Reducing American Exposure to Nitrate, Nitrite, and Nitroso Compounds:

The National Network to Prevent Birth Defects Proposal

Charles A. Black

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Summary

These comments are in response to a petition and supporting information submitted to the U.S. Secretary of Agriculture by the National Network to Prevent Birth Defects (NNPBD). The petition includes recommendations for governmental actions to reduce birth defects and other hazards said to be associated with the use of nitrogen fertilizers, nitrite as a food preservative, and certain pesticides.

The NNPBD recommends reducing the use of nitrogen fertilizers and substituting legumes as the principal means of reducing the health hazards to which it calls attention. Nitrite would be eliminated as a food preservative, and certain pesticides that may undergo reaction with nitrite would no longer be used under certain conditions. The following paragraphs summarize the main points made in the commentary.

1. As the prime evidence that nitrate is responsible for birth defects, the NNPBD cites an epidemiologic study in Australia in which the incidence of birth defects was greater in babies born to mothers who drank groundwater containing nitrate than in those born to mothers who drank rainwater. Evidence not cited by the NNPBD indicates that the association between nitrate and birth defects was fortuitous and actually caused by an unknown factor or factors.

2. The NNPBD reviews some epidemiologic studies linking nitrate intake to stomach cancer. Not reviewed are studies that do not support the thesis that nitrate causes stomach cancer. A set of mechanisms is known by which nitrate and nitrite may react in the body to cause stomach cancer, but whether the reactions are of significance at the levels involved in practice remains to be determined.

3. The NNPBD recommends eliminating the use of nitrite in meat curing as an important step toward food safety, citing stomach cancer as a hazard of nitrite ingestion. Adopting the NNPBD recommendation would be of minor value in reducing whatever stomach cancer hazard may be associated with the nitrite residues in cured meats. Far more nitrite is produced internally by the body than is ingested in cured meats. The evidence indicates that, on the average, 12 times more nitrite enters the stomach from saliva than from cured meats. This nitrite is produced by bacteria in the mouth from the nitrate present in the saliva. A much larger amount of nitrite appears to be formed by bacteria in the intestines.

4. Although the NNPBD advocates eliminating easily nitrosated pesticides, such as carbaryl, from pest control programs by public agencies in regions where well water is contaminated with nitrate, the nitrate content of well water is essentially irrelevant to whatever hazard would result from nitrosation of such pesticides. Nitrate is not directly involved in nitrosation reactions, and pesticides do not appear to undergo nitrosation in the environment. Moreover, the hazard associated with production of N-nitroso compounds in the body from the residues of nitrosatable pesticides normally ingested in food and water would very likely be too small to detect.

5. The NNPBD says that adopting its recommendation to reduce nitrogen fertilizer use and substitute legumes would have important economic benefits. One of these would be greater profitability for farmers. This inference is probably correct as a consequence of the normally greater percentage increases in commodity prices than percentage decreases in production that would accompany reduction of nitrogen fertilizer use and substitution of legumes.

6. The NNPBD says that substituting legumes for nitrogen fertilizers would decrease production costs. Reduction or elimination of nitrogen fertilizer use would of course decrease or eliminate nitrogen fertilizer costs. Cost per unit of product is the critical statistic, however, and this probably would be lower with nitrogen fertilizers than legumes under current economic conditions.

7. The NNPBD argues that substituting legumes for nitrogen fertilizers would improve the capability of American farmers to compete with foreign producers. The opposite would be true because the reduced production and higher domestic prices associated with substituting legumes for nitrogen fertilizers would decrease the export potential. The consequence of the substitution probably would be increased imports of lower-priced foreign commodities, followed by the erection of trade barriers to protect American agriculture.

8. The NNPBD presents the final argument that adopting its recommendation to substitute legumes

for nitrogen fertilizers would reduce the cost to taxpayers, who now are called upon to subsidize the purchase of nitrogen fertilizers to produce unneeded crop surpluses. Adopting the NNPBD proposal would indeed be expected to reduce the extent to which taxpayers would be assessed to pay for crop surpluses. Instead, they would pay for the lack of surpluses through higher prices for agricultural commodities.

Introduction

In a letter dated August 1, 1987, the National Network to Prevent Birth Defects (NNPBD) (Jansson, 1987) petitioned U.S. Agriculture Secretary Lyng to take actions that would reduce human exposures to nitrate, nitrite, and nitroso compounds. Accompanying the letter was a 93-page assembly of information relating to hazards posed by these substances. The letter summarizes the hazards and advocates reducing nitrogen fertilizer use and substituting legumes for nitrogen fertilizers as principal means of reducing the hazards. Also advocated are eliminating nitrite for food preservation and eliminating the use of easily nitrosated pesticides, such as carbaryl, for pest control by public agencies in regions where well water is contaminated with nitrate.

The purpose of this document is to comment on selected aspects of the evidence presented to the Secretary.

Birth Defects

The centerpiece of the NNPBD's case for birth defects caused by nitrate is research by Dorsch et al. (1984b), in which the estimated risk of bearing a malformed child in a local area in Australia was greater for mothers who drank groundwater containing nitrate than for those who drank rainwater. Reference was not found in the NNPBD document to two follow-up studies in which the seeming connection of nitrate intake in water and birth defects was called into question (Dreosti et al., 1984; Dorsch et al., 1984a).

