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# Cancer Risk and Fertilisers: Evidence from Developing Countries

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# CANCER RISK AND FERTILISERS: EVIDENCE FROM DEVELOPING COUNTRIES

## Jules N. Pretty, Gordon R. Conway

For some time nitrates derived from nitrogen fertilisers have been implicated in the causation of cancers. Theoretical models describing the chain of events from agricultural pollutant to cancer appear fairly complete, and hence lend weight to calls for restrictions on fertiliser use, despite the obvious potential losses in food production.

The key carcinogens in this chain are N-nitroso compounds. These are formed when nitrites, which have been in turn produced from nitrates, are combined through bacterial action with amines or amides derived from foods and various environmental contaminants. Most N-nitroso compounds tested have been found to cause cancers in many species of animals, notably in the stomach, liver, oesophagus and bladder. But, as yet, there is no direct evidence that these compounds cause cancer in man, though equally there is no reason to believe that humans should not be susceptible.

In humans most attention has centred on the risk of **gastric cancer**, principally because the stomach is expected to be the major site in the body for production of N-nitroso compounds. Evidence has now been produced to show that this nitrosation reaction does indeed occur, but the uncertainties are so great that it is still unknown whether the major exposure is from nitrosation or from intake of pre-formed N-nitroso compounds in the diet and from tobacco smoke.

Nonetheless the evidence for a link between incidence of gastric cancer and levels of nitrates in drinking water remains conflicting. In industrialised countries nitrate levels have been increasing over several decades, yet gastric cancer mortality has fallen on average by 30% since the early 1950's. Nitrate levels are also high in some localities in developing countries. According to various surveys in India and Africa, some 20-50% of wells contain nitrate levels greater than 50mg/l[1] and, in some cases, as high as several hundred mg/1, although these are mostly caused by domestic and livestock wastes rather than fertiliser use. It is usually wells in villages or close to towns that contain the highest nitrate levels, suggesting that domestic excreta are the main source. Livestock wastes are usually most important where drinking water troughs are situated close to wells, often producing levels in the hundreds of mg/l.

But, despite high nitrate levels, gastric cancer incidence is also falling in many developing countries (Table 1). The only recorded exceptions are amongst men and women in Recife, women in Cali and Malay men in Singapore. Only mortality rates in Chile, Colombia, Costa Rica, parts of Brazil, in Shanghai and amongst the Chinese population of Singapore are comparable to those in the industrialised countries. The question is, do any of these high levels correlate with exposure to nitrates, and if so, do the nitrates come from fertilisers?

1. The WHO guideline for safe levels in drinking water is 45mg nitrate/litre.

**Table 1 Changes in age-standardised rates of mortality and of incidence for gastric cancer in developing countries (Conway and Pretty, 1988)**

| Country | Period A | Period B | % Change in **Mortality** Period A to Period B | |
|---|---|---|---|---|
| | | | Males | Females |
| Costa Rica | 1976 | 1983 | - 8% | - 7% |
| Chile | 1950–51 | 1982 | - 46% | - 69% |
| Mexico | 1960–61 | 1982 | - 9% | - 13% |
| Puerto Rico | 1964–65 | 1983 | - 57% | - 54% |
| Uruguay | 1976 | 1984 | - 44% | - 59% |
| Venezuela | 1960–61 | 1983 | - 32% | - 37% |
| Hong Kong | 1960–61 | 1985 | - 53% | - 40% |
| Philippines | 1964–65 | 1976 | - 8% | - 6% |
| Singapore | 1971 | 1985 | - 7% | - 4% |
| Sri Lanka | 1960–61 | 1980 | - 19% | - 24% |
| Thailand | 1964–65 | 1976 | - 23% | - 25% |

