Volume Thirty-one

May, 1960

Number Eight

NUTRITION AND INFECTION

by NEVIN S. SCRIMSHAW, Ph.D., M.D.
Institute of Nutrition of Central America and Panama (INCAP)
Guatemala, C. A.

There are a large number of laboratory, clinical and field observations which demonstrate that the severity and outcome of infections is frequently worsened by malnutrition. The extensive literature includes so many conflicting and inconclusive studies, however, that the significance of the research carried out under circumstances where the effect of malnutrition can be clearly demonstrated is obscured. Furthermore, the adverse metabolic consequences of infections are frequently dismissed as relatively unimportant. The great majority of persons in the technically developed countries are sufficiently well nourished that these misconceptions do harm only in individual cases, but in the developing countries which have the greater part of the world's populations, both the effect of nutritional status on infection and that of infection on nutritional status are of tremendous significance.

Mortality in children 1-4 years of age in such countries varies from 20 to more than 40 times higher than in North America and Western Europe. In Guatemaia where the figure was 42.1 per cent in 1955, follow-up of individual deaths in one group of rural villages showed that 38 per cent of the children died with kwashiorkor and 25 per cent from disease of the digestive system, primarily acute infectious diarrhea'. In nearly every kwashiorkor case an episode of infectious diarrhea, measles, chicken pox, or other acute infections had been superimposed on underlying protein malnutrition several weeks before and seemed to have precipitated the appearance of kwashiorkor syndrome. Deaths in 24 to 48 hours from acute diarrheal infections were common although they are almost unthinkable in well nourished children. Furthermore, nearly all of the remaining 37 per cent were attributable to infections or combinations of infections which would not ordinarily be fatal to a well nourished child.

The way in which an infection can precipitate an acute nutritional crisis is now fairly well understood and documented. It has been known since the early part of the century that such severe bacterial infections as typhoid and paratyphoid fever, meningitis, pneumonia, malaria, streptococcal infections, and tuberculosis cause severe and prolonged loss of nitrogen due primarily to the toxic destruction of intracellular protein. Recent INCAP studies have shown not only that mild chicken pox is sufficient cause for a child to go into negative nitrogen', even when receiving an apparently adequate intake of protein, but also that an adverse effect on nitrogen balance can be consistently detected' with as mild and asymptomatic a viral invasion as that produced by yellow fever vaccine. The metabolic effect of any infection is compounded by the associated anorexia which results in decreased food intake and by the tendency of the mother to remove solid food and substitute thin starchy gruels when the child is sick. The nutrient loss in infections has particular significance for young children because of their relatively high requirements for protein and other nutrients per kilogram of body weight.

The mechanisms whereby nutritional deficiencies influence resistance to infectious diseases are much less completely known and are the subject of considerable controversy. They include the following:

1. Reduced capacity to form antibodies.

The potential mechanism which has received the greatest research attention is nutritional interference with antibody formation. The extensive studies of Cannon and several other investigators have left no doubt that severe protein deficiency in rabbits and dogs diminishes response to specific antibodies and those of Axelrod and other workers have demonstrated that specific vitamin deficiencies can interfere with both primary and secondary antibody response to antigen in rats and rabbits. For these observations in experimental animals to have practical application to clinical medicine, deficiencies of a severity comparable to that used in successful animal experiments must occur in human populations. These conditions are not often met in the technically advanced countries, although Wohl et al. found the antibody response to typhoid vaccine greatly slowed in 88 patients with serum albumin values below 4 grams per 100 ml. In children with severe malnutrition in Mexico, Olarte et al.' found a significantly reduced response to diphtheria antitoxin. More studies are needed to determine the practical importance and general applicability of these observations.

2. Interference with the production or activity of phagocytes.

A number of nutritional deficiencies including vitamin A", B-complex and ascorbic acid" appear to interfere with phagocytic activity. Furthermore, deficiencies of folic acid" and protein¹² when sufficiently severe interfere with leucocyte production. It is well known that one factor in the

(Continued on Page Four)

ABOUT THE AUTHOR

Dr. Scrimshaw is the 1960 recipient of the Osborne and Mendel Award for his work on malnutrition in children at the Institute of Nutrition of Central America and Panama (INCAP). He is the Director of INCAP as well as Regional Advisor in Nutrition, Pan American Health Organization, and Regional office for the Americas, World Health Organization.

