

PRESENT CONCEPTS OF VITAMIN B₁₂

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In 1926 Minot and Murphy demonstrated the therapeutic value of dietary liver in cases of Pernicious Anemia. Soon afterwards, as a result of their studies on the effectiveness of liver in Pernicious Anemia, Castle and his associates published their famous work, a theory of an Anti-Pernicious Anemia factor formed by the action of an "intrinsic factor" found in human gastric juice acting on an "extrinsic factor" found in the diet. Since that time research teams have attempted to isolate the active anti-anemic factor present in liver. These attempts came to a head in 1948 when research teams in England and the U. S. A. simultaneously isolated this factor, now known as Vitamin B₁₂.

Vitamin B₁₂ is a cobalt co-ordination complex containing cobalt, nitrogen, phosphorous, a cyane radical and traces of other elements. It is found most abundantly in glandular meats and fish solubles and to a lesser extent in muscle, milk and eggs. It is not found in all plant feeds. The presence of cobalt reflects the unknown part that element plays in body metabolism.

The discovery of Vit. B₁₂ and the mass of recent study directed to its part in the treatment of Pernicious Anemia have led to new concepts in the patho-physiology of that disease. It is now considered that Pernicious Anemia is a Vit. B₁₂ deficiency disease, and this deficiency is due to

impaired absorption of the vitamin from the gastro-intestinal tract because of an inherent or acquired absence of "intrinsic factor" in the gastric secretions of certain individuals. It is believed that this intrinsic factor facilitates the normal absorption of Vit. B₁₂.

Ternberg and Eakin have shown that Vit. B₁₂ in the presence of normal gastric juice becomes bound forming a complex. This complex was shown to enhance the development of megaloblasts in vitro. This work was confirmed by Callender and Lajtha who also demonstrated the fact that Vit. B₁₂ in the presence of normal gastric juice enhanced the ripening of megaloblasts to normoblasts in vitro. Vit. B₁₂ alone or gastric juice alone had little effect on the cell culture. The cells required combined activity of Vit. B₁₂ and intrinsic factor for growth. This idea of a complex, an Anti-Pernicious Anemia complex, fulfills Castles' theory.

Absorption.

The rate of absorption of Vit. B₁₂ from the human gastrointestinal tract is not known, nor is there any satisfactory methods known by which this rate could be measured. Experiments have shown that:

(1) the concentration of Vit. B₁₂ in the blood plasma and urine, following the ingestion of up to 10,000

ug of vitamin, at no time approached the plasma or urine levels produced by the intramuscular injection of 250 ug of Vit. B₁₂.

(2) Vit. B₁₂ is absorbed from the G. I. tract of patients with Pernicious Anemia in large doses, but the addition of normal gastric juice greatly increases this absorption.

(3) Parenteral injection of 25 ug of Vit. B₁₂ to patients with Pernicious Anemia, were followed by complete hematologic remissions, but it required 5000 ug (with no added intrinsic factor) orally to produce the same degree of remission.

Thus one must conclude that there is poor absorption of the vitamin from the normal gastro-intestinal tract and that Pernicious Anemia is a disease caused by a relative inability of an individual to absorb sufficient Vit. B₁₂ from his normal diet and therefore requires abnormal amounts of the vitamin to prevent the condition. Thus the success of liver therapy.

Referring back to the work of Calender and Lajtha who found that vitamin B₁₂ was active only in the presence of gastric juice, one must conclude that the vitamin is Castles' extrinsic factor and it requires the intrinsic factor to form the hemopoietic factor. Since an intramuscular injection of vitamin B₁₂ is so active in pernicious anemia, it seems likely that there are other sources of intrinsic factors in the body besides the gastric juice, since the vitamin is not active by itself.

Very little is known about the intermediate metabolism of Vit B₁₂. Chow has shown by experiment that the vitamin has no relation to protein metabolism or nitrogen balance. He has also shown that it has some unknown regulatory effect in the transformation of carbohydrate to fat, and that it probably acts as a coenzyme. Vit B₁₂ has been shown to pass through the placental barrier in rats and is present in the milk of the mother. Downing has shown that the vitamin has no effect on premature infants. This is most likely because they have acquired a reserve from the mother.

Vitamin B₁₂ has been shown to effect children's growth, especially when there has been a previous history of malnutrition and when the major source of calories is carbohydrate. It has been hypothesized and early clinical experiment has shown significantly that the vitamin is of benefit in chronically ill children. In healthy children it has no significant effect.

The relationship of folic acid to vit B₁₂ is unknown. The reason why some megaloblastic anemias respond to folic acid and not to vit B₁₂ is also unknown. There are many theories proposed but none have shown much strength.

Vit B₁₂ has a direct alleviating action on most cases of Sub-acute combined degeneration. This is in distinction to folic acid which has no effect on the condition and which some workers believe enhances the progress of the disease. Recently

some English workers have noted that the blood pyruvate level is raised in Sub-acute combined degeneration and that these blood levels returned to normal on administration of vit B₁₂. (6) The significance of the vitamin in pyruvate metabolism is not yet known.

Summary. Vitamin B₁₂ is a cobalt containing complex; thought to be

Castles extrinsic factor; it is not active by itself in vitro but requires the presence of intrinsic factor; it is absorbed poorly from the normal gut; it is thought to have an effect on carbohydrate metabolism and on growth; it may have some relationship to pyruvate metabolism.

References:

1. Lewis et al, Vit. B₁₂ in Natural Materials, Proc. Soc. Exp. Biol. and Med.
2. Callender and Lastha, On the Nature of Castle's Hemopoietic Factor, Blood, Dec. 1951.
3. Conley, Krevans et al, Observations on Absorption, Excretion, Utilization of Vit. B₁₂, Jour. of Lab. and Clin. Med., July, 1951.
4. Chow, B. F., Role of Vit. B₁₂ in Metabolism, South. Med. Jour., July, 1952.
5. Ungley, C., Sub-acute Combined Degeneration, Brain, 1949.
6. Earl et al, Blood Pyruvate Levels in Sub-acute Combined Degeneration, Lancet, Jan., 1953.

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