Diet in Relation to Dental Health*

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Vitamin D, Calcium and Phosphorus.

In searching for factors concerned in the etiology of caries and pyorrhea, and of tooth hypoplasia, the elements, calcium and phosphorus, and vitamin D have perhaps received more attention than any other dietary constituents, with the possible exception of vitamin C. This seems logical. While it would be readily admitted that all essential dietary components must be present in a diet that promotes and conserves good health, the relation of certain dietary defects to definite pathological conditions—vitamin C to scurvy, iron to anemia, iodine to goitre, etc.,—is unquestioned. Since teeth are composed chiefly of calcium and phosphorus, and since the metabolism of these elements is to a large extent controlled by vitamin D, it is not unreasonable to try to discover the influence of these factors specifically upon teeth. This paper will deal with calcium, phosphorus, and vitamin D only; other factors concerned with calcium and phosphorus absorption and metabolism will be considered in a later paper.

The earliest and most extensive work is that of May Mellanby (1, 2). She began by examining teeth in the dogs which Dr. E. Mellanby was using in his studies of rickets and her work has continued over many years. She studied, in this period, hundreds of dogs of various breeds, and thousands of their tooth sections. In many ways dogs are particularly good experimental animals. They readily adapt themselves to living under laboratory conditions; they have two sets of teeth similar in development to man's; they eat a mixed diet as does man. Most of the experiments were on young animals, begun at five to eight weeks of age and continued three to six months. A few experiments were made beginning with animals fourteen weeks old. Due to progressive improvement in the basal diet and hence in change of mineral content as well as in other factors; also to variation in the dogs' sizes and hence some difficulty in adjusting the food requirement, the results are not exactly comparable or clear cut. Moreover, at the time the work was started, it was not yet recognized that there are at least two fat-soluble vitamins, that is, vitamin D was not differentiated from vitamin A. Dr. Mellanby (3) showed that rickets was induced by a dietary deficiency which he believed identical with vitamin A. It was not until 1922 that McCollum (4) showed that whereas vitamin A is destroyed by oxidation, cod liver oil, which had been

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treated by passing a stream of oxygen through the heated oil, was still curative of rickets, although no longer so of ophthalmia. The distinction between vitamins A and D was taken into consideration in Mrs. Mellanby's later studies. The work on dogs was corroborated by study of rabbits and of rats, showing that the findings are not peculiar to the one species. With so large a number of animals on diets arranged to test the effects of low or lacking fat-soluble vitamins (A and D), the results, while not final, certainly demand consideration.

Dogs which had severe rickets, showed tooth defects evident to the most casual observer. The teeth were late in erupting and irregularly set; the jaw bone was spongy as are the ends of bones in rickets; the enamel was very soft and the total calcium low, roughly one third that of teeth of non-rachitic animals. Microscopic examination showed poorly constructed enamel and dentine with many interglobular spaces. However, actual decay did not occur. Mrs. Mellanby suggested that the experiments were not continued long enough to show decay. Similar structural defects were noted as fore-runners of decay in children's teeth. Antirachitic treatment, whether by addition of cod liver oil or egg yolk, irradiated foods or sterols (viosterol), or by exposure to ultraviolet radiation, resulted in improved tooth structure and higher calcium content. Increase of calcium phosphate, by addition of the inorganic salts or by increase of amount of milk fed, failed to show significant differences in the teeth.

A further observation of great interest, if the application to the human problem may be made, was the effect of the diet on the teeth erupted at different periods. In puppies, as with infants, calcification of the incisors is nearly complete by the end of the nursing period. These teeth are then fairly well perfected, even though the mother's bones and teeth may suffier. That this protection may not be complete is evidenced by the occurrence, although more rarely, of rickets in breast-fed infants. Since teeth calcify from the occlusal toward the apical area and from external to internal surfaces, there is usually a band of normally formed dentine even in the later erupted teeth. This band is narrowest with teeth being calcified just after weaning when the puppies were put on diets low in fat soluble vitamins. In Mrs. Mellanby's experiments, the teeth suffering most were the carnassials, which correspond somewhat to the first molars in man. The parallel, here, with human observations is striking. Usually decay occurs first in the molars and much more rarely in the incisors; usually, also, poorly formed and set teeth are most prone to decay. Carrying the parallelism further, decay most frequently occurs, primarily, in pits and fissures.