Dr. Scrimshaw received his Ph.D. degree from Harvard University and M.D. from the University of Rochester School of Medicine where he also was a post doctorate fellow; interned at the Gorgas Hospital, Canal Zone; later was assistant resident physician in Obstetrics and Gynecology, Strong Memorial Hospital; and was a Merck National Research fellow at Rochester. Dr. Scrimshaw and coworkers have published papers extensively on nutrition.



MEATY ORSELS

Studies in Iowa show that diets of pregnant women do not differ widely, except in quantity, from their regular life-time dietary habits. Those with good diet habits usually have had good diets most of their lives while those who have had poor diets usually continue to eat poorly during pregnancy.

One tendency for "fatty" adolescents is "just to sit" which encourages the deposition of fat. However, their lean contemporaries are very active. Lean teen-agers on an average have a total intake of 4600 calories per day compared to 3400 for the heavier ones.

A serving of chop suey supplies about 25 grams of protein and 380 calories when made with pork, onions, celery and bean sprouts. One-half cup of rice served with it contributes another 2.1 grams of protein and 102 calories.

Americans are growing taller, perhaps because of higher medical and nutritional standards. Army recruits in 1943 averaged 5'8.3" in height, in 1946 they averaged 5'8.6" and at the close of the Korean War some groups averaged 5'10".

The death rate in the U. S. has been reduced from 17.2 per 1,000 in 1900 to 9.4 per 1,000 in 1956. Recently there has been about a 1.5 per cent increase in net population per year.

Only a few "earn" good health. One has to accept his responsibility and work to attain it. Good nutrition is vitally important to good health.

The restriction of protein in reducing diets may be harmful. According to N. Jolliffe, M.D., it is axiomatic that every reducing diet should contain sufficient protein to guard against any deleterious effects of impaired nutrition.

FOR ADDITIONAL COPIES

If there is someone in your organization who would like a regular monthly copy of Food and Nutrition News, notify us and we will be pleased to add his name to our mailing list. Or if you wish additional copies of Food and Nutrition News for distribution, write to the National Live Stock and Meat Board, 407 South Dearborn St., Chicago 5, Illinois.

Nutrition Pot-Pourri . . .

Suggestions for Preventive Geriatrics

Nutrition is a vital, active process of biochemistry on which every cell of the body depends for nourishment and maintenance throughout life. It may determine whether a person lives to be 65 or 85. Therefore a person has to begin early in life for healthy senior citizenship.

In recent nutrition programs in metropolitan areas it was found that among senior citizens the diets of those with lower incomes were more likely to be poor. Many had inadequate nutritional intakes, especially of vitamin A and protein.

When overweight was a problem it was found that many individuals reduced the total calories in the diet but also omitted essential nutrients needed by the body. In general, they did not realize that nutrition was related to the feeling of well-being and vitality.

An older person who is reducing calorie intake needs to be selective in choosing foods containing protein and adequate amounts of calcium, iron, B vitamins, vitamins A, C and D.

Studies show that the NRC allowances are not excessive and that women between the ages of 30 and 70 need about the same amount of nutrients.

Most senior citizens welcome new ideas on integrating the correct selection of foods into interesting, appetizing, low-cost meals.

Health Problem—Fat Child

The obese child is a school health problem in Britain, according to Harvey Flack, M.D.

Fifty years ago for each 1,000 children, 130 were undernourished, 40 had rickets, 100 had defective footwear, 50 had inadequate clothing and 30 had heart disease. Today, out of each 1,000, there are only 17 in unsatisfactory physical condition, and two with heart disease.

Instead, obesity is a more prevalent problem. Of a recent group of 94 children sent to a nutrition clinic, 90 of them were overweight. Only four had some nutritional lack in their diets.

According to Dr. Flack and his coworker Dr. Eric J. Trimmer, children get fat from overeating, either from habit or from emotional disturbances. Habit overeating is more common and is usually a result of family habits. Three-fourths of fat children have a fat mother or father. Overeating due to habit may begin very early in life. Thus it is necessary to watch excessive gain and correct it at an early age.

