Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

The Vitamin B Complex

Volume XI | Friday, January 26, 1940 | Number 14

STAFF MEETING BULLETIN
HOSPITALS OF THE . . .
UNIVERSITY OF MINNESOTA

Volume XI | Friday, January 26, 1940 | Number 14

INDEX

Published for the General Staff Meeting each week during the school year, October to May, inclusive.

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William A. O'Brien, M.D.

I. LAST WEEK

Date: January 19, 1940

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:15 p.m.

Program: Movie: "Anesthesia"

Irregular Shedding of the Endometrium
Rodney F. Sturley

Discussion
John L. McKelvey

Present: 210

Gertrude Gunn
Record Librarian

- - - -

II. MOVIE

Title: "Polar Trappers"

A Walt Disney Short

Released by: R-K-O

- - -

III. ANNOUNCEMENTS

1. WEDDINGS

Jerome Hilger and Helen Backer, January 20, St. Paul. Dr. and Mrs. Hilger will spend their honeymoon in the East where he will take special work in Otolaryngology. They will return March 1st. Congratulations.

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2. BABIES

Mr. and Mrs. Andrew "Scotty" McGilp are the proud parents of a son, Murray Andrew "Scotty" McGilp, their third child - born January 19.

- - -

Dr. and Mrs. Harold F. Buchstein - a baby girl, weight 7 lb. 6 oz., January 23, at 5 a.m., their first child. Congratulations!

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3. CONTINUATION STUDY COURSE -

Dietetics - January 29-31, 1940, Center for Continuation Study.

- - -

4. MINNEAPOLIS SURGICAL SOCIETY

EIGHTEENTH ANNUAL FOUNDATION DINNER

of the

MINNEAPOLIS SURGICAL SOCIETY

Thursday, February 1, 1940 - - 6:30 P.M.

at the
Minneapolis Club

Guest Speaker

DOCTOR SUMNER L. KOCH

of
Northwestern University School of Medicine

"SKIN TRANSPLANTATIONS"

This announcement is again your invitation. Please notify the secretary by January 29 for reservations. The tickets are $5.00. Canapes and refreshments will be served at 6:30 and dinner at 8 P.M.

Harvey Nelson, Secretary
1935 Medical Arts Build.
Atlantic 7283

Formal Dress

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IV. THE VITAMIN B COMPLEX

'I' Chemistry and physiological significance of the principal components.*

Olaf Mickelson

A. Thiamin (vitamin B_1)

B. Riboflavin and nicotinic acid

'II' Clinical disorders associated with deficiency of one or more components.*

A. Thiamin deficiency

1. Nervous disturbances . . . . . Frederick W. Hoffbauer
2. Gastrointestinal disturbances . . Wm. H. Hollinshead
3. Cardiovascular disturbances . . . Wm. H. Hollinshead

B. Nicotinic acid (P-P factor) deficiency. Pellagra. . . . . Evrel Larson

C. Riboflavin (vitamin B_2) deficiency (ariboflavinosis). . . . Evrel Larson

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*Vitamins B_{3-6}, incl., have not been shown to be related to any clinical disorders in man, and are not considered in this review.

"I' CHEMISTRY AND PHYSIOLOGICAL SIGNIFICANCE OF THE PRINCIPAL COMPONENTS OF THE VITAMIN B COMPLEX

Olaf Mickelson

A. THIAMIN (vitamin B_1)

1. Historical

Lunin[1] (1881). Reconstructed a bread and milk ration of purified foods. Mice did not grow on this. Postulated the presence in milk of factors essential for life other than those then known.

Takaki[2] (1884). Surgeon General of Japanese Navy. Eradicated beriberi by substituting meat and legumes for a certain amount of polished rice. Believed the increased protein responsible for the change.

Eijkman[3] (1897). Accidentally produced polyneuritis in chickens fed only polished rice. At first thought the disease due to an infection but was convinced by his pupil Grijns of its deficiency nature.

Hopkins[4] (1906). Rats fed purified foods grew only when a small amount of milk was also given. Suggested the idea of accessory factors for normal growth.

Funk[5] (1911). Isolated nicotinic acid amide from rice bran and suggested identity of this with the anti-beriberi substance. Proposed name "vitamine."

Smith and Hendrick[6] (1926). Autoclaved yeast for 6 hours and destroyed the antineuritic substance, but this had no influence on the growth-promoting factor required by rats.

Jansen and Donath[7] (1926). Isolated vitamin B_1. No one was able to repeat this during the following six years. Other workers refined and simplified the procedure so that the formula was available in 1932.

Windaus, et al[8] (1932). Showed presence of sulfur in vitamin B_1 molecule and gave the correct empirical formula for it.

Williams[9] (1936). Conclusively proved the structure of vitamin B_1.

Williams,[10] Andersag and Westphal,[11] and Todd and Bergel[12] (1937). Synthesized the vitamin independently.

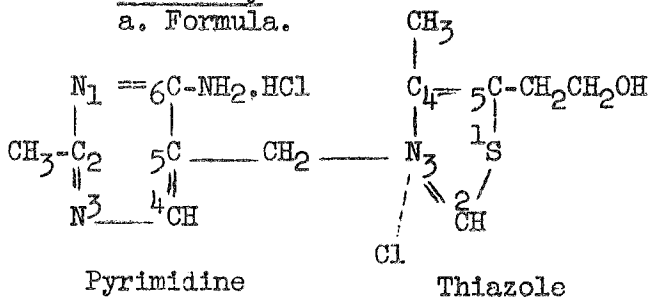
2. Methods of assay[13]

a. Biological
- 1) Animals
  - a) Preventive
    - (1) Chicks on an autoclaved ration.[14]
    - (2) Rats (Scheunert and Schieblich).
  - b) Growth or weight maintenance.
    - (1) Rat growth (Sherman, Mickelsen, et al[15])
    - (2) Maintaining or restoring weight of adult pigeons.
    - (3) Maintaining the appetite in dogs (Cowgill).
  - c) Curative.
    - (1) Pigeons.
    - (2) Rats (M.I.Smith, Kline, et al[16]).
  - d) Special tests.
    - (1) Bradycardia (Birch and Harris).
    - (2) Catorulin (Peters).
- 2) Plants.
  - a) Yeast-growth and fermentation (R.J.Williams, C.N.Frey).
  - b) Phycomyces Blakesleeanus (Schopfer, Sinclair[17]).
  - c) Cocci (Knight, West and Wilson[18]).
  - d) Higher plants.
    - (1) Germination of seeds (Kögl, Bonner and Roberts).
    - (2) Rooting of shoots.

b. Chemical
- 1) Azo test (Kinnersley and Peters).
- 2) Diazonium reaction (McCollum and Prebluda, Melnick and Field[19]).
- 3) Thiochrome (Jansen-Westenbrink, Hennessy and Cerecedo[20]).

