

development of a hematoma in the retro- or intraperitoneal spaces which, by pressure on intraperitoneal organs then presents the picture of a gastro-intestinal lesion. Extravasation of urine from the affected kidney may, at least for the first few hours after the injury, increase the pressure of this tumor-like mass. Combined injuries of the urinary and intraabdominal organs may result in early peritonitis, from lesions in the gastro-intestinal or urinary organs. Such a perforation of organs of both the gastro-intestinal and the urinary systems from a bullet or a stab wound may complicate the diagnosis. Injuries to the urinary bladder may be extra- or intraperitoneal. The urine emptying through the hole in the bladder may enter the soft tissue of the perivesical space, or the intraperitoneal cavity. Real peritonitis may result, or secondary pressure on the intraperitoneal organs from the accumulation of urine in the perivesical space.

Differential diagnostic problems between diseases of the male genital organs and the gastro-intestinal tract are fewer. One important clinical picture, though, may come up in males under the signs and symptoms of a fully developed peritonitis: tenderness and rigidity in either the lower left or right abdominal quadrant, distention, sickness and vomiting may be present. If the right lower quadrant is involved one may be inclined to make the diagnosis of an acute appendicitis.

Nevertheless, all this does not fit into the picture of an acute appendicitis or peritonitis. Blood count, especially white cells, may be normal or only slightly increased—rectal examination, which should never be forgotten in examining abdominal cases, may not reveal any pathology. The entire problem in such a case may be that of a relatively harmless acute deferentitis. There may be no swelling of the scrotal part of the vas deferens at all, but on palpation the finger feels in the inguinal canal the highly painful spermatic cord, causing the secondary, (but harmless) peritoneal reaction. If occurring on the right side it may easily be mistaken for an acute appendicitis. Sometimes it is difficult to differentiate between a hernia and a hydrocele, especially when both are combined and complicated by adhesions from wearing a truss.

It is obvious that many problems can arise from diseases of the female genital organs in differential diagnosis with the gastro-intestinal tract. The discussion of these features, however, would lead this paper too far and it can, of course, cover only a few of the many pictures and problems involved in differential diagnosis between gastro-intestinal and genito-urinary symptoms. It certainly has no ambition of being complete in this respect.

## The Role of the Fat Soluble Vitamins A and D in Nutrition\*

By

JACOB BUCKSTEIN, M.D.†

NEW YORK, N. Y.

### MODE OF ABSORPTION OF VITAMIN D AND FACTORS INVOLVED

VITAMIN D can be absorbed from the alimentary tract, and also after intramuscular injection and through the skin. Although the absorption of vitamin D is aided by the presence of fat, this does not apply however to absorption in the presence of mineral oil. Smith and Spector (*Smith, M. C. and Spector, H. Calcium and Phosphorus Metabolism in Rats and Dogs as Influenced by the Ingestion of Mineral Oil. J. Nutrition 20:19, 1940*) determined experimentally the effect of the ingestion of mineral oil in puppies on the metabolism of calcium and phosphorus. They noted that the mineral oil interfered with the utilization of vitamin D to such a degree that three times the amount of vitamin D was necessary to cure experimentally produced rickets when mineral oil was included to the extent of five percent of the ration. To such a degree did the mineral oil in the young dog interfere with the retention of calcium and phosphorus that normal calcification did not take place.

Efficient absorption of vitamin D is aided by the presence of bile. This is particularly shown by the fact that vitamin D cannot be properly absorbed from

the alimentary tract when a biliary fistula is established in an animal. However, if the animal is fed taurocholic acid or desoxycholic acid, the absorption of vitamin D is materially aided (*Greaves, J. D. and Schmidt, C. L. A. The Role Played by Bile In The Absorption of Vitamin D in The Rat. J. Biol. Chem. 102:101, 1933*). Obstructive jaundice also interferes with normal absorption of vitamin D.

In this connection, the work of Heymann (*Heymann, W. Metabolism and Mode of Action of Vitamin D. Am. J. Dis. Child. 55:913, 1938*) is of considerable interest. Experimenting with rats he ligated the bile ducts. Rickets which had been induced in rats who suffered from the experimentally produced obstructive biliary cirrhosis and jaundice required ten to twelve times as much vitamin D injected intramuscularly as was necessary for the cure of rickets in other rats.

The significance of the intramuscular injection was that it ruled out the possibility of impaired intestinal absorption. Similar results were obtained when the liver was damaged by the administration of carbon tetrachloride. The diminished antirachitic effectiveness of vitamin D was evidently due to the liver disease.

Although the exact mechanism is not clear, the unimpaired liver plays some role in the efficient utilization

\* Continued from August issue.

