NITRATE–RICH GROUNDWATER IN AUSTRALIA: A POSSIBLE CAUSE OF METHÆMOGLOBINÆMIA IN INFANTS

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Methæmoglobinæmia, cyanosis and fatal illness in infants can be caused by the ingestion of water which contains dissolved nitrates. Groundwater, derived from wells, bores or springs, which contains sufficient nitrate to cause illness in infants, is available and being used for domestic purposes in many rural and outback areas of Australia. These localities are described and the danger of feeding infants with groundwater is emphasized.

THERE are many causes of cyanosis in infants (Celermajer, 1972). One cause, methæmoglobinæmia, has long been known to result from contact with aniline-dyed clothing or other articles (Rayner, 1886) and, more recently, from the use of the local anæsthetic agent, prilocaine (Harley and Celermajer, 1970). In 1945 it was first reported in the U.S.A. that there was a relationship between the presence of nitrates in drinking water and development in infants of cyanosis caused by methæmoglobinæmia (Comly, 1945). In every case the water had been derived from underground sources (wells, bores or springs).

Groundwater which contains even small amounts of naturally occurring nitrate in solution is now known to have caused infantile cyanosis and death in several countries, including the U.S.A., Great Britain and Eastern Europe (Bucklin and Myint, 1960; Ewing and Mayon-White, 1951; Knotek and Schmidt, 1964). The danger from the use of such water is restricted to infancy when it is used, for example, to make up milk formulæ. Ingestion by adults or by children who are more than about one year old usually does not produce ill effects.

Groundwater is a major source of domestic water supply in many countries and, although it may be acceptable from the point of view of total salinity, taste and bacteriological purity, it sometimes contains nitrates in much higher concentrations than are found in surface water.

There do not appear to be any recorded cases in Australia of methæmoglobinæmia caused by the ingestion of water which contains nitrate, but the condition may have occurred without being diagnosed. The aim of this paper is to point out that groundwater which contains sufficient nitrate to cause cyanosis if given to infants occurs in widely scattered areas of Australia. Such water would normally be excluded from reticulated water supplies in urban areas. However, private bores or wells are common sources of water used for domestic purposes in country areas, particularly in the outback. Thus, nitrate-induced methæmoglobinæmia is most likely to occur in areas where medical facilities for its diagnosis and treatment are least readily available.

PATHOGENESIS OF NITRATE-INDUCED METHÆMOGLOBINÆMIA

In general, nitrates are non-toxic substances. The danger arises when any nitrate is reduced to nitrite, a powerful oxidizing agent, which causes hæmoglobin to be oxidized to methæmoglobin, thus preventing the transport and release of oxygen. Normally, less than about 1·7% of hæmoglobin is present as methæmoglobin, the latter being formed and reduced continuously (Bucklin and Myint, 1960). If the rate of its formation exceeds the rate of reduction and the proportion of methæmoglobin rises to about 10%, then cyanosis, which is not alleviated by oxygen administration, becomes apparent.

Non-pathogenic organisms which can readily reduce nitrate to nitrite are ubiquitous among the flora of the mouth, pharynx and colon (for example, *Aerobacter aerogenes*, *Streptococcus viridans* and *Escherichia coli*). Cornblath and Hartmann (1949) demonstrated that small quantities of nitrate introduced directly into the colon of a three-month-old child who had a colostomy produced methæmoglobinæmia and cyanosis within four hours because nitrite was formed and then absorbed into the

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blood stream from the colon. Nitrate-reducing bacteria are usually inhibited in the stomach, provided the pH is less than about 4·0 (Cornblath and Hartmann, 1948). Orally ingested nitrate is usually absorbed in the upper gastrointestinal tract before it can be reduced to nitrite by the gut flora; hence the relatively low toxicity of nitrates under most circumstances. However, gastro-enteritis has been associated with the onset of cyanosis caused by nitrate-induced methæmoglobinæmia, presumably because nitrate-reducing organisms are present at that time in the upper gastrointestinal tract (Comly, 1945; Cornblath and Hartmann, 1948).

Knotek and Schmidt (1964) studied infants in several communities near Prague, Czechoslovakia, where the domestic water supplies are obtained from underground and contain nitrate. They found "elevated levels" of methæmoglobin in 52% of otherwise healthy infants who were less than three months old, in 13% of those who were between 3 and 12 months old, but in none of those more than one year old. The unusual sensitivity of infants to the toxic effects of nitrate ingestion may arise for a variety of reasons. The oxygen dissociation curve of blood is displaced to the left in infancy and, therefore, offers less reserve than in adults to counter the effects of excess methæmoglobin formation; nitrate-reducing bacteria are able to grow in the stomach of babies where gastric pH is often less than 4·0 (Cornblath and Hartmann, 1948); and the physiological reduction of any methæmoglobin may be less efficient in the neonate than in older children or adults.