3. Units
   a. International Unit =
      = 0.5 Smith curative unit.
      = 2.0 Chase-Sherman units[21].
      = 1.0 Roscoe unit.
      = 20.0 mg. equivalents.
      = 3.0 micrograms crystalline vitamin B_1[22].

4. Chemistry
   a. Formula.



Pyrimidine Thiazole

3-(6 amino-2-methylpyrimidyl-5-methyl)-4 methyl, 5-B-hydroxyethylthiazolium chloride hydrochloride.

   b. Properties

      1) Water soluble - may explain loss on cooking when water is discarded.

      2) Destroyed by autoclaving at 15 lbs. pressure for 5 hours but only partly destroyed during cooking especially if reaction is acid.[23]

      3) Autoclaving cleaves the molecule into the pyrimidine and thiazole parts.[24]

      4) Sodium bisulfite cleaves the molecule into 2 parts when permitted to act on a pH above 5.[25]

      5) Stable to atmospheric oxidation but easily oxidized in solution by mild oxidizing agents.

   c. Activity of substituent parts and possible substitutes.

      1) Essential parts of vitamin B_1 molecule for physiological activity: an amino group on the pyrimidine, a 5-B hydroxyethyl group on the thiazole, a hydrogen atom in position 2 of the thiazole and a methylene bridge between the thiazole and pyrimidine.[26]

      2) Robbins and co-workers.[27] Polyneuritic pigeons were cured when the pyrimidine and thiazole parts of the vitamin were fed simultaneously but not if the 2 parts were fed 24 hours apart. Neither compound alone had any curative action. This was confirmed by Abderhalden[28] who showed that the amount required to produce a cure was more than 1,000 times the equivalent amount of the complete molecule necessary for a cure. Other animals require the complete molecule.[13]

      3) Some strains of microorganisms can grow on the pyrimidine part, others on the thiazole part, others require both parts, and still others require the complete molecule.

5. Physiological activity

   a. Carbohydrate metabolism.

Peters[29] catatorulin test showed a decreased oxygen consumption by avitaminotic pigeon brain tissue, and this could be increased by the in vitro addition of vitamin B_1. This brain preparation on a lactate substrate (a substrate is the substance on which the enzyme acts) can produce measurable amounts of pyruvic acid which disappears when vitamin B_1 is added. On the basis of this he believes that the main disturbance in avitaminosis B_1 is due to a faulty pyruvic acid disposal. The accumulated pyruvic acid inhibits the enzyme which

acts on lactic acid and consequently the concentration of this compound increases.

Lohman and Schuster[30] identified cocarboxylase as vitamin B_1 pyrophosphate and showed that it was as active as the vitamin itself in pigeons. Carboxylase is an enzyme in yeast which removes CO_2 from pyruvic acid with the formation of acetaldehyde, and this is then reduced to alcohol. The presence of cocarboxylase in animal cells was shown by Auhagen[31] who discovered this coenzyme. In yeast cocarboxylase is associated with carboxylase in the decarboxylation of pyruvic acid; in bacteria it very likely functions in the oxidative decarboxylation of pyruvic acid to give acetic acid. At present, the exact role of the vitamin in animals is not clear, for, although animal cells contain cocarboxylase, no carboxylase has as yet been found. In animals carboxylase undoubtedly functions in some phase of carbohydrate metabolism although just where it acts is still uncertain. This disturbance in carbohydrate metabolism may affect the nervous system in such a way as to produce some of the symptoms of beriberi.

Carboxylase-Cocarboxylase
(Vit. B_1 pyrophosphate)

$$CH_3\overset{O}{\overset{\|}{C}}COOH \longrightarrow CH_3CHO \longrightarrow CH_3CH_2OH$$

Pyruvic acid — Acetaldehyde — Alcohol

b. Fats.

Rats suffering from severe polyneuritis can be cured and kept normal for long periods of time by increasing the fat content of the deficient ration.[32] Rats which are permitted a choice of various foodstuffs, all of which are free from vitamin B_1, show an increase in their consumption of fats.[33] Evidently if some mechanism other than carbohydrate metabolism is available to supply energy, the animal is spared its need for vitamin B_1.

B. RIBOFLAVIN AND NICOTINIC ACID

1. Historical

Blyth[34] (1879) showed the presence of a water soluble yellowish-green fluorescent pigment in milk which he called lactochrome.

Goldberger and Lillie[35] (1926) tried to produce pellagra in rats on an experimental ration. The animals showed a symmetrical dermatitis which was believed analagous to human pellagra. The factor preventing the development of the condition was called vitamin G in America and B_2 in Europe.

Hogan and Hunter[36] (1928). The factor responsible for the cure of the dermatitis was destroyed by ultraviolet irradiation. Showed the presence of another vitamin, a deficiency of which also produces dermatitis (this is now known as vitamin B_6).

Goldberger and Wheeler[37] (1928). Produced a condition in dogs called blacktongue on a ration similar to that used by pellagrins in the South. Used this technique in assaying foods for the P-P (pellagra preventive) factor.

Warburg and Christian[38] (1932). Described a new water soluble enzyme from yeast which was yellow and showed a green fluorescence. This was necessary for the oxidation of Robinson's hexosemonophosphoric ester. When isolated[39] it was found to be composed of riboflavin phosphate and a protein.

Kuhn and co-workers[40]. On a vitamin B_2 low ration, they found a parallelism between the growth of rats and the intensity of the green fluorescence of their concentrate prepared from milk. Isolated 1 gram of the compound from 5400 liters of milk. This was originally called lactoflavin, but since all natural flavins were found to be the same, it is now called riboflavin.

Harris and co-workers, Koehn and Elvehjem[41] (1935). Flavin was inactive in "experimental pellagra" both in the dog and chick.

Fouts and co-workers[42] (1936). Showed riboflavin to be inactive in human pellagra.

Day and co-workers[43] (1931-7). Noted cataracts in rats maintained on a low flavin ration. Showed that the condition could be prevented by crystalline flavin.