† Asst. Prof. Clinical Med., Cornell Univ. Med. College.

of vitamin D. When liver disease is suspected, it would therefore be an indication for the administration of more ample dosage of vitamin D.

Because of the disturbance in fat absorption and the loss of calcium salts in the feces in celiac disease, large amounts of vitamin D may be helpful in controlling the disorder.

Absorption of vitamin D occurs mainly from the small intestine. It reaches the blood and then is distributed to meet the needs of the various tissues of the organism. In the normal human being the concentration of vitamin D in the blood is about 50 to 135 International Units in each 100 cc. of serum. In the fish, the liver is a special repository of vitamin D. In the human being however, no such special predilection for the liver is to be found; its distribution is much more general throughout the body wherever there is an accumulation of fat, provided an ample amount of the vitamin is available.

#### RESULTS OF DEFICIENCY OF VITAMIN D

ONE of the important results of a deficiency of vitamin D, is the development of rickets, a disease bound up with a disturbance of the mineral metabolism, so that normal calcification of bone does not take place. The minerals primarily involved are calcium and phosphorus. In some cases, the concentration of calcium in the blood is normal, but there is a deficiency of phosphorus. In this condition, the ends of the long bones exhibit an overgrowth of cartilaginous tissue of the ribs. Therefore the joints of long bones become enlarged. Along the ribs this increased prominence assumes the appearance of the classical "rachitic rosary." Because of the softness of the bones and their subjection to the weight of the body, the legs become bowed. Confirmatory evidence of the condition is to be found by means of the characteristic roentgen picture of the bones, and also by the demonstration of the low phosphorus determination in the blood serum on chemical examination.

Rickets may also result when the phosphorus in the blood is normal, but there is a deficiency of calcium in the serum. This is often referred to as "low calcium rickets." In this condition tetany may develop, presumably also as a result of low calcium.

Still a third type of rickets has been recognized, due to a deficiency of both the minerals calcium and phosphorus. This is the type known as osteoporosis. The interesting clinical therapeutic fact is that such rickets may be prevented, or in the already established condition, a cure obtained by the administration of vitamin D. The vitamin acts by restoring normal concentrations in the blood of both these minerals, calcium and phosphorus, provided the amount actually present is not too low. Vitamin D accomplishes this remarkable function by increasing the absorption of these essential minerals, from the alimentary tract, and also by preventing undue loss by excretion in the intestine (Sohl, A. T. *Physiology and Pathology of Vitamin D. Chapter XXIV. The Vitamins, 1939, The American Medical Asso.*)

It is possible that calcium and phosphorus already available and stored in the tissues may be mobilized by means of vitamin D, for deposition in bone and its normal structural development.

While the exact manner in which vitamin D acts to prevent or cure rickets remains an incompletely solved problem (Park, E. A. *The Therapy of Rickets. 115: 370-379, J. A. M. A. 1940*), the important fact remains from a therapeutic point of view, that the vitamin is remarkably effective in the cure of this serious disease. The minerals calcium and phosphorus and vitamin D thus have an important role to fulfill in facilitating normal structural growth and development. The diet should therefore contain a liberal quantity of all three factors. Liberal amounts of vitamin D in the presence of an adequate supply of these minerals will aid in a superior development of the skeletal structure. This is one reason among others why with an improvement in the economic status of people, the children often grow taller than their less fortunate parents reared in early poverty.

In this important field, the fish liver oils have played a prominent role, as readily available sources of natural vitamin D. Coupled with the fact that these oils are also excellent sources of vitamin A, one can readily understand the nutritional value of these commercially available sources of supply. Halibut liver oil, excellent as a source of vitamin A, also contains important quantities of vitamin D, and it therefore ranks among the superior substances in the promotion of skeletal growth. *The Interrelationship of Vitamin D and Calcium and Phosphorus*

However effective vitamin D undoubtedly has proven to be for the development of sound bony structure, one must never lose sight of the fact that the optimum usefulness of the substance is obtained in the presence of a liberal supply of both calcium and phosphorus, the prompt and best utilization of which takes place in the presence of this vitamin.

Osborne and Mendel (*Osborne, T. B. and Mendel, L. B. The Inorganic Elements in Nutrition. J. Biol. Chem. 34:131, Apr., 1918*) in 1918 showed the importance of calcium and phosphorus in the growth of bone. Although growth continued in spite of low levels of sodium, potassium, magnesium or chlorine, such growth was arrested when there was a diminished intake of calcium or phosphorus.

The relationship of the calcium phosphorus metabolism to disturbances of bony structure and the development of rickets was shown by Howland and Kramer (*Howland, J. and Kramer, B. Calcium and Phosphorus In The Serum In Relation to Rickets. Am. J. Dis. Child. 22:105, 1921*). They found the concentration of calcium in normal infants and young children to be from ten to eleven mg. per hundred cc. of serum. Examination made during active rickets showed the calcium concentration to be normal or slightly reduced. A definite reduction in the inorganic phosphorus of the serum always took place in active rickets.