Knotek and Schmidt (1964) blamed the widespread use of milk formulæ, which had been prepared with water containing nitrate, for the 115 cases of infantile cyanosis caused by methæmoglobinæmia in Prague over a 10-year period. Ten of these infants had died, a mortality of 8%. The same authors found that spores of *Bacillus subtilis* occur in many commercially prepared milk formulæ. These spores are normally harmless but can grow and reduce nitrate to nitrite, thereby causing methæmoglobinæmia under some circumstances. When lactic acid is added to the formula, infants can tolerate high concentrations of nitrate in the water without ill effect because growth of nitrate-reducing organisms is inhibited.

The concentrations of nitrate in drinking waters which have been reported to cause methæmoglobinæmia and cyanosis have been greater than 30 mg/l. and, in some cases, have been several hundreds of mg/l. (Comly, 1945; Bucklin and Myint, 1960). However, the American Public Health Association (1950) considers that water which contains as little as 10 to 20 mg/l. of nitrates may be unsafe for use by young children. Boiling such water is an attempt to "purify" it only increases the concentration of nitrate as a result of evaporation. In most cases the nitrate-reducing bacteria which create the problem are not initially present in the water.

NITRATE-RICH GROUNDWATERS IN AUSTRALIA

There are large areas of Australia where groundwater is available and being used for agricultural and, to some extent, also for domestic purposes. Figure 1 shows those localities where nitrate-rich groundwaters are known to occur. This figure was drawn on the basis of unpublished results of water analyses performed by the groundwater authorities in each State and on the published data of Murray and Siebert (1962) for Central Australia. There will undoubtedly be other localities of this type as knowledge of water resources increases. The concentration of nitrate in groundwater from each of these areas exceeds 10 mg/l. and in some cases exceeds 100 mg/l., particularly in the more arid regions of Australia. This water should not be given to children to drink, especially those less than 6 months old.

Nitrate-rich groundwaters are not confined to one particular geologic situation. For example, they occur in basalts in the Western District of Victoria and in south-eastern South Australia, but occur in dolomite aquifers[1] in Queensland and in alluvial deposits in the Hunter River (N.S.W.) and Gascoyne River (W.A.) valleys. Many of these groundwaters are derived from shallow aquifers (less than 30 metres from the surface). However, greater depth of wells is no guarantee that water will contain little dissolved nitrate. The overall salinity of many of these waters is low and there is no way of knowing by appearance or taste that nitrates are present. By contrast, nitrites very seldom occur naturally in groundwater.

It is sometimes inferred that nitrate in groundwater indicates the presence of organic pollution. While this may be so under some circumstances, most nitrate is produced by non-pathogenic nitrifying bacteria which live in soils. Rain-water filtering through certain nitrate-rich soils may enter an aquifer and later be available as sterile, nitrate-rich groundwater (Murray and Siebert, 1963; Lawrence, 1969). Some of this water is being used for human consumption in rural areas of Australia where supplies of surface water are limited and where privately owned water wells are common.

COMMENTS

The danger exists that infants will develop methæmoglobinæmia after ingesting only small amounts of water which contains nitrates when conditions exist for the reduction of the nitrate to nitrite before the absorption in the upper gastrointestinal tract. Nitrate-rich groundwater may be used for human consumption as commonly in Australia as it has been in some other parts of the world, notably in Eastern Europe. Nevertheless, it is possible that methæmoglobinæmia caused by the ingestion of such water could have occurred in the past in Australia without being recognized.

The clinical presentation of nitrate-induced methæmoglobinæmia often involves the onset of cyanosis in a baby a few weeks old who has previously been healthy (Ewing and Mayon-White, 1951; Bucklin and Myint, 1960). The cyanosis is unaffected by the administration of oxygen and the absence of signs of pulmonary or cardiovascular disease may make the diagnosis difficult unless it is specifically sought. A spectrophotometric determination of methæmoglobin in blood should be made, but this is unlikely to be possible in those places where the condition is most likely to occur. However, Harley and Celermajer (1970) have described a simple and rapid test to distinguish the "red-brown" blood of methæmoglobinæmia from the normal by visual comparison of drops of blood on filter paper.