Weight gain due to emotional problems should be dealt with psychologically and not with diet alone. The children's school work was better as the weight decreased, exercise increased and psychological adjustment improved.

Want Breakfast Ideas?

One reason given for poor breakfast habits is lack of time. The time is there and would be taken if enough interest were stimulated. Variety and appetite appeal provide the key to getting the breakfast skipper or skimper to sit down to an adequate meal at the start of the day.

The homemaker can build new interest in the morning meal by serving some of the following: rib steak, lamb cutlets, pork chops, broiled Canadianstyle bacon, broiled ham with boiled, fried, shirred, poached, baked or scrambled eggs; an omelet with jelly, green peppers, chives, or chipped meat; roast beef hash with poached egg; chipped beef served on toast, biscuit or potato. In addition, all kinds of smoked sausages or luncheon meats may be used for breakfast starters. Muffins, hot breads, pancakes plus a favorite jelly may be added for more appeal. Add a rich source of vitamin C such as grapefruit or orange and the menu is complete for a vigorous start to a bright

The Nutritive Value Of Cooked Meat

For you who need data on the nutritive value of cooked meat as it is consumed and eaten today you may order the publication, "Nutritive Value of Cooked Meat." This report, written by Ruth M. Leverton, Ph.D., and George V. Odell, Ph.D., is based on their research at the Oklahoma Experiment Station.

Common retail cuts of meat were analyzed in three portions—the extremely lean portion, the lean-marbled-with-fat portion and the fat portion. The results of these determinations are particularly valuable for those who calculate diets of persons who have different patterns of eating meat and fat.

The tables in this report present data on the weight yield of lean, marble, fat and waste portions; values for the energy, protein, fat, moisture, ash, phosphorus and magnesium for individual cuts; the range in energy, protein and fat content for cuts of cooked meat, and the value for the B-vitamins, calcium, potassium, and sodium content of selected cuts.

For example, one will find that $3\frac{1}{2}$ ounces cooked top round of beef contributes 262 calories, 37.7 grams of protein and 11.2 grams of fat if the marbled portion is eaten. If the lean only is eaten it would supply 216 calories, 39.3 grams protein and 5.3 grams of fat.

"The Nutritive Value of Cooked Meat" may be ordered from the National Live Stock and Meat Board, 407 South Dearborn Street, Chicago 5, Illinois, for 75 cents per copy.

Nutrition and Health Series

Other B vitamins and Ascorbic Acid

by RITA CAMPBELL WEAVER
Director, Department of Nutrition
National Live Stock and Meat Board

In addition to thiamine, riboflavin and niacin there are several other members of the vitamin B complex which are known to function in human nutrition. These will be reviewed briefly along with vitamin C or ascorbic acid.

Vitamin B₆ or pyridoxine was identified as a separate portion of the B complex in 1938. A deficiency of this vitamin may cause anemia, weakness, dermatitis and nerve disorders. It is known to be needed by both infants and adults. It has been estimated that 1 to 2 mg. is needed daily. This amount should be provided by an average diet. The best food sources of this vitamin are pork and variety meats; lamb, veal, beef and fish also supply it, as well as legumes, potatoes, bananas and oatmeal.

Since the discovery in the 1920's that liver was effective in the treatment of pernicious anemia, researchers have been searching for the constituent of liver which was responsible.

In 1948 vitamin B_{12} was isolated from liver and found effective in the treatment of pernicious anemia. Liver and kidney are the richest food sources of this vitamin followed by milk, muscle meats and fish.

The word pantothenic means "wide-spread" and was applied to the vitamin, pantothenic acid, because it occurs in a wide variety of foods. A deficiency of this vitamin in animals may cause emaciation, loss of hair and damage to the internal organs. It is provided by liver, kidney, heart, salmon, eggs and yeast. Medium amounts are provided by

pork, beef tongue, peanuts, broccoli, and mushrooms.

A deficiency of the B vitamin, biotin, has been produced in experimental animals by feeding raw egg white. Raw egg white contains avidin which unites with the biotin making it unavailable. Large amounts of biotin are provided by liver and other variety meats, yeasts, mushrooms and peanuts.

