancy and childhood should, of course, be considered in all cases of unexplained cyanosis. Aniline derivatives are used in the manufacture of some wax crayons, and this condition has sometimes been produced by ingestion of these crayons. The clinical picture depends on the amount of toxic substance ingested, but in all cases of slate-grey cyanosis and collapse, with nausea or vomiting, but without evidence of respiratory or cardiac disease, methaemoglobinaemia should be considered. If the cyanosis is unrelieved by oxygen therapy,

and blood withdrawn from a vein shows the characteristic chocolate-brown coloration, the diagnosis is certain. Methylene-blue, 1-2 mg. per kg. body weight, should at once be injected intravenously and the causal substance must be sought and eradicated. In very severe cases, exchange transfusion may be life-saving. It is stated that prolonged observation of the patient is needed because of the danger of neutropenia and agranulocytosis following the ingestion of sodium nitrite.

The *US Pharmacopeia* gives the average pharmacological dose of sodium nitrite as 0.060 G. or -1 grain, the *British Pharmacopoeia* as 0.03-0.12 G., or $\frac{1}{2}$ -2 grains. It has been established that a dose of 3 grains in an adult causes low blood pressure, pallor, sweating, nausea, dizziness and finally loss of consciousness.

Keohane and Metcalf¹⁵ showed, during the course of an investigation into the replacement of foetal by adult haemoglobin, that the haemoglobin of cord blood is more susceptible to methaemoglobinization by sodium nitrite solutions than is adult haemoglobin treated in the same way. This phenomenon had already been mentioned by Pellegrini and Mazzeo¹⁶ in a report of 5 cases of methaemoglobinaemia in which they attributed the increased sensitivity to the presence of foetal haemoglobin. Keohane and Metcalf¹⁵ showed, too, that the increased sensitivity to nitrite persists until about the time of puberty, and is not solely a property of foetal haemoglobin. The mechanism of the change in sensitivity is unknown.

Possible Contamination of Underground Water Supplies

In January 1959 all 3 infants of a set of triplets died at the Krugersdorp Hospital when 39 days old, following the administration of sodium nitrite instead of sodium chloride. This was the second recorded instance in South Africa of death from sodium nitrite poisoning, the first being at Krugersdorp as well. In 1953, 3 African children aged 11 months, 2 years and 5 years, died on that occasion.

At the 1959 inquest proceedings, Prof. D. G. Steyn of the University of Pretoria expressed the opinion¹⁷ that, though only these 3 fatal cases had been recorded in this country up to then, 'we must have had hundreds of cases of cyanosis from it (sodium nitrite). It appears that many of the deaths of so-called "blue babies" have been incorrectly diagnosed because the necessary tests are not made'. Professor Steyn ascribed this to the fact that the semi-arid regions of South Africa have 'underground water supplies (which) are frequently contaminated by nitrates and nitrites, and we are faced with the terrific danger of cyanosis to babies because their feeds are prepared from such water. Hundreds, perhaps thousands, of wells contain nitrite in amounts dangerous to infants'. Many authorities will not agree with this view.

There are two sources of nitrogen, as nitrites and nitrates, in South African soils and waters:

1. Oxidation of organic matter.
2. A small amount by fixation of atmospheric nitrogen, either through the aid of symbiotic bacteria in the soil, or through electrical discharges during thunderstorms, when nitric acid will be formed and washed down by rain.

Dr. G. W. Bond¹⁸ stated that the majority of wells or borehole waters show small amounts of nitrates as the result mainly of pollution. He found very few instances

of nitrite pollution, and then only in small amounts. This is understandable because, during the oxidation of organic matter, nitrites are an intermediate stage between ammoniacal nitrogen and nitrates and they are readily oxidized in water and soil to nitrates. This makes the risk of nitrite poisoning from wells and boreholes a small one.

SUMMARY

1. Seven cases of acute poisoning by sodium nitrite are described. They resulted from the ingestion of sausages, in the processing of which sodium nitrite instead of saltpetre (sodium nitrate) had accidentally been used.

2. All 7 patients recovered completely without ill-effects.

3. The public health investigations which followed the outbreak are described and an appeal is made for far more stringent identification measures when dealing with this highly toxic substance.

4. The literature is reviewed and the treatment described.

5. Finally, comments are made on the differing views regarding the degree of contamination of underground water supplies in South Africa with nitrites.

Thanks are due to my colleagues in the Johannesburg City Health Department, particularly in the Food Section, for their assistance and the meticulous investigations which followed the outbreak; to the South African Institute for Medical Research for the bacteriological investigations; to our Department's Chief Chemist, Dr. E. G. White, Ph.D., for all the chemical investigations and for information on underground water supplies; and finally to the Medical Officer of Health, Johannesburg, for his interest and permission to publish.

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