This important interrelationship of antirachitic vitamin to the minerals calcium and phosphorus was also demonstrated by the following contributions. Sher-

man and Pappenheimer (*Sherman, H. C. and Pappenheimer, A. M. A Dietetic Production of Rickets in Rats and Its Prevention by An Inorganic Salt. Proc. Soc. Exptl. Biol. Med., 18:193, 1920-1921*) showed the importance of the addition of potassium phosphate to the diet of rats in the prevention of rickets. The work indicated the importance of the mineral constituents of the diet as well as the fat soluble vitamin factor in the prevention of rickets.

Similarly Mellanby in 1925 (*Mellanby, E. The Effect of Cereals and Their Interaction with Other Factors of Diet and Environment in Producing Rickets. Medical Research Council, Special Report Series (London) No. 193, 1925*) showed the importance of an ample amount of calcium and phosphorus and fat soluble vitamin in the diet for the prevention of rickets in puppies. The causes of defective calcification of bone were found to be due to a deficiency of calcium and phosphorus in the diet as well as of the fat containing the antirachitic vitamin.

Sohl and his associates (*Sohl, A. T., Brown, H. B., Chapman, E. E., Rose, C. S. and Saurwein, E. M.: The Evaluation of the Phosphorus Deficiency of the Rickets-Producing Diet. J. Nutrition 6:271, May, 1933*) showed how restrictions in the amount of phosphorus could seriously limit growth even in the presence of liberal amounts of vitamin D. Growth was retarded when the level of phosphorus in the diet was low, even though the amount of calcium was high and ample amounts of vitamin A and D were administered. This work indicated the importance of phosphorus as well as calcium and vitamin D as factors essential for normal growth. The development or cure of rickets therefore depends on the role not only of vitamin D but of proper amounts of the minerals, calcium and phosphorus as well.

The essential function of vitamin D is to make the blood serum values of calcium and phosphorus normal by increasing the absorption of these minerals from the alimentary tract or by diminishing their loss through excretion by way of the alimentary tract.

In addition to the effect of vitamin D deficiency on the skeletal structures, the various other tissues of the body also suffer, leading particularly to weak and flabby musculature.

The presence of vitamin D deficiency when it has led to actual bone changes may of course be recognized by radiologic examination. This, however, represents an advanced stage of the disorder. Of greater importance are methods of recognition in the subclinical stage, before organic changes in the bony structure

have actually developed. This stage may be suggested by a determination of the concentration of calcium and phosphorus in the blood. Thus the normal value for phosphorus is 4-6 mg. percent and that of calcium is 9-11 mg. percent. A diminution in these values may be an early evidence of subclinical deficiency of vitamin D.

#### *Vitamin D Deficiency and Dental Caries*

Mellanby showed (*The Committee for Investigation of Dental Disease: The influence of Diet on Caries in Children's Teeth (Final Report), Medical Research Council, Special Report Series, No. 211, London, His Majesty's Stationery Office, 1936*) the importance of supplementary additions of fish liver oil in the prevention of dental cavities and the arrest in the progress of dental caries.

In this report Mellanby found "that a relatively high vitamin D content of the food can do much to diminish the incidence of caries if the vitamin is given during the development of the teeth; that a beneficial effect may be obtained if the vitamin is given at a fairly late stage of development, and that when it is given after the eruption of the teeth, the onset and spread of caries is delayed."

Mellanby administered from 700 to 1500 units of vitamin per day, McBeath had also shown the value of vitamin D in favorably influencing the condition of the teeth (*McBeath, E. C. Nutritional Control of Dental Caries. N. Y. State J. Med. 33:1086, Sept. 15, 1933*). In another study McBeath and Zucker (*McBeath, E. C. and Zucker, T. F.: The Role of Vitamin D in the Control of Dental Caries in Children, J. Nutrition 15:547, June, 1938*) recommended the addition of three teaspoonfuls of fish liver oil in the prevention of dental caries.

They reported their observations on the effect of vitamin D on the structure of the teeth over a period of four years on a group of 800 children. The children chosen for this study were from orphanages in and near N. Y. City. The findings of Mellanby were verified as to the effect of vitamin D on dental caries. Their observations led them to the conclusion that vitamin D as well as calcium and phosphorus played a specific role in the normal growth of the teeth and the prevention of caries.

During the period of the year when caries was most common, only the daily administration of 800 units of vitamin D was capable of preventing an increase in the disorder.

*(To Be Continued)*