Many of these puppies showed alternate layers of poorly and well constructed dental tissues directly dependent upon the alternating poor and good diets, during the time of active calcification. When the dogs were older, so that calcification was more nearly complete, when they were subjected to the poor diets, the teeth remained apparently normal (Compare, however, Steenbock's work discussed later in this paper).

Having shown the effect of inadequate or low supply of vitamin D on dogs' teeth, Mrs. Mellanby started to examine teeth of children. Here, again, her work has been extensive. She examined more than one thousand deciduous teeth, either shed normally or extracted. These she classified as (1) normal, with smooth enamel and no interglobular spaces in the dentine; (2) slightly, or (3) severely hypoplastic. She found only about fourteen percent structurally sound, while nearly two thirds were severely hypoplastic. Also, in general, the incisors were far better developed than the first and second molars. Even considering that some of the teeth examined were probably extracted because of defects, these findings are startling. Some permanent teeth were also examined. These were chiefly molars and all were found defective. Since these were available only by extraction, the results are less generally applicable than the results from the deciduous teeth. However, again the incisors, canines, and premolars were much better constructed than the molars, and the second molars were poorer than the first. In both studies the relation of structure to decay was striking. Well formed teeth rarely showed decay while in markedly hypoplastic teeth more than eightyfive per cent showed carious cavities. That poor tooth structure predisposes to caries was further borne out in cases when formation of secondary dentine was observed. If the diet contained adequate amounts of vitamin D while the secondary dentine was being formed, this was well calcified: if vitamin D was low or lacking, secondary dentine was of poor quality or not formed at all.

In this work on children's teeth, Mrs. Mellanby was assisted by Dr. Pattison, medical superintendent of King Edward VII Hospital, Sheffield. Dr. Pattison has further shown that the calcium content of saliva is greatly increased when an adequate amount of vitamin D is added to the diet. (5). Thus, in order to understand that increased vitamin D may stop the progress of caries by increasing the availability of calcium for formation of secondary dentine, it is not necessary to be arbitrary in regard to the moot question as to whether secondary dentine is calcified from within or without the tooth.

The next logical step was to determine whether giving children liberal amounts of vitamin D would prevent caries. Mrs. Mellanby and Dr. Pattison

with Dr. Proud, a dentist, undertook a study to discover this. (6). subjects were children with bone tuberculosis under twelve years in the King Edward VII Hospital. They were on the regular hospital diet which included about one and one-half pints of milk, ten to fifteen grams (about one-half ounce) of cod liver oil, and moderate amounts of fruits and vegetables, some meat and occasionally eggs. In the three series of experiments the children were grouped as follows:—(a) hospital diet; (b) hospital diet with additional milk, eggs, cod liver oil; (c) one-half to three-fourths pints of milk, no cod liver oil, high cereal especially oat meal; (d) hospital diet plus one to four cubic centimeters radiostol (viosterol). The teeth were carefully inspected at beginning and end, precautions being duly taken to eliminate personal bias of the examiners so far as possible. It is obvious again that more than one factor was varied among the several groups, although the chief variation was of vitamin D. The results led the investigators to the conclusion that increased vitamin D in whatever form showed marked benefit on the teeth in lessening the spread of caries and increasing the hardness of the teeth. That the effect was chiefly due to vitamin D is sustained by the rather better results when radiostol, the most concentrated source, was used.

Another investigation pointing to similar conclusions and rather widely heralded in the popular press was that of Tisdall and co-workers at Toronto. (7). Here the molar teeth of rats were studied; while rats do not have two sets of teeth and their incisors grow throughout their lives, the molars are similar in structure and function and in pathological manifestations to human molars. The diets given were all of about the same consistency (the importance of this will be discussed in the subsequent article) and were varied in contents of calcium, phosphorus, and vitamin D, both together and separately. On fully adequate diets, no caries developed in eighteen months. If the diets were adequate, except for vitamin D and phosphorus, fifty percent of the animals had developed caries by the end of thirteen months. When vitamin D was added in adequate amounts no caries developed. On diets which were inadequate as to minerals in general and good quality protein. as well as phosphorus and vitamin D, nearly all the animals showed caries within two months. Additions of vitamins A, the B complex, C, and E, failed to influence the teeth. (It should be pointed out that the rat does not require vitamin C, possibly being able to synthesize it). When, however, this poor diet, made normal with respect to phosphorus, was given, four of seven rats showed no caries in six months while if phosphorus was left low but adequate vitamin D given, no caries occurred in six, of a group of nineteen, in five months. No relation was found between bone ash or blood phosphorus and caries. On a low phosphorus diet, when vitamin D was adequate, animals whose blood phosphorus was low did not show caries. The percent of calcium in the diets was varied over a wide range without seeming to influence caries. The authors concluded that calcium has no influence and that low phosphorus and vitamin D are the most important factors in inducing caries. Since the human diet is more likely to be inadequate with regard to vitamin D than to phosphorus the former is the more important in the human problem. Parenthetically it must be said that knowing the mutual interdependence of calcium and phosphorus metabolism, it is difficult to accept the influence of calcium as nil if the influence of phosphorus is so great. These authors also give a preliminary report on the application of these results to children. After one year, children given vitamin D, in addition to their usual diets, showed no new decay and better health of gingivae and mucous membranes. The children to whose diets there had been no such additions, showed no improvement.