In the paper by Dreosti et al. (1984), water from sources drunk by the pregnant women who had an elevated estimated risk of producing a malformed child did not significantly affect the incidence of birth defects when it was concentrated by freeze drying and supplied as drinking water to pregnant rats. Moreover, the growth of rat embryos cultured in serum taken from pregnant women was the same, irrespective of the source of drinking water consumed by the women. The results of the investigation failed to verify the presence of an agent in the water that caused birth defects.

In the paper by Dorsch et al. (1984a), it was pointed out that the amount of nitrate ingested from the principal high-nitrate water source (containing 15 parts of nitrate per million — well below the "maximum safe level" of 45 parts per million used as a public health standard for infants in the United States) was only about 18 milligrams per person per day. The total intake of nitrate from all sources, including the water, was estimated at 128 to 138 milligrams per day. On the basis of this information, it was concluded that the additional amount of nitrate ingested from the drinking water was too small relative to the amount of nitrate consumed in other dietary sources to cause the observed difference in birth defects between the two groups of women. It was suggested that unidentified factors, not necessarily present in the water but correlated with water source and hence with nitrate, may have been responsible.

Commenting on the various findings in a letter to Dr. Dennis Keeney of the University of Wisconsin, Dr. Dorsch, the senior author of the paper reporting the epidemiologic association of birth defects with nitrate in drinking water, said that "Given the reservations raised in the two subsequent publications enclosed herewith, and the absence of substantiating findings from other studies as yet, I now believe the evidence for a causal association (with NO_3) is tenuous at best." Indications are, therefore, that the epidemiologic association of birth defects with nitrate in the drinking water observed in the Australian study is not to be regarded as evidence for a causal relation at this time. More evidence will be needed.

In New Brunswick, Canada, Arbuckle et al. (1988) investigated the association of nitrate in the drinking water with the risk of bearing a child with birth defects of the central nervous system in 130 cases of such defects over a period of 11 years. For women who drank water from private wells, an increase in nitrate concentration was associated with a moderate but statistically significant increase in risk; and for women who drank water from a municipal water system or a spring, an increase in nitrate concentration was associated with smaller but nonsignificant decreases in risk.

According to Klingberg and Papier (1979), about 10% of human malformations can be ascribed to environmental factors. These include viruses; parasites; drug therapy for cancer, epilepsy, and diabetes; bacteria; irradiation with ionizing energy; and exposure of mother and father to chemicals. An additional 25% of birth defects can be traced to genetic or chromosomal mechanisms. The cause of the remaining 65% of the defects is unknown.

The Centers for Disease Control (Edmonds and James, 1985) have the most comprehensive data on birth defects available for the United States. The records indicate that in the period from 1970 to 1983, during which there was a marked increase in usage of nitrogen fertilizers, the overall rate of malformations increased from 197 to 228 per 10,000 liveborn and stillborn infants. The incidence of 11 of the 33 major birth defects increased, the incidence of 17 was stable, and the incidence of 5 decreased. According to Schuman (1986), all but one of the increases were a consequence of better diagnosis. The one exception was "renal agenesis" or failure of the kidneys to develop. The reported increase in this defect has been found by Centers for Disease Control epidemiologists to be an artifact in coding and classification of their data (Schuman, 1988).

The Nitrate and Nitrate-Nitrogen Conventions

On the basis of the hazard of methemoglobinemia in infants, the U.S. public health standard for the "maximum safe level" of nitrate in drinking water was set many years ago at 45 parts of nitrate or 10 parts of nitrogen present as nitrate per million of drinking water. Although the distinction between the two conventions was pointed out by the NNPBD, the difference was not always observed correctly in interpreting the data quoted.

For example, on page 19, the NNPBD says that the study of birth defects by Dorsch et al. (1984b) in Australia "throws serious doubt on the wisdom of maintaining a 10 part per million standard for nitrate in drinking water," noting that "a nearly threefold increase in risk [of producing a malformed child] was experienced for women who consumed 5 to 15 ppm of nitrate in their water during pregnancy, and a fourfold increase for those consuming water with more than 15 ppm of nitrates." The NNPBD notes on page 3 of the petition letter that "the Dorsch study indicates the need to reduce the standard for nitrate contamination of drinking water to *less than 5 parts per million.*" From these quotations, it is evident that in this instance, the NNPD is using the convention of expressing the analytical results in terms of nitrate-nitrogen. Dorsch et al., however, expressed their nitrate concentrations as nitrate, which means that what they called 5 parts per million is equivalent to 1.1 parts per million according to the convention used by the NNPBD.

As noted in the preceding section, the findings by Dorsch et al. seem to have resulted from some unknown factor or factors, but not nitrate. If the findings were to be taken seriously as a hazard associated with nitrate, the current public health standard would be much further out of line for birth defects than suggested by the NNPBD.

Stomach Cancer

The NNPBD argues the case for reducing nitrogen fertilizer usage in part on the basis that the nitrate from fertilizers causes stomach cancer. This argument is not supported by cancer statistics, which show that the rates of incidence of and mortality from stomach cancer have declined in western countries during the past 30 to 40 years (National Research Council, 1982), a period when the use of nitrogen fertilizers was increasing dramatically.

In addition to reducing the use of nitrogen fertilizers, the NNPBD recommends eliminating nitrite as a curing agent in meat as an important step in improving food safety. The NNPBD presents some suggestive epidemiologic evidence linking stomach cancer to nitrite and nitrate, but seems to overlook evidence that does not support its thesis. Scientific papers that review both the positive and negative epidemiologic findings have been published by Fraser et al. (1980), Forman et al. (1985), and Forman (1987).