The Wisconsin group[44] (1933-7). Believed the syndrome of "scaliness" around the beak produced by feeding chicks a heated grain ration to be due to the same deficiency as human pellagra. Started work with dogs using a modified Goldberger blacktongue ration as a check on their attempts to concentrate the P-P factor. As the concentration progressed, the material cured blacktongue in dogs but had no influence on the syndrome in chicks. In May, 1937, nicotinic acid was isolated from a liver extract which was potent in the cure of blacktongue. Chicks showed no response to this compound. It was later shown that the chick deficiency was cured by pantothenic acid which had previously been shown by R. J. Williams[45] to be essential for the growth of yeast. The information about nicotinic acid and blacktongue was immediately sent to Dr. Spies[46] who used nicotinic acid on a number of human patients. Due to the marked peripheral vasodilatation produced by this compound, he made very careful toxicity studies before subjecting it to a complete clinical trial.

2. Methods of assay for flavin

a. Biological.
   1) Animals
      a) Growth
         (1) Rat - put on a quantitative basis by Bourquin and Sherman.[47]
         (2) Chick (Bethke[48]).
   2) Plants
      a) Microorganisms
         L. casei - the lactic acid production on a flavin-low medium is proportional to the concentration of the added vitamin. (Snell and Strong[49]).

b. Chemical

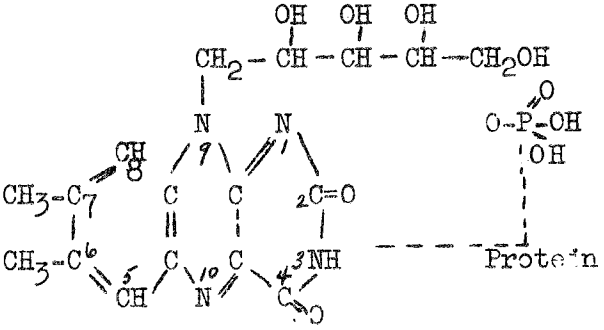
All of these depend upon the measurement of the fluorescence produced by an aqueous solution of flavin when exposed to ultra-violet light. A great many tests of this sort have been suggested but only a few of the more recent ones are listed.[50] Ellinger[51] critically reviewed many of these and concluded that the biological technique is the more reliable.

3. Units

a. Sherman-Borquin unit = 2.0 to 2.5 micrograms riboflavin.[52]

4. Chemistry

a. Formula



Riboflavin. Yellow oxidation enzyme of Warburg.

b. Properties
   1) Water soluble; heat stable in the absence of light.

   2) Labile to visible and ultraviolet light. Free flavin is rapidly destroyed in a solution exposed to sunlight for a period of four hours.[53] Exposure to light removes part of the ribose molecule leaving a $-CH_3$ group in place of the

sugar.[54] This compound is biologically inactive.

3) Easily reduced to the leuco form by chemical reagents or enzyme systems. When the leuco form is shaken in air, it is reoxidized.

c. Action of substituent parts

For biological activity at least one of the methyl groups in position 6 or 7 is essential; the absence of both produces a toxic compound. Only compounds containing d-ribose or l-arabinose have been found active.[55]

5. Physiological activity

a. Nerve degeneration

Chicks on a riboflavin deficient ration develop a paralysis of the feet associated with a curling of the toes. The nerves in these birds showed a characteristic degeneration; when crystalline flavin was added to the basal ration, the degeneration and paralysis did not develop.[56]

b. Relation to cortical extracts

Verzar and Laszt.[57] Flavin phosphate was able to maintain adrenalectomized rats but flavin itself had no influence. Cortin increased the life of these rats when only flavin was added to the ration. They maintain that flavin phosphate is formed from flavin only in the presence of cortin.

c. Enzymes

1) Yellow enzyme was first isolated from yeast by Warburg and Christian[38] who showed that it was composed of a specific protein and riboflavin phosphate. The enzyme functioned in the oxidation of the reduced coenzymes I and II. It was not found in animal tissues but schemes of respiration were proposed involving it. Recently it has been shown that flavin occurs in animals as diaphorase.

2) Diaphorase was first described by Green[58] and v. Euler.[59] It oxidizes coenzymes I and II but cannot react directly with oxygen. Was identified as flavin adenine dinucleotide[60] which is the same as the coenzyme for the d-amino acid oxidase enzyme. Both of these compounds are found in animal tissues.

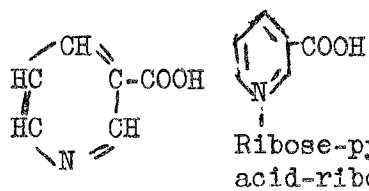
Path of hydrogen transfer:

Lactate ⟶ Cozymase ⟶ Cytochromes a,-b
dehydrogenase diaphorase

⟶ O_2 ⟵ HbO_2
cytochrome oxidase

6. Chemistry of coenzymes I and II

a. Formula



Nicotinic acid

Ribose-pyrophosphoric acid-ribose-adenine.

Coenzyme I (Cozymase)

Coenzyme II has a formula very similar to that of coenzyme I except that there is an extra phosphoric acid group in the molecule. The exact location of this is not known.

b. Properties

1) Water soluble in free form but difficult to extract from biological material because it is intimately associated with proteins.

2) Nicotinic acid is stable to heat and most chemical reagents. This is one of the most stable vitamins.

3) Activity of nicotinic acid derivatives. Only those compounds are active in animals and bacteria which have

a group in the position beta to the nitrogen capable of being oxidized to a COOH group.[66]

7. Methods of assay for nicotinic acid

a. Biological
   1) Animals
      a) Growth
         (1) Dogs are raised from weaning on a black-tongue producing ration. When they cease growing a standard dose of nicotinic acid is given and the growth response measured. They are then depleted to the same stage and the test material given. The content of nicotinic acid is calculated from the proportional weight increases.[61] This is the technique one would use if he wanted to determine the amount of this vitamin in a sample of liver.

   2) Plants
      a) Microorganisms. Nicotinic acid has been shown to be essential for a large number of bacteria. By using media deficient in this vitamin, these organisms have been used in assays. Haemophilus parainfluencae has been shown to require either coenzyme I or II and this is used in testing for these compounds.[62]

b. Chemical
   1) 2, 4-dinitrochlorobenzene (Karrer[63]).
   2) Cyanogen bromide oxidation (Swaninathan[64]).

c. Enzymatic
   Yeast fermentation - this determines only coenzyme I.[65]

8. Physiological Activity

a. Enzymes
   1) Warburg and Christian.[67] Isolated coenzyme II from R.B.C's. This substance together with a specific enzyme, glucose dehydrogenase, was necessary for the oxidation of hexosemonophosphate. Coenzyme I (cozymase) is required by the specific dehydrogenases for lactic, malic, glutamic, B hydroxybutyric acids, hexose diphosphate, triose phosphate and alcohol.