Many foods supply the B vitamin, para-aminobenzoic acid. This vitamin is important to growth in experimental animals.

Inositol, another of the B vitamins, is best known for its relationship to fat metabolism and the prevention of abnormal fat deposits in animals. Variety meats, and fruits and vegetables supply this vitamin.

The chemical name, "pteroylglutamic acid" is seldom used in connection with another of the B vitamins. More frequently it is called folic acid. It occurs in liver, green leafy vegetables, meat, fish, nuts, legumes and whole grain bread and cereals. This vitamin has been used in the treatment of macrocytic anemia and tropical sprue.

Choline and betaine are two other factors sometimes classified as B vitamins. Choline is synthesized from the amino acid methionine in humans. These substances are believed to function in preventing fatty livers. A deficiency of choline is unlikely since it is present in many foods.

In addition to these factors there are 6 or 7 other possible B vitamins. These are factors which are described as essential for experimental animals but not known to be of significance to humans.

Scurvy, the ascorbic acid deficiency disease, is said to have plagued the crew of Vasco de Gama as they sailed around the Cape of Good Hope. In the 15th century many of Jacques Cartier's men in Canada also suffered from scurvy. During the first New England winter in the colonies, the pilgrims suffered from this disease

Of all the vitamins, ascorbic acid is the most unstable to heat, oxidation, drying and storage. This vitamin is needed for the formation and maintenance of body tissues. Weak capillary walls and hemorrhages may occur when there is a deficiency. Changes in the bones, teeth, gums, and slower wound healing may be other results.

Today scurvy rarely occurs in the United States. However, the tendency to bruise easily, slow wound healing and swollen painful joints may indicate that the vitamin C supply is inadequate. In the chart the major sources of ascorbic acid are shown. The citrus fruits—oranges, grapefruits and lemons head the list followed by broccoli, strawberries, tomatoes, cabbage, melons, potatoes and liver.

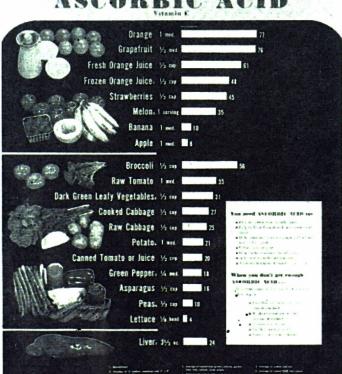
Research may some day reveal that additional B complex vitamins are needed by man. At present the "other" B vitamins described here are usually present in the average diet in sufficient amounts. To assure an adequate supply of the B vitamins and ascorbic acid each day the diet should contain meat, milk, eggs, citrus fruits and yellow and green leafy vegetables enriched or whole grain cereals and breads.

EDITOR'S NOTE

The illustrations in this series of articles are reproductions from a new set of colored "Food Value Charts." This 10 page set of 20"x30" charts is ideal for classroom, clinic or office use.

To order a set, send \$1.50 to: National Live Stock and Meat Board, Department NU 407 South Dearborn Street, Chicago 5, Illinois.







Meat and Meat Products, American Meat Institute Foundation, W. H. Freeman and Company, San Francisco, Calif. Pp. 438, Text edition \$8.00, trade edition, \$9.00.

This book, written by twenty-four research workers of the American Meat Institute Foundation, offers a concentrated and central source of scientific meat information. The two parts of the book, The Basic Science of Meat and The Science of Meat Processing, cover almost every phase of meat research results. The structure, histology, chemistry, microbiology, nutritive value, and palatability of meat are discussed. This

discussion includes the methods of analyses which would be of particular interest to those in meat research.

Mechanics of meat processing included are the quality factors, and preservation by refrigeration, freezing, thermal processing, dehydration, irradiation, chemicals and curing. Sausage products, packaging materials for meats and byproducts from meats comprise the remainder of the book.

"It is hoped that this book will be of broad general interest, and that it will be specifically helpful to scientists and executives in the meat and allied industries as well as to administrative and scientific personnel in universities and public agencies, and finally, that it will aid in the orientation and training of young scientists and students interested in the processing and preservation of meats," the preface states.