Recent papers include one by Dutt et al. (1987), who found that the Chinese in Singapore have a higher incidence of stomach cancer than the Malaysians and Indians. The Chinese have a higher dietary intake of nitrate than the Malaysians and Indians.

In a second recent paper, Al-Dabbagh et al. (1986) reported that among members of a group of workers in the United Kingdom who had been highly exposed to nitrate in fertilizer manufacturing plants for 10 years or more, there had been 3 deaths from stomach cancer within 20 or more years after the first heavy exposure. This number of deaths did not differ significantly from the 2.9 deaths expected from national statistics.

Takács (1987) investigated the incidence of cancer of the digestive organs (esophagus, stomach, intestines, colon, rectum, liver, and bladder) over a 17-year period in a high-nitrate county in Hungary, dividing the area into seven districts differing in nitrate content of the drinking water. Analysis of his data indicates that the total number of cases increased significantly with an increase in the nitrate content of the water. Data on stomach cancer were not broken out so that they could be tested separately, but about half of the total cases were stomach cancer. In this investigation, the average nitrate content of the water in the seven districts ranged from about 90 to 227 parts per million.

At this time, one can say that a set of mechanisms is known by which nitrate and nitrite may react in the body to cause stomach cancer. Whether the reactions are of significance at the levels involved in practice remains to be determined.

Stomach Cancer and Diet

Possible dietary causes of stomach cancer have been sought for many years. Perhaps the best clue thus far has emerged from the discovery that the marked decline in death rate from stomach cancer that has occurred in many countries through the years is closely related to the decline in death rate from stroke (Joossens and Geboers, 1981). Noting that the relationship between deaths from stomach cancer and stroke is similar among countries and that all the risk factors for stroke act through high blood pressure, these authors suggested that salt (sodium chloride) intake may be the dietary factor that links the two causes of death.

Although salt is a well known cause of high blood pressure, its possible mode of action in promoting stomach cancer has not been established. Joossens and Geboers (1981) pointed out that high salt intake produces gastritis in animals, is associated with atrophic gastritis in humans in areas where stomach cancer is prevalent, and delays emptying of the stomach, which would prolong the contact between the walls of the stomach and the various carcinogens in foods. Tatematsu et al. (1975) found that although salt had no apparent carcinogenic effect when added alone to the diet of rats, it increased the number of stomach cancers when it was added with the two carcinogens tested. This evidence suggests that the hypothesized relationship between salt intake and stomach cancer may be indirect. The decrease in stomach cancer associated with decreasing salt intake by populations in general might cover up small increases caused by greater exposure to carcinogens to which the stomach is sensitive.

According to a similar hypothesis proposed by Correa et al. (1975), stomach cancer may be the final result of a process that starts when the mucosal barrier lining the stomach is breached by abrasives or irritants, such as hard grains, salt, or surfactants. Chemical mutagens in the stomach contents then may reach the underlying epithelial cells and produce mutations. The mutated cells proliferate, resulting in atrophic gastritis. A final mutation or transformation allows one or more of these cells to become autonomous and invade other tissues.

Nitrate and Nitrite as Carcinogens

The average daily dietary intake of nitrate by a U.S. adult is estimated at 75 milligrams, to which vegetables are the principal contributor (65 milligrams). Intake of nitrite is 0.77 milligram, and cured meats are the major contributor (0.30 milligram) (Assembly of Life Sciences, 1981).

The total exposure of the body to nitrite and nitrate exceeds the intake because of internal production (Tannenbaum et al., 1974, 1978; Tannenbaum, 1979; Kurzer and Calloway, 1979; Hotchkiss, 1988). Both nitrite and nitrate appear to be produced by microorganisms in the intestines (Tannenbaum, 1979). The microbiological transformation of complex nitrogen compounds to ammonium and thence to nitrite and nitrate in sewage and soils is a well known microbiological phenomenon.

When nitrite is absorbed from the digestive tract into the bloodstream, it reacts with hemoglobin, as will be discussed later, and is changed to nitrate. Nitrite not absorbed is excreted in the feces.

Dietary nitrate is normally absorbed into the bloodstream before the contents of the digestive tract emerge from the small intestine. Most of the nitrate is removed from the blood by the kidneys. About half of the nitrate is eliminated in the urine within 8 hours after ingestion (a little is excreted in the feces), but part is recycled into the digestive tract via the saliva.

Some of the nitrate in the saliva is reduced to nitrite by bacteria in the mouth (Tannenbaum et al, 1974); a very small fraction of the nitrate present in food and drink should be similarly affected. Upon entering the stomach, the nitrite is changed to nitrous acid by the hydrochloric acid normally secreted in the gastric juice. Nitrous acid combines with a variety of nitrogenous compounds, including some present in human diets and others produced during digestion, to form N-nitroso compounds. A number of N-nitroso compounds are highly toxic and have been found to be animal carcinogens. They are mutagenic and are presumed to be human mutagens and carcinogens, although this has never been verified.