| Cancer Registry | Period A | Period B | % Change in **Incidence** Period A to Period B | |
|---|---|---|---|---|
| Ibadan, Nigeria | 1960–65 | 1970–76 | - 11% | -20% |
| Recife, Brazil | 1968–71 | 1973–79 | + 39% | + 28% |
| Sao Paolo, Brazil | 1969 | 1973 | - 8% | -12% |
| Cali, Colombia | 1962–64 | 1973–76 | - 14% | +16% |
| Kingston, Jamaica | 1958–63 | 1973–77 | - 35% | -15% |
| Puerto Rico | 1962–63 | 1973–77 | - 27% | -34% |
| Bombay, India | 1964–66 | 1973–75 | -3% | -6% |
| Singapore (Chinese) | 1968–72 | 1973–77 | -1% | -2% |
| Singapore (Indian) | 1968–72 | 1973–77 | -28% | -59% |
| Singapore (Malay) | 1968–72 | 1973–77 | + 12% | -25% |

In both Chile and Colombia extensive studies have sought to make the link between nitrogen fertilisers or nitrates and gastric cancer, but the conclusions are inconsistent. In Chile, the sole country in the world with natural nitrogen deposits, a correlation was observed between gastric cancer and per capita nitrogen fertiliser use – but this was not confirmed when nitrate levels in drinking water were measured. Urinary nitrate levels, a good measure of dietary exposure, were highest in regions of low cancer risk; while vegetables tended to have a high concentration of nitrate in both the high and low risk regions. However, later studies did reveal correlations between gastric cancer and both length of residence in high risk regions and agriculture as an occupation.

One of the highest rates of gastric cancer incidence in the world occurs in the Andes in Colombia (150/100,000). Here a precursor stage of the cancer, chronic atrophic gastritis, was found in the early 1970's to be present in more than 50% of adults over 40 years of age. Although the area is predominantly agricultural, commercial fertilisers were not being used intensively, and few of the drinking water wells contained large amounts of nitrate. People from the high risk area did have significantly higher salivary and urinary nitrate levels than those from low risk regions, but elevated nitrate concentrations were also found in people who did not drink the contaminated water. One suggestion is that ingested nitrates in this region come not only from drinking water but also from grains and vegetable roots. A recent study has also shown that the fava bean, a common vegetable in Colombia, contains a compound which produces a strong mutagen when nitrosated in the presence of nitrite. But, in general, other evidence suggests that vegetables in the diet probably provide protection against gastric cancer.

Although neither of these two cases contains clear evidence of widespread nitrate contamination of water, they have nonetheless both been strong components of the argument for restricting nitrogen fertiliser usage. Very little attention, however, has been paid to the possible role of N-nitroso compounds in the causation of cancer at other sites. Two such possibilities are bladder cancer in Egypt and oesophageal cancer in China.

The peak incidence for **bladder cancer** in Egypt occurs some 20 years earlier in life than in other countries, and it comprises about 30% of all male cancers and 12% of all female. It has long been clear that bladder cancer incidence is strongly correlated with infection by the parasite *Schistosoma haematobium*. The shistosome eggs become embedded in the bladder wall and seem to enhance tumour formation. However, schistosomiasis (also known as bilharzia) is not the only factor. In the Delta region there is also a high prevalence of bladder infection with bacteria capable of both producing nitrite from nitrate and combining it with amines and amides. Urinary nitrate levels tend to be high, and in relatively healthy young men the highest concentrations of N-nitroso compounds occurred in those infected with both reducing bacteria and schistosomiasis. Patients already showing clinical signs of bladder cancer also tend to have high levels of urinary N-nitroso compounds. Despite all this evidence, there is no firm information on contamination of drinking water with nitrates, though annual fertiliser applications to arable land are of the order of 300kg nitrogen/hectare.

**Oesophageal cancer** is very common in some provinces of northern China, where age adjusted mortality rates reach some 150/100,000 for men. But again the causative factors have not been clearly identified. A relatively high content of nitrate, nitrite and amines was found in some foods, such as pickled vegetables and some cereal products. Oesophageal cancer is correlated with consumption of pickled vegetables. Ground water nitrate levels were also highest in those regions with highest oesophageal cancer incidence; but the source of nitrate contamination is unknown. The strongest evidence for a link comes from a recent study, which found four times the concentration of N-nitroso compounds in the urine of inhabitants living in the high risk region compared to those in the low risk region.