This book is recommended as an authoritative reference on meat and meat products.

greater susceptibility of children with kwashiorkor to intercurrent infections is the feeble leukocytosis.

3. Alteration of tissue integrity.

The metaplasia and keratinization of epithelium as a result of vitamin A deficiency is one example of the effect of dietary deficiencies on possible tissue barriers to microbial invasion. Other possible ways are increased permeability of intestinal or other mucosal surfaces, reduction or absence of mucous secretions, accumulation of cellular debris and mucus to give a more favorable culture medium, loss of intercellular substance, interference with normal tissue replacement and repair, loss of ciliated epithelium from the respiratory tract and increased fluid in the tissues as found in nutritional edema.

4. Nonspecific inhibition of microorganisms.

The bacteriocidal effect of blood serum and other body fluids and tissues is often impossible to relate to any specific mechanism. They possess a nonspecific bacteriocidal effect which is diminished by some form of malnutrition and which is independent of antigen-antibody reactions. For example Guggenheim and Buechler13 hrve shown that the peritoneal fluid of rats deficient in thiamine, riboflavin or vitamin A has a decreased capacity to destroy innoculated S. typhimurium. Patients with severe malnutrition have been found by Dawson and Blagg" to have little or no salivary lysozyme activity against a variety of infectious agents. No agreement exists, however, on the importance of lysozymes and less is known of the possible nature of other nonspecific antimicrobial substances.

5. Nonspecific resistance to bacterial toxins

There is no doubt from the work of Werkman et al.15 that rats suffering from deficiencies of vitamin A or Bcomplex vitamins are more susceptible than controls to diphtheria toxin, even when antitoxin production is equal and the rate of disappearance of injected toxin is normal. This influence of nutrition on nonspecific resistance to bacterial toxins has also been observed in scorbutic guinea pigs, rats deficient in vitamins A and D or vitamin B complex, and sheep on diets low in minerals and vitamins A and D16. Nothing is known of the occurrence of this phenomenon in human malnutrition.

6. Endocrine influences.

The field of endocrine involvement in the relationship between malnutrition and resistance to infection is almost wholly unexplored. Adrenalectomized animals and Addisonian patients are both very susceptible to infection and there is evidence that cortical hormones may have a direct inhibiting effect on certain endotoxins. The better resistance to infection characteristic of diabetes under modern management is believed by Pollack17 to be primarily due to the positive nitrogen balance achieved with protamine-zinc insulin in contrast to the huge nitrogen losses associated with diabetic ketosis.

The discovery that specific vitamin deficiencies may interfere with the proliferation of certain viruses' has aroused much interest because it represents a situation in which nutritional deficiencies are antagonistic to the growth of a microorganism rather than synergistic. The finding has no direct practical application to human nutrition, however, since deaths from secondary bacterial complications are the most frequent cause of death in virus infections and these would the most likely to be increased by the deficiency. Another much misinterpreted observation comes from the studies of Schneider19 comparing the mortality from Salmonella infections in rats with high, medium and low resistance to bacterial strains with high, intermediate and low virulence. Of the nine pairs of observations, only one group, the rats with intermediate resistance fed organism of intermediate virulence, showed a significant nutritional effect. This is precisely the most common situation under field conditions in human populations.

It should be emphasized that supplementation or improvement of an already adequate diet should not necessarily be expected to improve resistance to infection. Part of the scepticism regarding the importance of malnutrition in influencing the consequences of infection arises from disillusionment with the unjustified claims that the consumption of specific nutrient supplements would prevent or alleviate infections regardless of the adequacy of the habitual diet.

From a review of animal and human studies16, certain generalizations can be made. The relationship between malnutrition and infection is usually but not always synergistic. When malnutrition affects primarily the host, synergism is likely to occur, and where the effect is on the infectious agent, antagonism is common. Bacteria, rickettsiae and helminth infections are regularly synergistic with nutritional deficiencies while viruses are more often antagonistic. Protozoa may fall in either category. Of the specific nutrients, protein deficiency tends to produce synergistic effects but deficiencies of the other essential nutrients may be either synergistic or antagonistic depending upon the circumstances. The mistaken impression that antagonism, as used in the above sense, may somehow be of value in clinical or preventive medicine, as well as the failure to recognize the importance of synergism, is of little consequence where malnutrition is rare. Where both malnutrition and infection are serious, however, as they are in most tropical and technically underdeveloped countries, lack of recognition of the importance of synergism jeopardized health and education programs. For such areas, efforts to control both infection and malnutrition are essential to the successful prosecution of public health programs and may be a crucial factor in saving the lives of many thousands of children.