Data summarized by the Assembly of Life Sciences (1981) indicate that the amount of nitrite entering the stomach per day from saliva (3.5 milligrams) is 5 times greater than that entering from dietary sources (0.77 milligram) and 12 times greater than that from cured meats (0.30 milligram). Eliminating nitrite as a meat curing agent thus would have relatively little effect on the amount of nitrite that enters the stomach, on the amounts of N-nitroso compounds formed, or on the incidence of stomach cancer that might result from these compounds. Eliminating any health hazard of nitrite in cured meats by prohibiting nitrite use would also eliminate any health benefits, chief among which is probably that of inhibiting the outgrowth of spores of *Clostridium botulinum* bacteria. These are the bacteria that produce the toxin responsible for botulism (Lechowich et al., 1978).

Indirectly, however, the diet contributes the nitrate that is reduced to nitrite in the saliva. The diet also contributes the nitrate that is reduced to nitrite by bacteria in the stomach of individuals with stomach acidity too low to form nitrous acid (the reactive form) (Ruddell et al., 1976; Forsythe et al., 1988). Hawksworth and Hill (1971) and Collins-Thompson et al. (1972) found that certain bacteria promote the reaction of nitrite with secondary amines to form N-nitroso compounds under near neutral conditions, at least at the relatively high concentrations of reactants tested experimentally in the media employed. The potential to form N-nitroso compounds thus may be greater in persons with near neutral stomachs than in those with normally acid stomachs.

The diet provides still another source of nitrite in the intestines, probably as a result of transformations of complex organic nitrogen compounds. On the basis of data published by Tannenbaum et al. (1978), Black (1978) calculated that 30 milligrams of nitrite may be formed per day in the intestines. This amount is 39 times greater than the 0.77 milligram of nitrate that enters the stomach from dietary sources and 100 times greater than the 0.3 milligram of nitrite ingested in cured meats. Whether the bacteria that are believed to mediate the formation of N-nitroso compounds in near-neutral stomachs form correspondingly greater amounts of these compounds in the intestines is not known. If the N-nitroso compounds formed have a carcinogenic effect, the primary influence would be expected to be in the large intestine, but they might also result in cancers at other locations, including the stomach.

The evidence related to the salt hypothesis proposed by Joossens and Geboers (1981) suggests merely that salt irritates the lining of the stomach and increases the susceptibility of the tissues to whatever carcinogens may be present. The N-nitroso compounds, which are probable but not confirmed human carcinogens, are only one class of carcinogens in the food supply whose effectiveness in generating stomach cancers might be enhanced by a high intake of salt. Before it can be decided that intakes of nitrate either are or are not great enough to make a significant contribution to stomach cancer, better evidence than that now available will be required.

Forman (1987) suggests that, on balance, vegetables, which usually supply most of the dietary nitrate, may actually supply protection against stomach cancer because they contain vitamin C and other inhibitors of the reaction of nitrite with secondary amines to form N-nitroso compounds. Epidemiologic findings lending some support to this view include those by Haenszel et al. (1972), Risch et al. (1985), Forman et al. (1985), and Fontham et al. (1986).

If eventually the evidence does indicate that nitrate and nitrite are a significant factor in stomach cancer in humans, it may become important to separate the contribution of nitrogen fertilizers from the inherent properties of the plant products and the digestive system. For example, within most of the practical range of nitrogen fertilizer use, the concentrations of the various nitrogenous components of plants are controlled mostly by the inherent nature of the plants. Nitrogen fertilizers have a far greater relative effect on the yield of plant products than on the concentrations of nitrogenous substances. Where nitrogren fertilizers are used in quantities approaching those producing maximum yields, however, the relative increases in concentration of nitrogenous components may exceed the relative increases in yield; this is especially true of nitrate, which is a temporary storage form of nitrogen that accumulates in the stems and leaves of some kinds of plants pending its use to promote growth (if present, nitrite occurs only in traces). For nitrate-accumulating plants fertilized in this high range, decreasing the amounts of nitrogen fertilizers applied would reduce whatever stomach cancer hazard may be presented by nitrate. Within this high range, a decrease in nitrogen fertilizer use will also decrease the concentrations of protein and nonprotein forms of organic nitrogen in foods and, hence, the nutritional value.

Also important in evaluating the effect of fertilizers on the possible stomach cancer hazard of nitrate and nitrite would be further development of understanding about the production of these forms of nitrogen in the body and how this may relate to nitrogen fertilizer use. It would seem a priori that reducing nitrogen fertilizer use in the range near maximum yields should decrease nitrite and nitrate formation in the intestines because of the decreased concentration of nonnitrate nitrogen in the plant products consumed.

Nitrosatable Pesticides

Among the substances that may react with nitrous acid to form N-nitroso compounds are certain pesticides. In the petition letter to the Secretary of Agriculture, the NNPBD noted that "There is a need to eliminate the use of easily nitrosated pesticides like carbaryl for public spray programs, in regions where well water is contaminated with nitrates. The combination of carbaryl and nitrite may explain the reports from New Jersey, New Mexico, Idaho, and California that public spray programs for gypsy moth and other pests caused birth defects and abortions."

Several factors need to be taken into account in considering the possible hazard from the formation of N-nitroso compounds from pesticides. First, nitrate is ubiquitous and is found in well waters generally. But nitrate occurs in most groundwaters and well waters at concentrations less than 50 parts per million. Pesticides usually are found in groundwaters in concentrations below 1 part per billion if they are found at all. Concentrations up to 20 to 50 parts per billion or higher are found only occasionally (Craigmill et al., 1987).