A similar study was made by McCollum and his associates. (8). The diet contained $77\frac{1}{2}$ to $79\frac{1}{2}$ per cent oatmeal, adequate with respect to calcium and phosphorus. To this basal diet was added in varying proportions, butter fat, cod liver oil or viosterol, with and without tomato juice. The latter substance showed no influence. Of the others, viosterol gave the best results, sustaining the conclusion that vitamin D specifically influences the occurrence of caries.

There is other evidence reported in the literature that rickets or the conditions inducing rickets predispose to poor teeth. Delay in tooth eruption has long been considered a symptom of rickets. A statistical study of this delay was made by Blum and Mellion (9) who found that while time of eruption of the first tooth showed a good deal of variation with normal children, even mild rickets caused definite delay, not only in the first but in subsequently erupted teeth. Dr. de Vries (10) states that hypoplasia of the first molars and permanent incisors is most frequent in children with histories of early rickets, i. e. that there was hypoplasia of the teeth being developed at the time the child had rickets. He also reports bad decay in the temporary teeth of such children. Hess (11), studying two groups of children from infancy to five to nine years, reported that the group with histories of mild rickets showed slightly greater incidence of caries than the group with no evidences of rickets. Therefore, he points out, that while rickets may be of importance, it is far from the whole story. Caries does occur with no sign of rickets and on the contrary there may be marked rickets with good teeth, a condition often found in the negro. Moreover, rickets is rarely seen in the tropics while caries is rampant. He further urges that distinction be made between caries, a disease of dentine (mesodermal tissue), and soft enamel (ectodermal tissue) and notes that low calcium, as in Mrs. Mellanby's experiments, discussed above, results in poor quality of enamel rather than in caries.

Leaving out the involvement of rickets, there is much direct evidence as to the effect of ample vitamin D on mouth and tooth health. Templin and Steenbock (12), studying calcium conservation in the adult, noted that on very low calcium diets, the teeth were affected and that additions of vitamin D proved corrective. Bödecker and Applebaum (13) found caries developing in rats on diets deficient in vitamin D. The molars were most involved, but all teeth showed some decalcification. They also noted bacterial plaques on the tooth surfaces. The finding of such plaques is also discussed in Bunting's studies (14) and influences his opinion regarding the importance of bacteria as affecting caries. This theory will be discussed in a later paper but it is of bearing on the present subject because high calcium was found to influence the hardness of teeth and therefore the progress of caries, yet these hard teeth may show caries and soft teeth may not do so invariably. Bunting furthermore considers that structure is undoubtedly important, since decay occurs much more often in pits and fissures, i. e. in poorly formed teeth, than on smooth surfaces. Many workers (15-22) have confirmed the findings of poor structure and tooth arrangement, including malocclusion, on diets low or deficient in vitamin D.

With all this emphasis on the value of vitamin D it is well to add a warning. Clinically there is no longer doubt that excessive dosages of viosterol are dangerous. Early symptoms of vitamin D toxemia are loss of appetite with hypercalcemia, followed by kidney damage. There are also a few reports on specific damage to the teeth after administration of high amounts of vitamin D (23, 24). Whether these effects are due to vitamin D itself or to a toxic substance which may occur with it in irradiated sterols, is not determined. Practically it is beside the point since it is difficult to give excessive doses without the use of irradiated sterols (viosterol, radiostol). Since, also, these excessive doses could not be given before the use of irradiated sterols became common, this can not well be the main cause of caries. It has been suggested that the rampant caries in the tropics may be explainable on the basis of high vitamin D (tropical sunlight) with low calcium and phosphorus intake. (31). This should not be taken to mean that viosterol should never be given, but only that it should be given with care and under observation.