   2) When either dogs or pigs are brought down with a severe nicotinic acid deficiency, the coenzyme content of the liver and muscle is decreased but that in the brain, kidney cortex and blood is unchanged.[68] This seems to indicate that the liver and muscles serve as a storehouse for this vitamin. Its concentration in the other organs has to remain at an approximately normal level for the maintenance of life.

b. Animals

   So far nicotinic acid has been shown to be essential for man, the pig, dog and monkey. The rat, guinea pig, chick and pigeon have not shown any deficiency when kept on a nicotinic acid deficient ration for long periods of time.[69]

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Unpublished results.

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'II' CLINICAL DISORDERS ASSOCIATED WITH DEFICIENCY OF ONE OR MORE COMPONENTS OF THE VITAMIN B COMPLEX

A. THIAMIN (VITAMIN B_1) DEFICIENCY

1. Peripheral Neuritis

Frederick W. Hoffbauer

Beriberi, a metabolic disorder endemic in the Orient, has long been recognized as due to a deficiency of Vitamin B. One of the most striking features of this disorder is the presence of polyneuritis. This manifestation has been shown to be due to deficiency of vitamin B_1 or thiamin. Hence the occasional reference to this substance as the "antineuritic vitamin." Within the past decade the concept has arisen that the polyneuritis of many clinical disorders other than beriberi is due to a deficiency of thiamin. In some instances a causal relationship appears to be fairly well established, in others it remains as yet only a suspicion. The concept places new emphasis on the importance of nutrition and affords a new approach to the solution of many diagnostic and therapeutic problems.

As observations have progressed, it has become apparent that some objective for the recognition of thiamin deficiency would be of considerable value. The most promising finding to date appears to be a determination of the daily excretion of the substance. Thiamin chloride being water soluble is excreted in the urine. The capacity of the tissues to store the vitamin is limited, hence whenever the saturation point is exceeded, increased elimination occurs. If the excretion is large, one can assume that the diet contains an amount above the bodily needs. If the amount is small, low dietary intake plus depletion or threatened depletion of bodily stores can be suspected. At the present time the available microchemical methods are too complex to permit use as a routine procedure. A few reports are available in which such studies have been carried out. Harris and Leong (1) state that a daily excretion of less than 12 international units raises the presumption that the vitamin intake is inadequate. Wilder and his associates at the Mayo Clinic (2) have recently investigated the time required to deplete the body stores. Four subjects were maintained on a diet more deficient in thiamin than is usually reported in association with beriberi. During the last eleven weeks of a twenty one week period of observation, the daily urinary output of thiamin averaged about 14 gamma (42 international units). Anorexia, fatigue, loss of weight, and inconstant tenderness of the calf muscles were observed in all four cases. The onset of these symptoms was much later than had been anticipated. Recovery promptly followed the parenteral administration of relatively small doses of thiamin chloride. The failure of development of striking neurological symptoms in these subjects is worthy of note.

The exact role that thiamin plays in the maintenance of the normal function of the nervous system is not known with certainty (see Part I). Polyneuritic manifestations are prominent in both human beriberi and in experimental deficiency states produced in animals. These manifestations have been attributed to a neuritis, or more precisely, a degeneration of peripheral nerves, both motor and sensory. The process appears to affect those nerves which have the longest course from the cord to the periphery. Thus weakness of the extensors of the foot may be noted first, later similar changes in the calf and thigh muscles occur. Sensory disturbances are manifested by severe pain, burning, paresthesias, and occasionally exquisite muscle tenderness. Microscopic examination of the affected nerves of patients dying of beriberi has been reported to show degenerative

changes in the myelin sheath-Vedder[3]. This fragmentation and disintegration of myelin has been assumed to represent the pathological change characteristic of vitamin B_1 deficiency. There is reason to suppose, however, that such changes are not specifically due to B_1 deficiency, but rather result from inanition. The recent studies of Prickett[4] and others have failed to confirm the belief that degenerative nerve changes are due directly to the lack of sufficient thiamin. Despite the disagreement as to histological changes, there is no question that a deficiency of B_1 produces marked functional changes in the peripheral nerves. In support of this view is the fact that experimentally produced nervous disorders disappear rapidly following administration of thiamin. For example the spastic paralysis occurring in the dog when thiamin intake is inadequate disappears within a few hours following the administration of the vitamin. This rapid return to the normal functional state makes it seem quite unlikely that the disturbance is one of actual axon dogeneration.

Of the various clinical disorders in which the polyneuritis has been attributed to a deficient thiamin intake, beriberi, alcoholism, pregnancy, and diabetes have been most extensively studied. Typical outspoken cases of beriberi are uncommon in the United States. An occasional case is observed in Louisiana. The relative rarity in the poorer classes of the South has been explained by Cowgill[5] as due to the liberal use of pork, molasses, and corn meal in the diet. Such foodstuffs, however otherwise deficient, do contain a fair amount of vitamin B_1. Nevertheless, mild degrees of thiamin deficiency as evidenced by neuritis are noted in some cases of pellagra.

It is probable that neuritis developing in chronic alcohol addicts is usually related to faulty nutrition. Minot, Strauss, and Cobb[6] found that in a group of 53 alcoholics with evidence of neuritis, 51 had subsisted on a diet containing little fresh food or protein. The caloric requirement was maintained through the use of concentrated carbohydrate foods plus that yielded by the alcohol. These investigators were able through the use of adequate diets supplemented by a Vitamin B_1 concentrate to effect a clinical cure in each instance. In addition they were able to relieve the neuritic symptoms in a group of these patients by administration of the vitamin while the subjects continued to consume their customary amount of alcohol. The finding of manifestations of other vitamin deficiencies in these patients lends support to the theory of faulty nutrition.

The development of polyneuritis in pregnant women suffering from pernicious vomiting has been claimed to be due to a lack of sufficient thiamin chloride. It is thought that the factors concerned are inadequate intake and increased requirement incident to the heightened metabolic needs during pregnancy. Favorable response has followed the parenteral administration of thiamin chloride in some cases (Theobald - 7). Not all cases of neuritis developing during pregnancy are due to nutritional deficiency. As has been pointed out by Berkwitz and Lufkin[8] a toxic factor must also be considered.