Second, nitrate does not form nitroso compounds. These compounds are formed in the presence of nitrite, which usually is present in only traces in groundwaters if it can be found at all. When Mallik et al. (1981) added three different pesticides and nitrite to soil in quantities several hundred times greater than those that would be found in practice, they detected a maximum of 1.4 parts of nitrogen present as a nitrosamine per million of soil with one of the pesticides and traces with the other two. When the pesticides were added in excess but no nitrite was added, no nitrosamines were found.

Third, carbaryl, the pesticide mentioned repeatedly by the NNPBD as an easily nitrosatable substance, is relatively unstable in soil. In a field experiment by LaFleur (1976), carbaryl was applied to a sandy soil in South Carolina at 13 times the normal maximum rate of application. Carbaryl appeared in the groundwater at a depth of 1.1 meters (about 3.6 feet) within 2 months, reaching a maximum concentration of 60 parts per billion of water at the end of the second month. By the end of the 16th month, however, no carbaryl could be detected in the groundwater.

According to Kearney (1987), pesticides are not known to be nitrosated in the environment. Kaplan and Kaplan (1985) found that N-nitrosodimethylamine, an N-nitroso compound that has been identified as an undesirable contaminant in foods, alcoholic beverages, cosmetics, and pesticides, is degraded by microorganisms in soil and water. Pesticides similarly are subject to microbial degradation. Presumably, therefore, any pesticides that might be nitrosated in soils would be subject to degradation.

If nitrosation of pesticides occurs, the most likely site would be in the stomach, where the contents are acid and the nitrous acid that takes part in the reaction would be produced by the action of the hydrochloric acid in the stomach on the nitrite swallowed in the saliva and present in the diet (Lechowich et al., 1978). Almost all of the nitrite would be derived from reduction of nitrate in the saliva. The nitrite in the saliva would reflect all sources of nitrate, of which drinking water supplies less than 3% on the average (Assembly of Life Sciences, 1981). Therefore, the presence of nitrate in the groundwater is generally essentially irrelevant to nitrosation of pesticides in either the environment or the human body.

Fourth, the extent of nitrosation of the insignificant residues of pesticides ingested would be very small because of the low concentrations of the reactants and the existence of a large excess of competing dietary components that can undergo nitrosation with the small amount of nitrous acid present. Research on the nitrosation of carbaryl, the pesticide mentioned by the NNPBD, was published by Rickard and Dorough (1984). They introduced 0.25 micromol of radiocarbon-tagged carbaryl insecticide and 1160 micromols of sodium nitrite into the stomachs of rats and guinea pigs and then determined how much of the carbaryl was nitrosated. The proportion of the carbaryl nitrosated was 0.02% in rats and 1.54% in guinea pigs. (Nitrosation in humans probably would be similar to that in guinea pigs because the stomach contents are strongly acid in both species, and acidity favors nitrosation.) These small degrees of nitrosation were achieved only with the high concentration of nitrite mentioned (which would be equivalent to a dose of 16.6 grams [0.6 ounce] for a human weighing 70 kilograms [154 pounds], or 3,900 times the average combined daily intake of nitrite in food, drink, and saliva). When lower concentrations of nitrite were used, the yield of nitrosated carbaryl was reduced in the guinea pigs, and none could be detected in the rats. With nitrite in the normal range, the proportion of the carbaryl nitrosated would have been vanishingly small and undetectable even with the radioactive tracer. The amount of carbaryl supplied was 5,000 times greater than the amount that would be ingested by the animals (which weighed 200 to 250 grams each) in 10 milliliters of water containing carbaryl at a concentration of 1 part per billion (a high concentration for carbaryl in groundwater). Although the concentration of nitrosated carbaryl formed from a 1 part per billion concentration with the nitrite from the saliva would be too slight to detect, it undoubtedly would be well under 0.015 part per billion.

Fifth, the hazard associated with the minute concentrations of nitrosated pesticides that might be formed with the concentrations normally present would very likely be too small to detect. It is a rare compound that can be found to have an effect in animal systems when it is present in concentrations of only 1 or a few parts per billion of food and drink. The authors of a recent publication on chemical hazards in the environment (Craigmill et al., 1987) were unaware of any instance in which pesticide residues in groundwater had been vertified as a human health hazard.

Methemoglobinemia

The one well verified and well understood hazard relating to nitrate and nitrite is infant methemoglobinemia. Most writers who wish to attack nitrogen fertilizers as a health hazard do so on the basis of methemoglobinemia. Although the NNPBD called attention to methemoglobinemia it did not emphasize this hazard, perhaps because its principal concern is birth defects. The methemoglobinemia hazard has existed for many years, but it can be circumvented easily, and the condition can be cured within minutes. Illnesses and fatalities thus are rare.

Methemoglobinemia is caused by nitrite that in most instances is produced in the body by microbiological reduction of nitrate. Methemoglobinemia is a condition that may affect human infants, generally in their first few months of life. A few months may be required in infants to develop enough stomach acidity to inhibit bacterial growth in the stomach and upper small intestine, from which the nitrate supplied by the diet and the saliva is normally absorbed by older people. When infants are affected by diarrhea, the stomach acidity is lessened further. Then bacteria may be active throughout the alimentary tract. If food or drink high in nitrate is ingested, the bacteria may reduce the nitrate to nitrite, which is absorbed into the blood. In the blood, the nitrite is oxidized by the hemoglobin to form nitrate, and the hemoglobin is reduced to methemoglobin, which does not carry oxygen to body cells. Death may ensue in severe cases (Black, 1983).