Perhaps vitamin D has received so great emphasis in the study of this problem because it is a comparatively new weapon in fighting rickets and

other disturbances of calcium and phosphorus metabolism. While it does permit the organism to utilize small amounts of these elements to much greater advantage than is possible without it, it cannot *replace* these elements or promote good health with sub-minimal amounts of them. That this is true regarding tooth and mouth health, directly, as well as that of other body tissues, is sustained by several investigators. Hess (11) pointed out that milk in the diet was of value for the teeth, although it is not antirachitic. (Sometimes milk may contain traces of the antirachitic factor but the amount is so small and so variable that it cannot seriously be considered as the reason for the value of milk). Kramer and Howland (25) explained the occurrence of hypoplastic teeth as being due either to low calcium or low phosphorus or both. They note also that there is not seasonal variation in the development of caries, as there is with rickets, wherefore the cause is not primarily low vitamin D but rather low supplies of the elements themselves.

Davies, in Massachusetts (26), reported a very striking study supporting the value of milk for the teeth. Children of elementary school age were examined, medically and dentally, in two towns and their diets studied by means of home visits. The diets in the two towns were very similar except that in one, a dairy town, 64 per cent of the children consumed a quart or more of milk daily, while in the second but 16 per cent received that amount of milk. In the first town, 35 per cent of the children had no carious permanent teeth and 11 per cent had five or more; in the second town only 17 per cent were without carious permanent teeth and 22 per cent had five or more carious teeth. The difference is more striking when first molars are considered. In the dairy town only 17 per cent had all first molars carious or extracted (a high enough figure indeed!) but in the second town 46 per cent had all first molars carious or extracted. A study from the Mayo clinic (27) seems superficially, to refute this evidence. Two groups of school children, one with perfect teeth, the other with high occurrence of caries, were observed. Quite full data as to dietary history from infancy, heredity, etc., were The chief difference was that the good-tooth group consumed considerably larger amounts of fruits and vegetables while the poor-tooth group actually drank more milk. However, the diets of the second group also contained large amounts of cereals and candy. (The effect of high carbohydrate will be discussed in a later paper). If, as the author concludes, fruits and vegetables are more effective in protecting teeth than milk, this cannot be taken as support for the theory of the value of an alkaline ash diet, (discussed in a later paper) since milk yields a high alkaline ash. A more probable explanation is supplied by the work of Chaney and Blunt (28) who found that orange juice, added to a high cereal diet, increased retention, in children, of both calcium and phosphorus. Blunt (29) suggests that this is due to the double acid-base effect of the orange juice, i. e., acid in the digestive tract but alkaline after combustion. It may be further pointed out that milk contains calcium and phosphorus, not only in good amounts but in optimum proportions; also that children are able to absorb and utilize calcium much less well when it is taken in the form of vegetables than in milk (30).

Consequently adequate sources of calcium and phosphorus and of vitamin D must be considered in maintaining dental health. Vitamin D is the least generally distributed of all the known dietary factors and, therefore, very apt to be low or lacking in the average dietary, both of adults and children. Of the common foods, egg yolk is the only one supplying it in any significant amounts. 'Egg yolk was early shown to be both preventive and curative for rickets. (32). One egg yolk daily was preventive in the formulae of bottle-fed babies. Even severe rickets in children was cured by adding one to two egg yolks daily to diets of milk and cereal. (33). However the diet of the hen or the amount of ultraviolet she receives makes a great difference in the vitamin D content of the egg—even as much as tenfold. (34). Since it is seldom possible to know much about such conditions, in buying in open market, even eggs cannot be relied upon as a potent source of the vitamin in the diet.

Milk, or rather milk fat, may contain small amounts of vitamin D, depending again upon the cow's ration. If the cows are on good diet, the milk shows small amounts, roughly one-hundredth of that in good cod liver oil. (35). Since both milk and butter may easily be taken in relatively large amounts, this has some importance, if one is able to know conditions of the animal producing the milk. Cod liver oil in the cow's ration makes slight if any difference in the vitamin potency (36) and tends to decrease the milk flow. (37). Recently this problem has been met by feeding irradiated yeast to cows. By this means milk of standard vitamin D potency may be practically obtained. Such milk has seemed to show unusually good antirachite effects in comparison with other sources of vitamin D of similar unit content. (38). Human milk may be low or entirely lacking in vitamin D. (39, 40). It may be slightly increased by giving cod liver oil to or directly irradiating the mother. (41, 42). It would seem better that some source of this vitamin be directly administered to the infant.

