

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET - - CHICAGO 10, ILL.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - Eight dollars per annum in advance

Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.

SATURDAY, SEPTEMBER 18, 1943

SALMONELLA INFECTIONS

The genus *Salmonella* comprises gram-negative and non-spore forming bacilli with known microscopic and cultural characteristics and with considerable pathogenic significance for human beings and animals. In a recent review of the present status of the *Salmonella* problem, Bornstein¹ says that the human diseases caused by members of this group may be termed *Salmonella* fever, septicemia or gastroenteritis regardless of the type that causes the infection, although there are differences in relative incidence.

The clinical course of salmonella fever is milder and less typical than that of typhoid. With few exceptions fever and malaise are the dominating symptoms, usually lasting from one to three weeks. In some cases leukopenia is present. Not infrequently the appendix is removed. Blood cultures may be positive early in the disease and stool cultures may be positive at the onset or may remain negative for weeks. In the septicemic forms the distribution and pathologic effects of *Salmonella* are similar to those caused by the pyogenic cocci. Intestinal involvement is usually absent in adults. Diagnosis may be difficult, but blood invasion is evident from the high remittent fever and early finding of positive blood cultures or from the localization of the infection in various tissues. Gastroenteritis from *Salmonella* is rarely fatal in adults except in those who have been weakened by other disease or old age. There is an interval of eight hours to one day between the consumption of the contaminated food and the first symptoms. Vomiting is usually the first sign, but it may be absent. Diarrhea in adults is less severe than in dysentery and the stools are rarely bloody. In infants there is a greater variety of manifestations than in adults. With proper care the disease usually subsides in less than one week. Surgical removal of purulent lesions or drainage of abscesses produces good results comparable to those obtained in other pyogenic infections.

1. Bornstein, Siegbert: The State of the *Salmonella* Problem, *J. Immunol.* **46**: 439 (June) 1943.

Treatment of these infections with polyvalent anti-*Salmonella* serum has not been tried extensively and preliminary trials have been inconclusive. Vaccine therapy of acute infections is not of value and may be harmful. Chemical interest has recently been concentrated on sulfonamide therapy. Choice of drug varies with the clinical picture and the type of *Salmonella* causing it. Although some of the sulfonamides appear promising, final conclusions cannot yet be drawn.

Bornstein points out that these infections constitute an important public health problem. Food which has not been prepared or kept with necessary cleanliness may become the source of *Salmonella* infection. Eggs should not be consumed in a raw condition as in mayonnaise. The control of *Salmonella* infection in animals is a veterinary problem of importance. The human source of infection must not be neglected. Bacteriologic examinations in all cases of diarrhea and their contacts as far as possible together with complete reporting of bacteriologically diagnosed *Salmonella* infections would, after a few years, clarify the question of relative public health importance of the various *Salmonella* types. It would doubtless lead also to the establishment of much more effective control measures.

CHRONIC FLUORINE INTOXICATION

Distribution of the element fluorine is so widespread throughout nature that a small intake of the element is practically unavoidable. Fluorides are general protoplasmic poisons, probably because of their capacity to modify the metabolism of cells by changing the permeability of the cell membrane and by inhibiting certain enzyme systems. The exact mechanism of such actions is obscure. The sources of fluorine intoxication are drinking water containing 1 part per million or more of fluorine, fluorine compounds used as insecticidal sprays for fruits and vegetables (cryolite and barium fluosilicate) and the mining and conversion of phosphate rock to superphosphate, which is used as fertilizer. The fluorine content of phosphate rock is about 4 per cent. During conversion to superphosphate, about 25 per cent of the fluorine present is volatilized and represents a pouring into the atmosphere of approximately 25,000 tons of pure fluorine annually. Another source of fluorine intoxication is from the fluorides used in the smelting of many metals, such as steel and aluminum, and in the production of glass, enamel and brick.

The known effects of chronic fluorine intoxication are those of hypoplasia of the teeth, which has been called mottled enamel, and of bone sclerosis. The classic epidemiologic studies of McKay¹ clearly demonstrated the relationship of the fluorine content of the domestic water supply to the anomaly of mottled enamel of the teeth. The condition is now known to be endemic in isolated communities on every continent. In the United

1. McKay, F. S.: Mottled Enamel: The Prevention of Its Further Production Through a Change of the Water Supply at Oakley, Ida., *J. Am. Dent. A.* **20**: 1137 (July) 1933.

States there are about four hundred known endemic areas distributed among twenty-eight states. Dean and McKay² succeeded in the unique epidemiologic experiment of arresting the production of the endemic mottled enamel at Oakley, Ida., Bauxite, Ark., and Andover, S. D., by changing the common water supply from one containing amounts of fluorides toxic to calcifying dental enamel to one the fluoride content of which does not exceed the permissible maximum, i. e. 1 part per million. Children using domestic waters containing as little as 1 part per million of fluorine experience only a half to a third as much dental decay as comparable groups using fluoride-free water, such as the Lake Michigan or the Mississippi River waters. The same inverse relationship has been observed in England, South India and North Africa. Apparently teeth require traces of fluorine for optimum dental health, although excessive amounts may result in the disfiguring condition known as mottled enamel.