In a few instances in Europe (Phillips, 1971), preformed nitrite ingested in the food is suspected to have caused methemoglobinemia. These cases occurred when infants consumed canned spinach that had been allowed to stand after the cans were opened. Bacterial reduction of nitrate to nitrite had occurred before the infants ate the spinach. Green leafy vegetables, such as spinach, may be high in nitrate. A small part of the nitrate in even fresh spinach has been found to be changed to nitrite upon long standing under refrigeration (Aworh et al., 1980). Paschold and Hundt (1986) also described the postharvest formation of nitrite in spinach.

A number of infant deaths from methemoglobinemia occurred before the cause was discovered in 1945 and for a few years after that time until doctors became aware of the hazard and the treatment of the disease. Now the use of low-nitrate water by infants during their first year is recommended if their regular source of water is high in nitrate. Cured meats are not recommended during the first 12 weeks of life.

An appreciation of the cost of the methemoglobinemia hazard for infants relative to the investment in nitrogen fertilizers may be derived from some rough calculations. If one-tenth of the babies born each year were supplied for their first year with bottled water because their source of drinking water was high in nitrate, if bottled water cost $0.75 per gallon, and if the babies consumed 1 liter or 1.06 quarts of water per day (the Environmental Protection Agency's convention for a 10-kilogram or 22-pound child), the total cost would be about $26 million annually. This amount is equivalent to about 0.7% of the cost of the nitrogen fertilizer used annually. If each dollar spent for nitrogen fertilizer returns $2 in crop value, the cost of the bottled water would be about 0.35% of the crop value resulting from nitrogen fertilizer use.

Adults escape the hazard and can tolerate high-nitrate water because the nitrate is absorbed into the blood from the acid part of the digestive system. It is then excreted in the urine. Adults and older infants also have a higher concentration of the enzyme that changes methemoglobin back to hemoglobin than do infants younger than 4 months (Johnson et al., 1987).

Substituting Legumes for Nitrogen Fertilizers

The petition letter submitted by the NNPBD recommends reducing nitrogen fertilizer use and increasing the use of legumes as a substitute. (Legumes convert atmospheric nitrogen to organic forms that can be transformed in the soil to inorganic forms, principally nitrate and ammonium, that nonleguminous plants can absorb.) Three important economic benefits are said to follow if the recommendation were to be adopted:[1] (1) Farmers would make more profit. (2) Production costs would decrease, and as a result farmers could compete with foreign producers. (3) The cost to taxpayers would be reduced. Additionally, the NNPBD notes that legumes are valuable in soil erosion control, and they offer a "complete alternative" to nitrogen fertilizers. These advantages will be examined in turn.

The NNPBD derives support for its economic contentions from an econometric analysis by Olson et al. (1982). The same analysis will be used as a basis for these comments. Olson et al. examined the economic consequences of converting U.S. agriculture to "organic" (largely "nonchemical") farming, one of the characteristics of which is the elimination of commercial nitrogen fertilizers and the substitution of legumes and other sources of supplemental nitrogen for crop production. The economic consequences of reducing the use of nitrogen fertilizers and increasing the use of legumes would be analogous to, but less marked than, those of converting U.S. agriculture to organic farming. A report on the social and economic impacts of restricting pesticide use in agriculture, an analogous issue, was developed by a task force chaired by Eddleman (1980).

[1] The economic benefits listed are direct statements that may be inferred from the following quotations and related discussion from the NNPBD submission: (1) "We believe that the curtailment of overfertilization of crops is not only in the national interest, but also in the interest of the farmer in terms of profit margins and profitability." (2) "The type of program outlined by Olson and colleagues reduces farm costs so much that American farmers would in fact become efficient enough to meet the pricing challenges of foreign farmers." (The "program" is explained further in the text of these comments.) (3) "Nitrogen fertilizer is a major factor in crop surplus payed for by the tax-payer. . . . There is really no excuse in a period of intense crop surpluses for farmers to overfertilize crops that are to be bought by the U.S. tax-payer."

Farm Profits Would Increase

The NNPBD says that farmers could make more profit by reducing their use of nitrogen fertilizers and substituting nitrogen fixed from the atmosphere by legumes. The analysis by Olson et al. (1982) is cited as support for this view. In this analysis it was found that changing U.S. agriculture from conventional farming to organic farming, with exports sufficient in both instances to require the use of almost all available cropland, would result in an estimated total increase of $14 billion in farm profits for the major crops studied.

The contention about increased profitability is probably correct, but the reason seems more likely to be an increase in prices of the crops than the decrease in cost of production, which the NNPBD favors as the reason. The NNPBD does not call attention to the fact that in the analysis by Olson et al. the estimated U.S. prices for the crops studied ranged from 60 to 283% higher under the organic farming system than under the conventional high-export system. The higher prices were no doubt a result of the low production with the organic system. The percentage increase in price of a commodity normally exceeds the percentage decrease in supply, so that for moderate decreases in supply the total value of the commodity increases.