Before discussing the vitamin D potency of the fish oils, it will be well to try to clarify the standard of evaluation. The official unit of the Council on Pharmacy and Chemistry of the American Medical Association is "that amount of vitamin D which, when uniformly distributed into the standard vitamin D deficient diet (Steenbock's), will produce a narrow and continuous line of calcium deposits on the metaphyses of the distal end of the radii and ulnae of standard rachitic rats." This is often called the Steenbock unit. The American Drug Manufacturers Association (A.D.M.A.) unit is ten times the Steenbock unit. Knowledge of the vitamin and methods of assay have advanced so rapidly that recently a new unit, "U. S. P. x - revised 1934", has been made official by the U. S. P. Vitamin Advisory Board, to be used in evaluation by the Food and Drug Administration. This is the same as the "international unit" and equals 3.25 A.D.M.A. units. At the moment it seems to add to the confusion, but as it comes into use and replaces the others it will make accurate comparisons easier.

The classic source of vitamin D is cod liver oil which was long administered empirically before the relation of the vitamin to rickets was known. With development of methods for biological assay it has been shown that cod liver oils vary widely, depending upon season, amount of fat in the cod's liver, etc. Oils put out by reliable drug houses now specify a minimum potency, biologically determined. Claims of many of the drug houses, both for cod liver and other fish oils and preparations, have been checked by the American Medical Association Council, so there is no difficulty now in getting a reliable source. Fish oils other than cod have been shown to be even richer. Halibut ("Haliver"), tuna, salmon, sardine and herring, are some of the edible fish showing high potency not only in the liver, but in the case of the latter three, in body oil as well. (28).

Ultra violet radiation is a good source of vitamin D. This is true whether the source is artificial (carbon or mercury arc) or from sunlight. The latter, however, is a source of ultraviolet only in certain localities and during certains seasons of the year. That is, ultra violet is filtered out from sunlight by smoke and by certain atmospheric conditions such as haze and fog. It probably reaches the earth not at all or in insignificant amounts when the sun is below 35° from the horizon, i. e., in winter, outside of the tropics and at the ends of the day (43, 44, 45). In general, high altitudes receive more ultra violet than low. Direct irradiation must be carefully controlled to avoid serious burns and overdosage. For these reasons irradiation of food has been developed recently. (46). With cereals this at least probably serves to balance any anti-calcifying effect. Irradiation of milk, both fluid and powdered, has been reported as having value. (38) However over-irradiation causes unpleasant taste and odor, finally even destroying the activation and also vitamin A. The production of milk high in vitamin D potency, by feeding irradiated yeast to the cows, would seem to be the preferable method. Many other foods have been successfully activated, nearly all foods except sugar and rancid oils may be. So far these have not come into general use.

The most fascinating outcome of the knowledge of inducing vitamin D potency by irradiation of foodstuffs has been the elucidation of the nature of the vitamin itself. That ergosterol, chemically related to cholestorol, is the "pro-vitamin" has been established by work contributed from several laboratories (47). Irradiation changes ergosterol in certain of its chemical as well as biological properties. "Viosterol" has been officially adopted as the term for irradiated ergosterol; the English term is "radiostol".

As sources of calcium it is perhaps sufficient to stress milk and cheese. Without the liberal use of milk it becomes all but impossible to insure sufficient amounts of calcium in a child's diet. Vegetables may well serve as a good source in the adult diet. Phosphorus is contained in good amounts in milk and is relatively high in egg yolk, legumes, cereals, meat, and fish.

Summary

Liberal but not excessive amounts of vitamin D must be supplied to the organism to insure good teeth and mouth structure and health of the mouth tissues. Such a supply is difficult to maintain without the use of one of the fish oils. Adequate supplies of calcium and phosphorus are also essential to dental health.

Literature Cited

- 1. Mellanby, E., Jour. Physiol. 52, xi. (1918); Lancet I (1919), 407.
- 2. McCollum, Simonds, Becker, and Shipley. Jour. Biol. Chem. 53, 292, 1922.
- 3. Mellanby, M. Physiol. Rev., 8, 545. 1928; Lancet II 767, 1918; Med. Res. Council Special Rpt., No. 159, 1931.