To explain the relatively high incidence of neurological lesions in diabetes, various theories have been proposed. The two possible explanations given by most writers are sclerosis of the nutrient arteries of nerves, and vitamin deficiency. Proponents of the former theory have fairly conclusive evidence upon which to base their contention (Waltman and Wilder[9]; Jordan[10]). Although many have suggested, on theoretical grounds, that vitamin deficiency may be a causative factor in diabetic neuritis, there are surprisingly few instances in which this has actually been proven. Needles[11] has recently reported the development of neuritis in 3 diabetics during a period in which the vitamin intake, as calculated from their diets, seemed adequate. The number of cases of diabetic neuritis seen at the University Hospital is not large. No attempt has been made to review the results of therapy in these cases. In some the administration of thiamin

chloride has appeared to be beneficial. One case in which thiamin chloride therapy failed to produce any beneficial effect may be mentioned. The patient, a female, 65 years old, was observed for a period of eight weeks. She received 6 mg. of thiamin chloride daily in addition to her diet. Over this period no appreciable change in the degree of neurological involvement was noted. The numbness, paresthesias, and altered tendon reflexes remained unchanged. At the present time, information is inadequate to state that the majority of cases of diabetic neuritis are caused by an inadequate amount of vitamin B_1. Until the question is decided, however, it would seem wise to assure the diabetic of an ample intake of the vitamin.

Evidence of thiamin deficiency may be expected to occur in some cases of disease of the gastrointestinal tract where such factors as diet restriction, anorexia, vomiting, or diarrhea are present. Likewise whenever metabolic processes are accelerated, as in hyperthyroidism or febrile states, the increased need for vitamin B_1 must be met.

In infections such as poliomyelitis or herpes zoster where the infecting agent has a predilection for the nervous system, there is little reason to suppose that thiamin deficiency can play any but a minor role. Nevertheless, the administration of large doses of the vitamin has been reported to produce beneficial results in a number of neurological disorders. This has been ascribed to a non-specific effect of thiamin on neuritis rather than to the correction of an assumed deficiency (Clough[13]). Experimentally, thiamin chloride has no demonstrable pharmacological action. That is, it appears to be effective only where a previous deficiency of the substance has existed. Nevertheless, there is considerable clinical evidence to suggest that thiamin is of value in the treatment of toxic or infectious disorders of the nervous system, particularly where the peripheral nerves are involved. This has been the experience of members of the neurological staff of this hospital.

The first essential in the treatment of any vitamin deficiency should be the provision of an ample diet. Assuming the daily requirement of man to be about 1 mg. (333 international units), early cases should respond to the administration of 5 mg. doses daily. If the deficiency state is marked or if there is reason to suspect faulty absorption of the substance, the parenteral administration of 5 to 10 mg. per day should rapidly correct the disorder. The toxicity is low and relatively enormous doses can be given without fear of an untorward reaction.

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2. Gastrointestinal Disturbances

Wm. H. Hollinshead

Thiamin is essential for the normal function of the gastrointestinal tract. The nature of the dysfunction due to a lack of this vitamin is not clearly understood.

The initial symptom of avitaminosis B_1 in man and animals is anorexia. It is the only characteristic symptom referable to the gastrointestinal tract definitely due to vitamin B_1 deficiency. Inanition is secondary to the anorexia. Glossitis, epigastric distress and tenderness, flatulence and constipation are observed in many deficiency states and are associated with the inanition and secondary multiple dietary deficiency. The anorexia disappears promptly following vitamin B_1 therapy.

The explanation of the anorexia is obscure. Cowgill[1] does not believe that vitamin B_1 owes its restoration effect upon the appetite to an increased flow of gastric juice which it might produce. Elson and Sample[2], Alverez and his co-workers, and Sure and Harrelson[3] were unable to detect any change in gastric acidity in clinical or experimental vitamin B_1 deficiency. Gastric acidity has been found normal in true beriberi. Jaffe and Jolliffe[4] attributed the low and absent gastric acidity frequently noted in chronic alcoholism with polyneuritis to a vitamin deficiency other than that of B_1.

Sure and his co-workers[5,6] demonstrated no change in the in vitro peptic digestion in thiamin deficiency but noted marked reduction in pancreatic lipase and esterase digestion. No impairment of fat digestion as a result of vitamin B_1 deficiency has been demonstrated in animals.

A number of investigators attribute the beneficial effect of vitamin B_1 on the appetite to the return of gastrointestinal tonus. Cowgill, Sparks and Collins, and Vort and Ramoii[7,8,9] have observed gastrointestinal atony in vitamin B_1 deficiency and have noted a return of appetite associated with a return of normal motility. Tuohy has reported a case of atony and dilatation of the stomach in an elderly male which disappeared following thiamin chloride therapy.

The mechanism of gastrointestinal atony in B_1 deficiency is not understood. Moliton and Sampson found that vitamin B_1 has no direct effect on the tone of the intestinal muscle of vitamin B_1 deficient rabbits in situ or in the isolated specimen. The rapidity of improvement following thiamin chloride therapy is against an organic change. Some investigators[10,11] believe that ulcers of

the stomach are specific lesions of vitamin B_1 deficiency. This has not been substantiated.

Glossitis is observed in many deficiency states and has not been proven to be due specifically to a lack of vitamin B_1.

Clinically it is difficult to evaluate the vitamin status in disorders of the lower gastrointestinal tract. There is the question of a disturbance arising primarily from vitamin deficiency and the factor of a secondary deficiency state resulting from restricted diets and inadequate absorption of ingested foods.

At present it appears that the only dysfunction of the alimentary tract due to avitaminosis B_1 is atony. There are no definite morphological changes. The observed anorexia is probably a response to a general systemic disturbance.

The essentials of treatment are:

(1) A well-balanced diet adequate in proteins, minerals, and other vitamins as well as vitamin B_1.

(2) The correction of underlying surgical or medical conditions leading to a depletion of vitamin B_1.

(3) In severe cases of deficiency, pure vitamin B_1 in the form of thiamin chloride should be given orally or parenterally. Parenteral administration is necessary where absorption by mouth is debatable.

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3. Cardiovascular Disturbances

Wm. H. Hollinshead

To our present knowledge, a deficiency of vitamin B_1 is the only vitamin deficiency in man associated with cardiac dysfunction.

It has long been recognized that cardiac dysfunction is part of the classical picture of beriberi. The typical clinical pathological picture of oriental beriberi heart disease has been adequately reviewed by Alameer and Wenckebach, Keefer, and Scott and Herriman,[1,2,3,4] and Weiss and Wilkins and others[5,6,7] have described the cardiac manifestations of vitamin deficiency associated with other conditions more common in this country--notably chronic alcoholism, gastrointestinal disorders, dietary faddism, chronic infection, pregnancy, diabetes, and hyperthyroidism. The clinical pathological picture while varying in degree is essentially the same.

The chief pathological changes in beriberi heart disease are:

(1) Dilatation of the heart, particularly the right side of the heart.

(2) Edema of the tissues and effusion of fluid into the serous cavities.

(3) Usually associated degenerative changes in the motor and sensory elements of the peripheral nerves.