The large financial benefit to farmers from changing to organic farming in the analysis by Olson et al. (1982) was a consequence of the assumption in their analytical conditions that all farmers were using either the organic system or the conventional system. If organic farming is more profitable than conventional farming under free-choice competitive conditions, farmers would move in that direction to benefit from the extra profit. The fact that few have done so indicates that an important reason that farmers have so largely abandoned legumes as sources of nitrogen and have gone to nitrogen fertilizers is that they perceived greater profit possibilities in the use of nitrogen fertilizers. As long as nitrogen fertilizers are available at a low price and farmers are free to use them as they wish, individual farmers cannot afford to lose the profit these fertilizers provide. This is true even though the aggregate value of the commodity they are producing declines as a consequence of the increased national production that results from the use of nitrogen fertilizers by the many farmers producing this commodity. If an individual farmer fails to use nitrogen fertilizers up to the quantity that corresponds to the maximum net profit, this farmer is merely foregoing part of the profit that could have been made with appropriate use of nitrogen fertilizers. The same of course may be said for legumes, which at one time were widely preferred over nitrogen fertilizers.

Production Costs Would Decrease

The second economic advantage given by the NNPBD as a reason for decreasing the use of nitrogen fertilizers and substituting legumes is that production costs would decrease, and American farmers then could compete economically with foreign producers. To buttress this argument, the NNPBD calls attention to the analysis by Olson et al. (1982) in which the total U.S. production costs for organic farming and conventional farming were estimated under the hypothetical conditions in which the export demand was sufficient to require the use of almost all the available land in both systems. Under these conditions, changing to organic farming decreased the total cost of producing the major crops studied by $2.5 billion nationwide.

Reducing the use of nitrogen fertilizers would of course decrease the cost of this crop production input. No direct cost that can be compared with the cost of nitrogen fertilizers is assigned to the legume nitrogen proposed as a substitute. The atmospheric nitrogen utilized by legumes is free, as is true also for that used in nitrogen fertilizer manufacture. Nonetheless, there are indirect costs. For nitrogen fertilizers, these include manufacturing costs and the cost of the natural gas used in production. For legume nitrogen, the indirect costs would include reductions in production of and income from nonleguminous crops. The legumes would remove from production some land that otherwise could be used to produce nonleguminous crops that could be sold to generate income. (The leguminous crops that leave the largest amounts of fixed nitrogen in the soil are mostly used on the farm as livestock feed and are not marketed to the extent characteristic of grain crops.) Part of the decreased production of nonleguminous crops would result from the nitrogen deficiency with legumes as the source of supplemental nitrogen. Legumes removed as crops rarely leave in the soil enough nitrogen to meet the needs of succeeding nonleguminous crops for more than 1 or 2 years. Some do not supply enough nitrogen for even one following crop.

Two important conditions that affect the ability of U.S. farmers to compete in the world market are the prices their products will bring in the United States and the cost of producing a unit of the product. Although farm profits probably would be increased by the higher prices noted in the preceding section for crops grown under the organic system, the higher prices would not enhance the economic competitiveness of U.S. farm products in the world market. Rather, the anticipated consequences would include decreased exports of U.S. agricultural products, increased imports of lower-priced foreign products, and the establishment of trade barriers to protect American agriculture against these imports.

For evaluating the likelihood that U.S. agricultural products would be purchased by foreign countries, the cost per unit of product is more appropriate than the total cost given by Olson et al. (1982). The aggregate production costs were $2.5 billion more in the conventional high-export alternative than in the organic alternative, due mainly to the fertilizers and pesticides used in the conventional system. For this extra $2.5 billion, the farmers produced an estimated 84% more wheat, 61% more corn, 208% more feed grains other than corn, and 223% more soybeans. These large increases in production suggest lowered unit costs.

A further inference regarding cost competitiveness on a per unit basis may be derived from a different comparison in the paper by Olson et al. in which the aggregate costs of organic farming were compared with those of conventional farming under circumstances in which exports in the conventional system were based on historical trends in world trade. In this comparison, the aggregate costs of producing the major crops studied were estimated to be $2.7 billion more with organic farming than with conventional farming. The reason for this is presumably that although no costs for commercial fertilizers and other processed chemicals would be incurred in the organic system, the shortfall of production and the increase in crop prices would encourage the planting of many more acres, and all these extra acres would have production costs. In the analysis by Olson et al., the production in the conventional system considerably exceeded that in the organic system, but the number of acres under production in the organic system was estimated to be 55% greater than in the conventional system. This version of the conventional system is probably more realistic for present circumstances than the one referred to by the NNPBD in which almost all the available land was cropped by conventional farming to supply high export demand. When compared with the historical-export-trend conventional system, the organic farming alternative evidently increased both the aggregate production cost and the production cost per unit of product. The specific costs per unit, however, cannot be calculated from the data included in the paper by Olson et al.

The strong emphasis on row crops as opposed to close-growing legumes in conventional farming promotes soil erosion on the land in production. At the same time, conventional farming reduces soil erosion on much relatively erodible land of low productivity that would be in production if organic farming were the national system (Barrons, 1988; see also Heffernan and Green, 1986). This beneficial effect is a consequence of the greater productivity and greater economic efficiency of conventional farming, and the tendency for the concentration of production on the best land. Although there are exceptions, this land generally has a relatively low erosion hazard.

