A REVIEW OF NITROGEN DIOXIDE PNEUMONIA, A RECENTLY DISCOVERED MALADY IN SILO FILLERS

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The first two recognized cases of this disease, which I reported, occurred August 27, 1954. I have chosen to call this condition "Nitrogen Dioxide Pneumonia". This disease, however, is not confined to people who fill silos, but afflicts others in many occupations and places and, probably, is a factor in other obscure respiratory illnesses.

There have been nine other reported cases of NO_2 pneumonia in silo-fillers since the first two cases in 1954. This is 11 known cases.

There are four other names associated with this condition: Silo Filler's Disease, Farmer's Lung, Thresher's Lung, and Silage Gas Poisoning.

Nitrogen dioxide gas also has been described as a health hazard in the following occupations: Manufacture of Nitric Acid, nitration of cellulose and other organic materials as in the manufacture of explosives, dyes, lacquers, and certain types of film and celluloid, in the bleaching of cotton and raw silk, in the metal industry doing etching with aqua regia, cleaning of tanks and towers, decomposition of artificial fertilizers, manufacture of sulfuric acid, welding with an acetylene torch or electric arc. Inhalation of smoke from burning X-Ray films has caused the disease.

An important place where we should look for the possibility of Nitrogen Dioxide Pneumonia is in smog.

The etiology of the condition in silo fillers: The presence of a concentration of nitrates below 0.5% in growing plants, such as corn and alfalfa, is a normal finding. Some of the factors which increase the amount of nitrates to be found in the plants are as follows: No. 1: High nitrate soils due to fertilization, No. 2: Drought, particularly if it occurs when the plants are relatively immature. No. 3: Increasing light intensities.

These same nitrates which get into the cornstalks, incidently, and then cause nitrogen dioxide pneumonia after fermentation, also cause another disease in humans. Many farms and some of the shallow wells on farms have had enough nitrite and nitrate contamination to impair the health of both men and animal. This comes from the use of organic or commercial fertilizer in fields near the wells. There have been numerous reports of methemoglobinemia in infants where their formulas were prepared with water from wells with a high nitrate content.

Other consequences of high nitrate in forage and silage might be mentioned in passing. One is nitrate forage poisoning in cattle. Another is the explosion of silos. There also has been confirmation of the existence of Nitrogen Dioxide Pneumonia in cattle; and this is very interesting, because we think this is caused by the fermentation of silage in the cows' stomachs. The cows then belch up their own NO_2 and inhale it.

The thought might occur to you that, inasmuch as cattle can get fatal methemoglobinemia and nitrosohemoglobinemia by eating cereal grasses such as oats, wheat, barley, and corn, it is possible that people may also, at times, get into the same trouble. Is it possible that some people are suffering from nitrate poisoning caused by the ingestion of cereals grown in drought-stricken lands?

How does potassium nitrate in the corn plants change into nitrogen dioxide? First of all, potassium nitrate in the corn plant, by anaerobic fermentation, is changed into potassium nitrite and oxygen. The nitrite in the silage combines with organic acids, such as lactic acid, to form nitrous acid (HNO_2). As the temperature of the ensilage rises with fermentation, the HNO_2 decomposes into water and a mixture of nitrogen oxides, which include NO, NO_2, N_2O_3, N_2O_4, and N_2O_5. Nitrogen dioxide, which is NO_2, and N_2O_4, which is its dimer, are the oxides that are really responsible for the toxicity of this gas in silo filler's disease. In the lung, the five oxides all change to NO_2 and N_2O_4. These, then, react with water in the respiratory tract to produce nitric and nitrous acids. This is why I call this Nitrogen Dioxide Pneumonia.

Nitrogen dioxide is toxic in concentrations above 5 parts per million and is detectable by its odor above 5 parts per million, but is not visible as a heavy yellowish-brown gas, until the concentration reaches 75 - 150 parts per million.

All the known cases of Nitrogen Dioxide Pneumonia have occurred after a latent interval which may vary from hours to days. This could be due in part to the mucous barrier that exists between the air and the actual tissues of the bronchial tree. In addition, the latency is caused by the duration of time it requires for an inflammatory response to develop once the acids have reached the mucosal cells. It has been suggested that histamine release may play a part in the exudative phase.

The clinical picture in humans can be divided into six types:

1. Acute pulmonary edema (or fulminating pneumonia)
2. Acute Bronchopneumonia
3. Bronchiolitis fibrosa obliterans following sub-acute bronchopneumonia. The importance of the X-Ray picture in bronchiolitis fibrosa obliterans lies in the similarity of its appearance to miliary tuberculosis.
4. Bronchitis
5. ...with a question mark...Pulmonary fibrosis (Late sequela)
6. Possible bronchial asthma. (Late sequela)

The differential diagnosis of silage gas poisoning: You have a patient coming into the hospital who has been exposed to a gas in a silo and now has a respiratory illness.

What kind of gas is it? There are three kinds of silage gas poisoning: One is due to carbon dioxide, one is simple oxygen lack, one is the oxides of nitrogen. Under ordinary circumstances, when there is sufficient

moisture for the production of normal plants, high concentrations of nitrates do not occur in the forage plants and the chemical reactions that produce toxic concentrations of NO_2 do not take place. "Farmer's Lung", also known as "Thresher's Lung", should be differentiated from this condition. According to Dickey and others, this is an acute pneumonitis due to hypersensitivity to substances in moldy hay dust.

Treatment for NO_2 pneumonia:

1. Steroids. Three of the cases reported received steroids with ensuing dramatic improvement. These patients recovered. However, four other survivors of this disease were not treated with steroids and, at the time of this writing, are alive and well. There has been a total of four deaths.

2. Oxygen is imperative. Pressure oxygen should be of value in some cases.

3. Bronchodilators.

4. Digitalis. Circulatory failure secondary to the pulmonary failure will occur, and Digitalis may be of some temporary benefit.

5. The detergent aerosols can be used.

6. Antibiotics have been used to prevent secondary infection and to treat secondary bacterial bronchitis and pneumonia, and this is definitely important.

7. Atiopine, I.V. fluids, venesection are contra-indicated. Sedation and narcotics should be cautiously administered.

It should be emphasized that, in patients with bronchiolitis fibrosa obliterans, recovery is considerably hastened by steroids and, in some cases, death actually prevented.

I would like to present a hypothesis which may be of some value in preventing this disease. In the first place, we know that this pneumonia is caused by nitrous and nitric acids. NO_2 and N_2O_4 change to these acids after they are inhaled.

Secondly, we know that there is a latent interval which, in part, may be due to the mucous barrier between the atmospheric air and the bronchial mucosa.

It would seem then, that the application of a neutralizing agent such as sodium bicarbonate, to the mucosa of the respiratory tract, during the latent interval, would be a rational method of preventing tissue destruction. The manner in which this could best be performed would be by aerosol. A preparation is available which not only includes a physiological amount of sodium bicarbonate but which also includes a safe detergent "Alevaire). I believe that if this were administered in time to patients known to have been exposed to the fumes of nitric acid or other nitrates, or to silage gas containing nitrogen dioxide, the treatment should prevent or minimize this disease. The end.