Several mechanisms are responsible for edema formation in dietary deficiency, singly or in combination. Edema may be essentially cardiac in origin. It may be secondary to a lowering of the plasma proteins. In certain instances, edema is unexplained by either of the above causes, and is due to some disturbance of tissue permiability. The disturbance is fundamentally dietary in origin. The edema disappears readily following the administration of vitamin B_1.

As in other types of heart disease, activity, infection, and other agents producing strain on the heart are of etiological importance in the development of heart failure in beriberi heart disease. Muscular activity seems most important. Many authors have stressed the fact that decompensation seldom develops in nutritional deficiency where there exists an incapacitating neuritis, even though definite heart involvement is demonstrable.

The condition may affect a normal or a previously damaged heart. It may be a complicating factor in any type of heart disease.

Incidence of Beriberi Heart Disease

Beriberi heart disease may develop in infants and children. Here it is often of the acute type. Among adults, males are more frequently affected. Weiss found that one in every 160 charity patients admitted to two large services at the Boston City Hospital had demonstrable evidence of beriberi heart disease. Jolliffe and Goodhart found the incidence to be 1/3 of all chronic alcoholics admitted to the New York Psychiatric Hospital.

History

In all instances, the nutritional history is grossly abnormal. Often there is a chronic underlying disorder. Chronic alcoholism is very common.

Signs and Symptoms

Fatiguability and palpitation with tachycardia are the most frequent early evidences of the disease. Dyspnea may appear slowly or suddenly in paroxysmal form. Sudden fatal collapse associated with pulmonary congestion may occur. Weiss has described spontaneous attacks of syncope associated with asystole due to a hyperactive carotid sinus reflex developing as a result of dietary deficiency. This condition responded quickly to Vitamin B_1 therapy.

Dependent edema also develops early. In advanced cases, anasarca exists with fluid in the abdomen, chest, and pericardium. The presence of edema alone does not indicate heart failure. Venous engorgement, the tender hepatomegaly are confirmatory evidence of cardiac decompensation.

The common types of arrythmia are not observed, although gallop rhythm is frequently present in severe cases. Changing systolic and diastolic murmurs are often heard on auscultation over the precordium and disappear following therapy. The systolic blood pressure is usually unchanged. The pulse pressure is often increased producing a moderate degree of Corrigan pulse.

Cardiac enlargement is almost always present. It is the most typical finding of the disease, and can be best demonstrated by fluoroscopic examination. All of the cardiac chambers are dilated, particularly the right ventricle and right auricle. The right auricle may be enormously dilated. If decompensation exists, the shadow of the great veins is enlarged on x-ray.

There are no typical electrocardiographic changes. The most common finding is a marked decrease in voltage, especial-

ly of the T waves, and a tendency towards inversion of the T waves in leads 3 and 4. Prolongation of the electrical systole (Q-T interval) and prolongation of the P-R interval has been observed. These changes are indicative of myocardial damage and disappear rapidly and completely following adequate therapy.

Several explanations of the mechanism of heart failure in vitamin B_1 deficiency have been proposed.

The Vagus Theory: The oldest hypothesis as to its cause is that it is due to degeneration of the vagus nerves. Histological evidence of destruction of the vagus nerves in this disease is inadequate. There is no evidence that paralysis of the vagus nerves can cause heart failure as seen in beriberi.

Carter and Drury[8] found that the bradycardia produced in pigeons on vitamin B_1 deficient diets could be abolished by section of the vagus nerves and by atropine. On the other hand, the bradycardia produced in rats is sinus in origin and not due to vagal influence[9]. In man, tachycardia is present. The nature of the disturbance apparently varies in different species. The hyperactive carotid sinus reflex observed by Weiss suggests a functional alteration of vagal tone. Its rapid disappearance following vitamin B_1 therapy is against an organic change.

The Water Retention, or edema hypothesis: This is the most commonly accepted theory. A number of investigators believe that a lack of vitamin B_1 leads to a fundamental metabolic disturbance resulting in edema of both the skeletal and cardiac muscle. Wenckebach[2] and Keefer[4] have described hydropic degeneration of the myocardium which robs the heart of its powers of resistance and deadens its powers of contraction." Keefer points out in explanation of the electrocardiographic changes observed that muscle edema decreases muscle contractility but does not influence its conductivity.

Weiss and Wilkins[5] were able to demonstrate hydropic degeneration in but 50 per cent of their cases and observed similar changes in other types of heart disease. They believe that changes in both the vagus nerves and the myocardium are responsible for the cardiovascular disturbances in this disease.

The rapid improvement noted in beriberi heart disease following vitamin B_1 therapy suggests that the fundamental disturbance is undoubtedly physiological in nature, and that the pathological changes observed are purely secondary.

Treatment

Beriberi heart disease characteristically responds readily to vitamin B_1 therapy. All cardiovascular manifestations of the disease disappear completely following adequate treatment.

In severe or acute decompensation due to vitamin B_1 deficiency, full doses of thiamin chloride are indicated. Twenty to fifty mgm. of thiamin chloride should be given daily either intravenously or intramuscularly. Weiss and Wilkins have given as much as 130 mgm. daily in divided doses.

Improvement is rapid in patients with severe congestive failure and may be striking. Improvement has been seen to follow within 2 hours after the first injection.

As improvement takes place, the dosage is reduced to 10 mgm. per day or every other day. Later the dose is reduced still further, and given by mouth, providing intestinal absorption is adequate.

The diet must be adequate in vitamin content and in other necessary constituents.

As the diagnosis of "beriberi heart" is sometimes doubtful, a trial of vitamin B_1 therapy for several weeks is indicated when the condition is suspected. High vitamin B_1 intake has no untoward effect on a normal heart or in other forms of cardiac disease.

Proof that the cardiac manifestations

were due to thiamin deficiency is obtained when the heart returns to a more normal size, the electrocardiogram becomes normal, and signs of heart failure disappear, coincident with administration of thiamin chloride.

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B. NICOTINIC ACID (P-P FACTOR) DEFICIENCY. PELLAGRA.

Evrel Larson

Definition

Pellagra is a disease characterized by skin lesions, gastrointestinal disturbances, and nervous and mental changes, now known to be due to a deficiency of nicotinic acid.