 4. Mellanby and Pattison, Brit. Dental Jour., 47: 1045, 1056, 1926. Brit. Med. Jour.,
- 2: 1079, 1928.
- 5. Pattison, C. L., Brit. Med. Jour., 3: 6. 1926.
 6. Mellanby, Pattison, and Proud, Proc. Royal Soc. Med., Section of Odontology) 16: 74. 1922-23.
- 7. Agnew, Agnew, and Tisdall. Jour. Amer. Dental Assoc., 20: 193. 1933.
- Whittle, Klein, and McCollum, Jour. Dental Res., 13: 189. 1933.
- 9.
- Blum and Mellion. Jour. Amer. Med. Assoc., 86: 677. 1926. DeVries in Abt's Pediatrics III. 118. Saunders Co., Philadelphia. 1924. Hess, A. F. Dental Cosmos 73: 849. 1931. 10.
- 11.
- Templin and Steenbock, Jour. Biol. Chem., 100: 217. 1933. 12.
- **1**3. Bödecker and Applebaum, Dental Cosmos 74: 335. 1932.
- 14.
- Bunting, Dental Cosmos 72: 399, 1930. Grieves, Jour. Amer. Dental Assoc., 9: 467, 1922. Barker, Jour. Amer. Dental Assoc., 18: 17, 1931. 15.
- 16.
- 17. Kronfeld and Barker, Jour. Amer. Dental Assoc., 19: 105. 1932.
- Beck and Weber, Jour. Amer. Med. Assoc., 18: 197. 1931. Gottlieb, Dental Cosmos 62: 1209. 1920. 18.
- 20. Marshall, Jour. Amer. Dental Assoc., 14: 2207. 1927.

- Blackberg and Berke, Jour. Dental Res., 12: 349, 695. 1932.
- Weinmann, Jour. Dental Res., 10: 411. 1930. 22.
- 23. Downs, Jour. Dental Res., 12: 363. 1932.
- 24.
- Blackberg and Berke, Jour. Dental Res., 12: 609. 1932. Kramer, Amer. Jour. Dis. Child., 30: 195. 1925; Kramer and Howland, Jour. Nutri-25. tion 5: 39. 1932.
- 26. Davies, E. S., Mass. Agr. Exper. Sta., (Amherst) Bull. 241. 1928.
- Kappes, L. O., Amer. Jour. Dis. Child., 36: 268. 1928. 27.
- Chaney and Blunt, Jour. Biol. Chem., 66: 829. 1925. 28.
- Blunt and Cowan, Ultra Violet Light and Vitamin D in Nutrition. Univ. of 29. Chicago Press. 1930.
- 30.
- Sherman and Hawley, Jour. Biol. Chem., 53: 375. 1922. Hess, A. F., Rickets Osteomalacia and Tetany. Lea and Febiger, Phila., 1929. 31.
- Hess, Jour. Amer. Med. Assoc., 81: 15. 1923. Casparis, Shipley, and Kramer. Jour. Amer. Med. Assoc., 81: 818. 1923. 32.
- 33.
- 34. Hart et al, Jour. Biol. Chem., 65: 579 1925.
- 35.
- Coward. Quart. Jour. Pharmacy I. 534. 1928. Steenbock, Hart, et al. Jour. Biol. Chem., 74; lxxiii. 1927. 36.
- Hart, Steenbock, Kletzien, and Scott-Jour., Biol. Chem., 71: 271. 1926-27. 37.
- Hess and Lewis-Jour. Am. Med. Assoc., 101: 181, 1933. 38.
- Outhouse, Macy, and Brekke, Jour. Biol. Chem., 78: 129. 1928. Hess and Weinstock, Amer. Jour. Dis. Child., 34: 244. 1927. Weech, Johns Hopkins Hosp. Bul., 40: 244. 1927. 39.
- 40.
- 41. 42.
- Hess et al, Jour. Amer. Med. Assoc., 88: 24. 1927. Godfrey, Jour. Preventive Med., 5: 1. 1931. Godfrey and Larsen, do. 25. 1931. Tisdall and Brown, Amer. Jour. Dis. Child., 34: 721. 1927. 43.
- 44.
- 45.
- 46.
- Frawley, Amer. Jour. Dis. Child., 41: 751. 1931. Steenbock, Jour. Amer. Med. Assoc., 84: 1003. 1925; Hess do., 1910. Hess and Windaus, Proc. Soc. for Expt. Biol and Med. 24: 461 1927.