The current evidence for a relationship between nitrates and cancers is thus at best mixed. Recently, Forman and colleagues at the Imperial Cancer Research Fund in the UK.

concluded following an epidemiological study that probably "nitrates do not play an important role in determining gastric cancer incidence", but this of course does not preclude their playing a more important role in other cancers.

Thus evidence does not support any reductions in the use of nitrogen fertilisers in developing countries, particularly in the light of well-established benefits to food production. Furthermore, with developing country populations expected to continue growing and opportunities for expansion of production into new areas declining, significant future growth in crop production will have to come from intensification, and this currently implies increasing fertiliser use.

But we should not be complacent. The risks of nitrate contamination of water appear greatest in regions where inorganic nitrogen fertilisers are used intensively; particularly in seasonal climates where high yielding cereal varieties are cultivated with irrigation. Nitrates are flushed into surface and ground water at the onset of the rainy season, and irrigation water provides a direct conduit for nitrate to surface and ground water. Moreover during reuse nitrate levels may become progressively concentrated. There is a need for closer examination of nitrate levels in water and foods, and of cancer incidence in seasonal climates. Further analysis is also required of the role of N-nitroso compounds on cancers other than of the stomach.

In the meantime increased promotion of certain dietary inhibitors of nitrosation in the body, for example vitamins C and E, will help to ensure that, should N-nitroso compounds be unequivocally shown to be inducers of cancer in humans, their effect will be minimised.

# References

Conway, G.R. and J.N. Pretty. 1988. *Fertiliser Risks in the Developing Countries: A Review.* IIED, London.

Conway, G.R. and J.N. Pretty. 1988. Fertiliser risks in the developing countries. *Nature* (in press).

MAFF. 1987. Nitrate, Nitrite and N-Nitroso Compounds in Food. The twentieth report of the Steering Group on Food Surveillance. The Working Party on Nitrate and Related Compounds in Food. *Food Surveillance Paper No 20*. HMSO, London.

Forman, D., S. Al-Dabbagh and R. Doll. 1985. Nitrates, nitrites and gastric cancer in Great Britain. *Nature*, 313: 620–625.

Forman, D., S. Al-Dabbagh and R. Doll. 1985. Letter to editor. *Nature*, 317: 676.

Armijo, R. and A.H. Coulson. 1975. Epidemiology of stomach cancer in Chile – the role of nitrogen fertilisers. *Int. J. Epidemiology*, 4: 301-309.

Armijo, R. et al. 1981. Epidemiology of gastric cancer in Chile: II - Nitrate exposures and stomach cancer frequency. *Int. J. Epidemiol*, 10: 57-62.

Cuello, C. et al. 1976. Gastric cancer in Colombia. 1. Cancer risk and suspect environmental agents. *J. Natn. Cancer Inst*, 57: 1015-1020.

Hicks, R.M. 1983. The canopic worm: role of bilharziasis in the aetiology of human bladder cancer. *J. Roy. Soc. Med*, 76: 16-22.

Hicks, R.M. et al 1982. Association of bacteriuria and urinary nitrosamine formation with Schistosoma haematobium infection in the Qualyub area of Egypt. *Trans. R. Soc. trop. Med. and Hyg*, 76: 519-527.

Lu, S.H. et al. 1986. Urinary excretion of N-nitrosamino acids and nitrate by inhabitants of high- and low-risk areas for esophageal cancer in Northern China: endogenous formation of nitrosoproline and its inhibition by vitamin C. *Cancer Res*, 46: 1485-1491.

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The Sustainable Agriculture and Rural Livelihoods Programme of IIED promotes and supports the development of socially and environmentally aware agriculture through policy research, training and capacity strengthening, networking and information dissemination, and advisory services.

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