There is no fixed answer to the question of the relative competitiveness of U.S. farmers under organic and conventional farming. The same is true for the use of nitrogen fertilizers versus legumes. Both answers depend upon the conditions. To judge from farmers' current practices, which reflect their efforts to turn a profit as they compete in the marketplace with other farmers, they would be losers with organic farming for the time being, and they would be losers to forego the use of nitrogen fertilizers, even with crop values as low as they are.[2] But the profitability of using nitrogen fertilizers obviously depends upon their cost. If their cost were high enough relative to crop values, little or no profit would result from their use, and farmers would stop using them. This was the situation that existed for most farmers in pre-World War II days, when only relatively small amounts of nitrogen fertilizers were used, and the national agricultural system approached what now would be called organic farming.

[2] The great increase in nitrogen fertilizer usage occurred prior to 1981. From 1981 onward, the consumption has remained at about 11,000,000 short tons annually, except for decreases in 1983 (the year of the "payment-in-kind program") and 1986 and 1987 (when the acreage-reduction program was taking land out of production). The use on corn, which receives about half of the nitrogen used in fertilizers, has ranged from 132 to 140 pounds per acre in the 1981 to 1987 period.

Taxpayers' Costs Would Decrease

The third point in the NNPBD's list of economic advantages from reducing nitrogen fertilizer use and increasing the use of legumes as a substitute is that the cost to taxpayers would decrease. The NNPBD quotes information from the Conservation Foundation to the effect that in 1986 taxpayers bought 28% of all fertilizer and 40% of all pesticides used on corn and wheat.

The NNPBD's statement that "Nitrogen fertilizer is a major factor in crop surplus payed for by the taxpayer . . ." is probably correct, but this is not the whole story. If nitrogen fertilizer use were reduced or eliminated, crop production would indeed decline, and surpluses would be reduced. But taxpayers would not necessarily be spared. According to the analysis by Olson et al. (1982), adoption of the organic farming system would increase farm profits by $14 billion for the major crops studied. The reason is that the estimated increases in crop prices ranging from 60 to 280% for the crops studied were more than enough to offset the percentage decreases in total production. The consequence thus would be that although taxpayers might not be assessed through taxes to pay for crop surpluses, they would pay for the lack of surpluses through increased prices for agricultural commodities. If the decreased supply and higher prices of U.S. agricultural commodities were to lead to trade barriers to keep out lower-priced foreign commodities, as suggested in a preceding section, taxes would not be involved, but consumers would be called upon to forego access to foreign products as a source of relief from the higher prices of U.S. commodities.

The principal benefits from the yield-increasing, efficiency-enhancing advances in agricultural science and technology have not been captured by farmers. Rather, the prime beneficiaries have been consumers, who have benefited from the lower commodity prices. Annual rates of return to the public on agricultural research expenditures are of the order of 50% (Evenson et al., 1979). Failing to use the knowledge developed through this research reduces returns to the public, but it will generally increase farm profits.

The Legume Alternative

The NNPBD looks upon legumes as "a complete alternative" to nitrogen fertilizers for farmers. There are both quantity and quality aspects to this issue.

From the quantity standpoint, legumes provide to succeeding crops some nitrogen that they have captured from the atmosphere. The quantities of fixed nitrogen added to the soil depend upon the nature of the leguminous crop and other factors, but they are rarely enough, when added to the nitrogen made available to plants from the soil organic matter, to meet the full nitrogen needs of succeeding nonleguminous crops for more than 1 or 2 years, as noted previously. Legumes thus have limited quantitative capabilities to supply nitrogen for other crops.

The NNPBD gives no details on the qualitative aspect, but to judge from the extensive comments on the hazards of nitrate and the consistently favorable light in which legumes are presented, it appears that the nitrogen supplied by legumes is viewed as being superior in some way to the nitrogen supplied by commercial fertilizers. The end product of microbiological transformation of legume nitrogen in the soil is nitrate, as is also true for urea and other fertilizers that supply nitrogen in forms other than nitrate. If similarly distributed in the soil, nitrate derived from legumes is lost just as readily as nitrate derived from commercial fertilizers.

From the standpoint of loss from the soil, legume nitrogen has the advantage of being converted to nitrate rather slowly (Ladd et al., 1981). Therefore, under some conditions, the amount of nitrogen lost from fertilizer-derived nitrate may greatly exceed the loss from an equal addition of legume nitrogen (Muller, 1987). There are also other conditions under which the nitrogen lost from legume-derived nitrate may exceed the loss from an equal addition of fertilizer nitrogen (Adams and Pattinson, 1985).

Legumes that are planted in solid stands, as is generally true of alfalfa and clovers, are well recognized for their value in controlling soil erosion in comparison with row crops, such as corn and cotton. Not all legumes have this beneficial effect. For example, soybeans are recognized as erosion enhancers. They generally are planted in rows, and they loosen the soil so it is more susceptible to erosion.

From the standpoint of crop composition, it is principally the leafy vegetables, such as spinach, from which most of the dietary nitrate is derived. The greater the supply of nitrate in the soil, the greater is the concentration of nitrate in the leaves. Whether the nitrate concentration in the leaves is greater with legumes or fertilizers as the source of nitrogen will depend mostly upon how much nitrate the sources supply and when it is available. The nitrate content generally may be greater with nitrogen supplied by fertilizers than legumes because legumes have natural limitations on their nitrogen supplying capability and may not provide as much nitrogen as the succeeding crops can use efficiently in increasing growth. When nitrogen fertilizers are as economical as they are at present, however, they can be used in large enough quantities to produce nearly the maximum yield before the maximum economic return is exceeded.

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