[1] The relatively porous and permeable rock which yields groundwater.

The intravenous administration of a 1% solution of methylene blue, 2 mg/kg of body weight, provides a rapid cure for methæmoglobinæmia, no matter what its cause. However, prevention is preferable to cure. The public should be made aware of the danger of feeding infants

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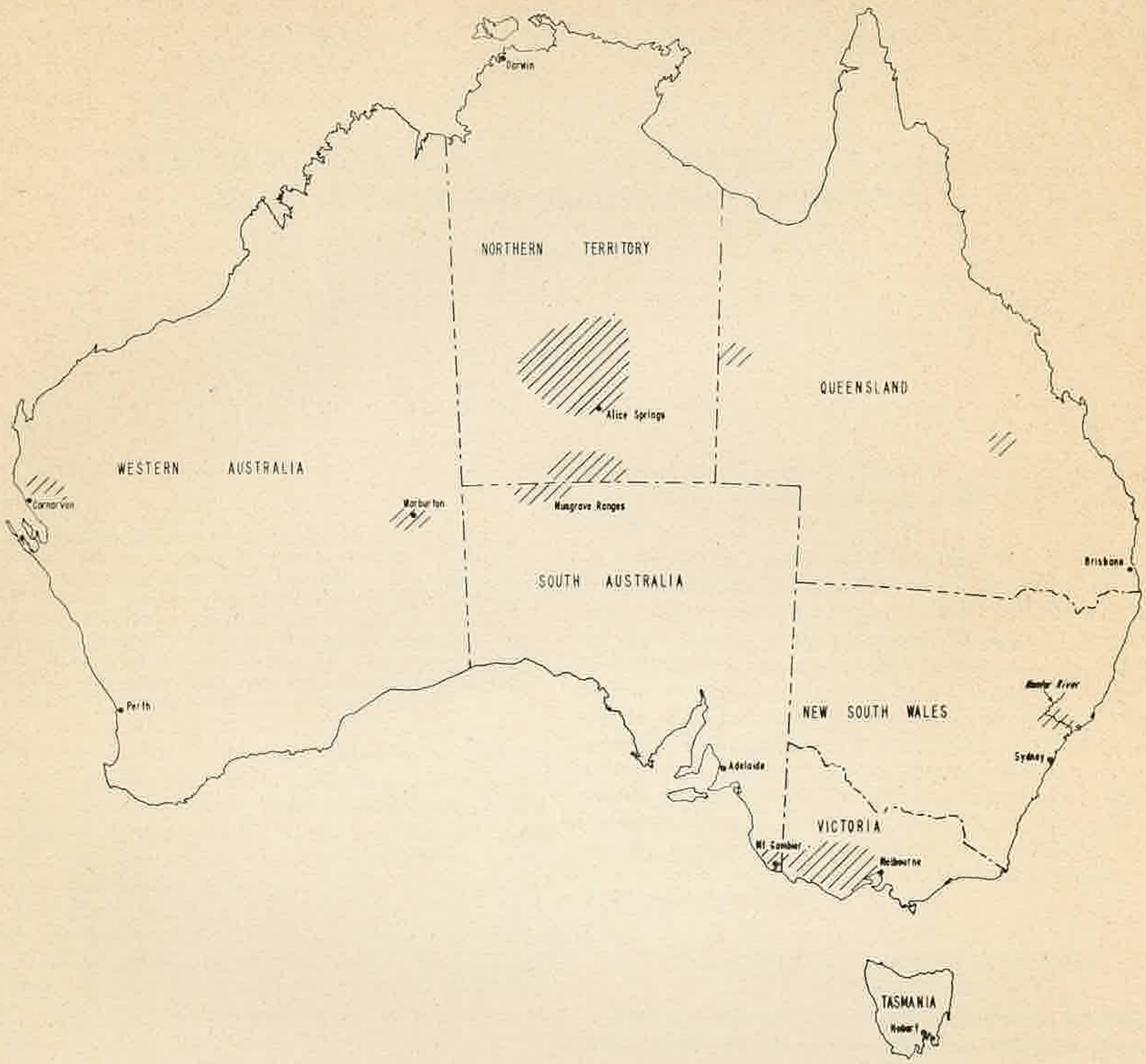

FIGURE 1: Areas of nitrate-rich groundwaters in Australia.

with water which contains nitrates, even though that water is sterile and palatable. This danger is largely restricted to the use of water derived from springs, bores or wells. A chemical analysis of such water, including an assay for nitrate, should always be performed before it is used for human consumption.

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