BIBLIOGRAPHY

1. Behar, M., W. Ascoli and N. S. Scrimshaw. An investigation into the causes of death in children in four rural communities in Guatemala. Bull. Wld. Hlth. Org. 19, 1093 (1958).

2. Peters, J. P. and D. D. Van Slyke. Quantitative clinical chemistry interpretations. V. I 2d ed. Baltimore, Williams & Wilkins Co.,

1946, p. 678.

3. Scrimshaw, N. S., D. Wilson and R. Bressani. Infection and kwashiorkor, J. Trop. Pediat. (in press).
4. Gandra, Y. R. and N. S. Scrimshaw. Unpublished data.

Cannon, P. R. Dietary protein and antimicrobic defense. Nut. Rev. 7. 161 (1949).

6. Axelrod, A. E. The role of nutritional factors in the antibody responses of the anamnestic process. Am. J. Clin. Nut. 6, 119 (1958).

7. Wohl, M. G., J. G. Reinhold and S. B. Rose. Antibody responses in patients with hypoproteinemia—with special reference to the effect of supplementation with protein or protein hydrolysate, Arch. Int. Med.

83, 402 (1949).
8. Olarte, J., J. Cravioto and B. Campos. Inmunidad en el nino desnutrido. I. Produccion de antitoxina difterica. Bol. Med. Hosp. Inf.

Mexico 13, 467 (1956).

9. Hassan, M. U., Ibrahim and L. C. Khanna. The relation of vitamin A to white cells in human blood and normal white cell counts in the Punjab. Indian J. Med. Res. 36, 33 (1947). 10. Orskov, V. J. and O. Moltke. Studien uber den Infektionsmechan-

isums bei verschiedenen Paratyphus Infektionen an weissen Maussen. Ztschr. Immunitatsforch 59, 375 (1928).

Doan, C. A. Folic acid (synthetic L. casei factor) an essential panhematopoietic stimulus. Experimental and clinical studies. Am. J. Med. Sci. 212, 257 (1946).
 Guggenheim, K., E. Buechler and S. Halevi. The effect of protein

deficiency on the resistance of rats to infection with spirochetes of relapsing fever. J. Infect. Dis. 88, 105 (1951).

13. Guggenheim, K. and E. Buechler. Nutrition and resistance to infec-

tion. Bactericidal properties and phagocytic activity to peritoneal fluid of rats in various states of nutritional deficiency. J. Immunol. 54, 349 (1946) 14. Dawson, C. E. and W. Blagg. Further studies on the effect of human

saliva on the Cholera vibrio in vitro. I. Dental Res. 29, 240 (1950). 15. Werkman, C. H., F. M. Baldwin and V. E. Nelson. Immunology significance of vitamins, resistance of avitaminic albino rat to diphtheria toxin. Production of antitoxin and blood pressure effect. J.

Infect. Dis. 35, 549 (1924).

16. Scrimshaw, N. S., C. E. Taylor and J. E. Gordon. Interactions of nutrition and infection. Am. J. Med. Sci. 237, 367 (1959).

17. Pollack, H. Altered prognosis in the diabetic with infection. Ann. New York Acad. Sci. 63, 311 (1955).

18. Terzian, L. A., N. Stahler and H. Miller. Relation of antibiotics, vitamins and hormones to immunity to infection. J. Immunol. 70

vitamins and hormones to immunity to infection. J. Immunol. 70. 115 (1953). 19. Schneider, H. A. Nutrition and resistance-susceptibility to infection. Nutrition Fronts in Public Health. Nutrition Symposium Series No.

3. New York, National Vitamin Foundation, Inc., New York, 1951, pp. '118-132.