History

Pellagra was first described by Gaspar Casal, a Spanish physician, in 1735, who also pointed out that the disease was related to a deficient diet.[3,31] It was subsequently described by Frapolli in Italy in 1771, where it was widespread, and he first applied the name pellagra, meaning "rough."[4] Prior to the twentieth century, only sporadic cases were reported in the United States, but in 1907 there was a definite outbreak of the disease in the South, most marked in Alabama. Following this, for about eight years, there was an alarming increase in the number of cases, especially among the poorer classes in rural communities and among the inmates of orphanages and asylums, where it reached epidemic proportions.[11] This outbreak was further characterized by its acute nature and rapidly fatal course. Following the work of Goldberger and his associates in 1914 and 1915, the incidence was markedly decreased and the etiology clearly established as being a food deficiency.[11,12,13] In 1937, nicotinic acid and nicotinic acid amide were reported as being effective in curing blacktongue in dogs, a disease considered by many investigators to be analogous to human pellagra.[25,26,30] During the same year, human pellagra was successfully treated by the use of nicotinic acid, and since that time, many confirmatory reports have appeared in the literature.[26,27,31,32,33]

Incidence

Pellagra affects the negro and white races in about equal proportion and may occur at all ages. It has been regarded as a disease affecting principally the poorer classes but this is not necessarily true; it may occur in any individual partaking of a diet low in fresh animal products, lean meat, and the leguminous protein foods.[11,12,13,28] It is also common in alcoholics and is frequently encountered in association with chronic conditions interfering with nutrition, namely, mental disease, gastro-intestinal malignancy or chronic disorders, and chronic infectious processes. It has been found to occur most frequently in the spring of the year.

Clinical Manifestations

Dermal Lesions

The skin lesions of pellagra may occur anywhere upon the body although the dorsa of the hands and feet, the axillae, elbows, wrists, knees, areas beneath the breasts, and the perineal region are the most common sites.[26,27] In many cases the lesions are first noted on the exposed areas of the body. They are usually bilaterally symmetrical and are separated from the surrounding skin by a sharp line of demarcation. The onset is marked by an erythema of the affected area accompanied by burning and pruritis. Later the area becomes swollen and often fiery red in color and vesicles and bullae may develop. After a period of time ranging from a few days to several months, the swelling decreases, the color becomes a reddish brown, and desquamation begins. The underlying skin may remain abnormally thickened and permanently pigmented.[32]

The effect of sunlight on the skin of pellagrins is marked. This is noted particularly in the alcoholic cases such as seen during the summer months in this and other vicinities. In these individuals the skin lesions are usually confined to the areas exposed to the sun. In more severe pellagra, however, such as the endemic pellagra of the southern states, skin lesions are often noted in areas not exposed to the sun. The sunlight sensitivity of pellagrins has not been explained adequately. It has been suggested that porphyrinuria, which Spies and his associates[36,37] believed an integral part of the pellagra syndrome, might be the underlying cause of the photosensitivity. Watson[38,39] has shown, however, that the reaction which was believed by Spies and his co-workers to indicate porphyrinuria, is not due to porphyrin, but rather to indol acetic acid, the chromogen of the substance to which Nencki and Sieber gave the name "uro-rosein," in 1882. This substance bears no relation to the porphyrins. The "uro-rosein" reaction depends not only on the presence in the urine of indol acetic acid, but also on the presence of a suitable oxidizing substance such as nitrite.[39,40] This question is under investigation at present by Dr. John Layne who finds that many urines, even from normal individuals, contain indol acetic acid, but that they usually do not contain the oxidizing substance which is so commonly present in pellagra (and in other gastrointestinal diseases).

There is often a mild increase of coproporphyrin in the urines of cases of alcoholic pellagra, but not more than is often encountered in liver disease, or in various forms of poisoning (lead, arsenic, etc.) in which light sensitivity There is no reason to believe, therefore, that the light sensitivity of pellagra is in any way related to the porphyrins.

Gastrointestinal Lesions

The earliest sign occurring in this group of lesions is characteristically a glossitis, involving in the early stages the tip and lateral margins of the tongue, producing reddening and swelling. As the condition progresses, penetrating ulcers are common, which may become infected by Vincent's organisms. Stomatitis, gingivitis, and pharyngitis may occur to varying degree. These signs are accompanied by burning sensations of the mouth, esophagus and stomach. In the severely ill pellagrin, nausea, vomiting, ptyalism, and diarrhea appear frequently; in the sub-clinical case, one or all of these symptoms may occur. Gastroscopic examinations of pellagrins disclose the diseased mucous membranes of the stomach to be similar in appearance to those of the oral cavity. Ureteritis and vaginitis may also occur.[27,28,31,32]

Nervous and Mental Symptoms

Subclinical pellagrins exhibit features which remind one of neurasthenia: multiple complaints such as fatigue, insomnia, anorexia, palpitation, nervousness, and headache. Various types of psychoses occur in severer cases: one frequently sees excitement, mania, depression, and delirium.[1,33] The most common symptoms are confusion, loss of memory, disorientation, and confabula-

tion. It is notable that long-standing mental disorders are not as a rule reversible. Peripheral neuritis is frequently encountered in association with other symptoms of pellagra--this is undoubtedly due to an accompanying thiamin deficiency.[26,33]

Treatment

After the full significance of diet in the development of the disease was recognized,[11,12,13,28] the administration of a high caloric diet, rich in protein and vitamins, supplemented with large amount of pellagra preventive materials such as yeast, wheat germ or liver extract became the accepted treatment.[32] This proved to be beneficial in most cases but impractical because it frequently necessitated the hospitalization of patients for several weeks; The administration of adequate amounts of nicotinic acid or one of its compounds is followed quickly by disappearance of many symptoms.[5,14,23,26,27,31,32,33] Twenty-four to 72 hours suffice to allow subsidence of redness and swelling of the tongue, gums, mouth, throat, and vagina. Over the same period of time, nausea and vomiting, ptyalism, and diarrhea usually disappear. Acute lesions of the skin will blanch within 43 hours after administration of nicotinic acid, but where the continuity of the skin is broken and the lesions are moist, ulcerated, dry or pigmented, a longer period of therapy is necessary. There is a dramatic alleviation of the acute mental symptoms, which may disappear overnight. Chronic psychoses, as previously mentioned, may not respond completely to therapy. The dosage of nicotinic acid varies considerably in the opinion of different writers. The common oral dosage is from 100 to 500 mgm. per day, given in 50 mgm. doses.[1,31,33] Patients vary considerably in their requirements. For parenteral administration, the total daily dose varies from 40 to 80 mgm.. It may also be given intramuscularly. The administration of large amounts of nicotinic acid, especially by the parenteral route, is accompanied in many patients by flushing of the face, a rise in skin temperature, and a sensation of heat. However, there is usually no drop of blood pressure accompanying these symptoms. The daily human requirement of nicotinic acid is about 20 mgm. per day (Elvehjem).

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C. RIBOFLAVIN DEFICIENCY (ARIBOFLAVINOSIS)

Evrel Larson

Definition

Ariboflavinosis is a deficiency state characterized by a feeling of ill health, loss of strength and weight, a typical cheilitis, and a dermatitis involving the skin of the angles of the mouth and sometimes that of the alae nasi and vestibules of the ears and nose.