Møller and Gudjonsson³ described in 1932 a peculiar form of bone sclerosis in workers exposed to cryolite dust for a number of years. An exhaustive study of the various aspects of fluorine intoxication was made by Roholm.⁴ Loss of weight, impairment of growth in young persons, loss of appetite, anemia and cachexia are mentioned among the general symptoms of chronic intoxication. Cases of fluorine osteosclerosis were reported by Wilkie,⁵ Bishop,⁶ Shortt,⁷ Pandit and his associates⁸ and Linsman and McMurray.⁹ The bone changes are those of thickening of the bone lamina and an increase in the whiteness of the bone shadows on the roentgenogram to an actual opacity of the bones and calcification of the ligamentous attachments. Anemia was present in some of the cases and was probably due to the displacement of the bone marrow by thickened trabeculae. In Pandit's experience, continued residence over fifteen years in the endemic area was necessary in the case of adults to bring about symptoms of chronic intoxication. The incidence and severity of the disease had a definite relationship to the economic and nutritional status of the community. A pronounced deficiency of the vitamin C factor in the diet was especially associated with a severe incidence of the disease. Factors other than the amount of fluorine in the water supply may assume a contributory role in the development of chronic fluorine intoxication.

VITAMIN DEFICIENCY BY INTERFERENCE

Vitamin deficiency may occur in man or animals despite the presence in the diet of a normally adequate amount of the appropriate vitamin. Perhaps the most widely known example of this is the occurrence of a vitamin K deficiency—characterized by a low prothrombin level in the blood and a consequent tendency to hemorrhage—in man or animals when bile salts are prevented from reaching the intestine. Whether present in the diet or synthesized by intestinal micro-organisms, fat soluble vitamin K is of little value to the body in the absence of these salts, which are necessary for its proper absorption. Other examples of such "secondary vitamin deficiencies,"¹ include avitaminoses observed in animals fed a diet containing a constituent which destroys or makes unavailable a particular essential food factor.

Results of studies on the biotin problem have greatly contributed to our knowledge of vitamin deficiency by interference. The biotin deficiency syndrome was first observed in rats fed a diet containing a large percentage of uncooked egg white. The deficiency symptoms exhibited by the animals were first thought to be due to toxicity of uncooked egg white, but subsequent investigation revealed that something in the egg white combined with the biotin and thereby made it unavailable. The interfering substance proved to be a protein, which has since been given the descriptive name avidin.² Cooked egg white is not at all antagonistic to biotin. Biotin deficiency can be experimentally produced in human subjects by incorporating large amounts of dehydrated egg white (200 Gm. a day) in their diet for several weeks.³ However, biotin deficiency probably never occurs normally in man in the manner in which it was experimentally produced.

The story of Chastek paralysis⁴ in silver foxes discloses an extremely interesting example of avitaminosis by interference. When the meat in the diet of foxes being raised for their fur was replaced, for economic considerations, with 10 per cent or more of raw fish, hundreds of animals became ill for no apparent reason and died. The syndrome was characterized by anorexia, weakness, progressive ataxia and spastic paraplegia. Death followed within eighteen to seventy-two hours after onset of the neurologic symptoms. Concerted efforts of a number of investigators have unraveled the story of what happened on the fox farm of Mr. Chastek and on numerous other fox farms in this country. Raw fish has been found to destroy vitamin B₁. Foxes

2. Dean, H. T., and McKay, F. S.: Production of Mottled Enamel Halted by a Change in Common Water Supply, *Am. J. Pub. Health* **29**: 590 (June) 1939.

3. Møller, F. P., and Gudjonsson, V.: *Acta radiol.* **13**: 269, 1932.

4. Roholm, K.: "Fluorine Intoxication," London, H. K. Lewis, 1937.

5. Wilkie, J.: Two Cases of Fluorine Osteosclerosis, *Brit. J. Radiol.* **13**: 213 (June) 1940.

6. Bishop, P. A.: Bone Changes in Chronic Fluorine Intoxication, *Am. J. Roentgenol.* **35**: 577 (May) 1936.

7. Shortt: *Indian J. M. Res.* **25**, 1937.

8. Pandit, C. G.; Raghavachari, T. N.; Rao, D. Subba, and Krishnamurti, V.: Endemic Fluorosis in South India: A Study of the Factors Involved in the Production of Mottled Enamel in Children and Severe Bone Manifestations in Adults, *Indiana J. M. Res.* **28**: 533 (Oct.) 1940.

9. Linsman, J. F., and McMurray, C. A.: Fluoride Osteosclerosis from Drinking Water, *Radiology* **40**: 474 (May) 1943.

1. Jolliffe, Norman: Conditioned Malnutrition, *J. A. M. A.* **122**: 299 (May 29) 1943.

2. Eakin, R. E.; Snell, E. E., and Williams, R. J.: Concentration and Assay of Avidin, the Injury Producing Protein in Raw Egg White, *J. Biol. Chem.* **140**: 535 (Aug.) 1941.

3. Sydenstricker, V. P.; Sengal, S. A.; Briggs, A. P.; De Vaughn, N. M., and Isbell, Harris: Observations on the "Egg White Injury" in Man and Its Cure With a Biotin Concentrate, *J. A. M. A.* **118**: 1199 (April 4) 1942.

4. Green, R. G.; Carlson, W. E., and Evans, C. A.: A Deficiency Disease of Foxes Produced by Feeding Fish: B₁ Avitaminoses Analogous to Wernicke's Disease of Man, *J. Nutrition* **21**: 243 (March) 1941.