History and Incidence

Cheilitis has been noted frequently in pellagrins and has commonly been considered part of the pellagrous syndrome[30]. However, it was observed that neither cheilitis nor the rhagades occurring at the corners of the mouth were cured by the administration of nicotinic acid when the patient remained on a diet deficient in the vitamin B complex. This finding was reported in 1938 and constitutes the first and only clinical sign of human riboflavin deficiency which has been proven up to the present time.[25] The lesions were found to occur in several experimental subjects before any frank signs of pellagra were evident and healed very slowly under treatment with nicotinic acid but there was a rapid involution when yeast or liver extract were used; in addition, it was noted that relapse quickly occurred when these substances were discontinued.[22,25] During the last six months several reports on the successful treatment of clinical riboflavin deficiency by the use of the synthetic drug have appeared in the literature.[29a,b,34] It may appear in any race and at any age.

Clinical

The lesions at the angles of the mouth begin as a pallor of the mucosa of the lip not involving the buccal mucosa. This

condition is soon followed by maceration and within a few days superficial transverse fissures appear, usually bilaterally, exactly at the angles of the mouth.[25] Very little inflammatory reaction occurs. The fissures extend into the skin of the mouth angles as much as one half inch in some cases. The lips become abnormally red about the same time, and scaling usually occurs. The lesions resemble those described as perleche.[34] Occasionally one also sees a fine scaly slightly greasy desquamation on a mildly erythematous base in the nasolabial folds, on the alae nasi, and in the vestibules of the nose and ears. Recently filiform excrescences of a seborrheic nature have been described. These lesions are said to vary in length up to 1 mm. and to be scattered over the face, characteristically located in the naso-labial folds, but appearing on the alae nasi, bridge of the nose, or on the forehead above the eyebrows. These lesions improve following the administration of natural or synthetic riboflavin but fail to respond to diets poor in vitamin B complex or to nicotinic acid.[34] In one case, mild conjunctivitis and photophobia was noted to occur in conjunction with the other symptoms. The general complaints of feeling of ill health, and loss of strength and small amounts of weight are almost always present and sometimes are very prominent.

Treatment

Yeast and the old unconcentrated form of liver extract are potent sources of riboflavin. The synthetic form gives excellent results when used in therapy. This is administered by mouth in doses varying from 2 to 60 mgm. per day depending upon the patient's response, by vein or intramuscularly[29a] in doses of from 5 to 20 mgm. per day, all given in divided doses t.i.d. The parenteral method of administration seems most effective. The lesions heal quickly, in 3 to 10 days as a rule and tend to recur quickly when the treatment is stopped (in the absence of an adequate diet).[25,29a,b,34] Dietary management consists of adequate amounts of milk, green vegetables, and lean meat.

Comment

Ariboflavinosis appears to be a well established clinical entity, which the clinician must observe from time to time especially in conjunction with deficiencies of other vitamins. It should be watched for especially in the chronic alcoholic. The daily human requirement is about 1 mgm./day (Hogan).

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V. GOSSIP

According to a speech teacher at the Colorado State Teachers College of Education, the 9 "chief" annoying habits of speakers are as follows: mumbling; longwindedness; obvious lack of preparation; "in closing" remarks running on and on; hesitant "ahs," "uhs," and "ers"; folksy remarks addressed to someone in the audience; a show of temper over a disturbance in the room; vagueness about facts; mispronunciation of common words. 500 persons from 59 occupations were asked to name their pet peeves against public speakers. There were many more than the above, but these were first.... We have been asked to suggest to some of our speakers that they refrain from speaking so close to the microphone. This is a minor suggestion, for week in and week out the members of our group succeed in offending very few of our listeners by carelessness in speech.....The following letter from Russell H. Frost, formerly of Buena Vista Sanatorium, Wabasha, now superintendent and medical director of G. B. Cooley Sanatorium, the Tuberculosis Sanatorium of Ouachita Parish, Monroe, Louisiana writes "There are many things I have missed since leaving Minnesota, August 15, last, not the least of which has been the Staff Meeting Bulletin of the University Hospital, a most excellent publication. It would be like a breath from home to receive it again here if this can be arranged. Please convey my best regards to Drs. O'Brien, Myers, Wangensteen and the other friends in and about the school and hospital."....The first bulletin of the Minnesota Dietetic Association made its appearance January 22, 1940. Lorraine V. Frawley is editor, Angeline Mannick, assistant editor, and Elizabeth Ryan, business manager. The other four positions are held by dietitians who are not members of our staff. The issue contains a message from the president, editorial page, news about the dietitians' dinner at the Gold Room of the Radisson Hotel, January 31, at 7:30 p.m., an article on continuation study, food for thought (a discussion of the dietary needs of older people), educational articles, social column, and some verse, jokes, and personals. The bulletin has a very attractive cover and arrangement...The University has acted as host this week to Lester J. Evans (medicine) and Geddes Smith (publications) of the Commonwealth Fund of New York. They are here in the interest of the projects which they are supporting at Minnesota: medical and hospital postgraduate education, psychiatry in childhood, growth and development studies. They are also interested in the progress of Dental Research, Biochemist Wallace Armstrong, who was on a traveling fellowship last year. According to Time, Mrs. Stephen Vanderburg Harkness of Manhattan set aside $10,000,000 to "do something for the welfare of mankind." By 1926, when she died, she had left $38,000,000 to the Fund. Now it is $50,000,000. Last year the Fund gave $2,000,000 to Research and Public Health. Its chief interests are public health support, especially in the south; fellowships for young teachers in medicine and future general practitioners; bringing British students to America; assisting in postgraduate medical and hospital programs; building rural hospitals; publishing books; and assisting in research. M. H. Manson, formerly of our staff, is a member of their hospital group. It is always good to receive visitors from the Fund who not only assist us by critically appraising what we are trying to do but also by bringing us news from other centers where similar programs are being conducted. It is said of visitors in general that anyone can be fooled, if he only spends one day. P.S.- The Commonwealth representatives spend four days...According to a University of Minnesota report, students who lived in the dormitories made better scholastic records than those who lived at home (second), fraternities or sororities (third), and rooming houses (fourth). Co-operative cottages led all groups in scholarship. In the first study comparisons, students with similar high school records and college aptitude ratings were tested. This report is of interest in connection with previous studies which indicate that the children of those who occupy the "lower" stations in life and those with limited incomes are much better students than those who come from the more privileged homes. It is probable that there is purposeful selection (ambition) in the lower income group.....