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NEW ENGLAND PEDIATRIC SOCIETY

A meeting of the Society was called to order by the President, Dr. Lewis Webb Hill, Boston, at 8:15 P. M., on May 6, 1932 who spoke as follows:

This meeting represents an attempt to arrive at conclusions concerning the rational use of the vitamin preparations in pediatric practice. There is one man whose work on deficiency diseases and allied subjects has been so brilliant and so applicable to the everyday work of each one of us that any such meeting as this could not be complete without his presence—Dr. Alfred Hess of New York.

DIET, NUTRITION AND INFECTION*

BY ALFRED F. HESS, M.D.†

IT is a commonplace that the relationship is intimate between composition of the diet and susceptibility to infection. However, the extent of this relationship and its importance in clinical medicine has only just begun to be realized; in fact we are still uncertain as to the limits of altered susceptibility. From the standpoint of disease, diet, nutrition and resistance to infection should be regarded as an etiologic unit rather than as a triad. In appraising dietaries from this point of view, not only the several vitamins should be considered, but the various inorganic and organic constituents which likewise may be implicated in bacterial infection. It would lead too far afield, however, to consider these various aspects of the subject, so that I shall confine myself to the rôle of some of the vitamins, basing my conclusions mainly on observations made during the past ten to fifteen years in a child-caring institution. As my experience has been concerned chiefly with the antirachitic, antiophthalmic and antiscorbutic vitamins, in other words with vitamins D, A and C, I shall limit my comments to these specific nutritional factors. Furthermore, I shall take into consideration only clinical data, to the exclusion of experiments on animals.

After an experience of several years with the effect of *ultraviolet rays* in the prevention and cure of rickets, an effort was made to lessen the incidence of infection in the institution by means of irradiation with the mercury vapor lamp. As is well-known, respiratory infections constitute one of the last vestiges of institutionalism in hospitals and asylums for children and, during the winter months, plague and torment their foster-parents. Our first attempt, undertaken in 1926[1] with the confidence born of inexperience, was most disappointing. In the course of the winter, in spite of irradiation carried out every other day for a period embracing four months, quite as many infections occurred among the group of infants who were irradiated as among those who lived under the same régime except that they were not irradiated. It may be added that the irradiated group evidenced an initial increase in weight which, however, did not continue during the subsequent months.

Two years later a similar investigation was carried out[2] with the only difference that a carbon arc lamp was used as the source of radiation, as it was thought that these rays might be superior because they more nearly resemble the spectrum of the sun. Again our efforts were fruitless. In spite of systematic exposures to these rays no relative diminution in the incidence of respiratory infections occurred during an observational period of three months.

The following year, 1929, the problem of infection was attacked in a different way[3]. Rickets was prevented by means of the usual doses of cod liver oil, in other words of three teaspoonfuls daily for babies three months or more of age. The diet was composed of full amounts of pasteurized milk, cereals, orange juice, and of vegetables for the older infants. In order to render exposure as infrequent as possible, what was termed "aseptic nursing" was carried out in one ward—physicians, nurses and attendants coming in contact with the infants were required to wear surgical masks which were changed daily; hands were scrubbed thoroughly and frequently; visiting was allowed but once a month and visitors were provided with masks; fondling and petting of infants were prohibited and nurses who had colds or infections were temporarily excluded from service. Once again our attempts at prophylaxis resulted in failure; infections

*Read before the New England Pediatric Society at its meeting, May 6, 1932.

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were frequent in spite of all hygienic precautions and the inclusion of cod liver oil in a dietary which already was liberal. A graph (Chart 1) is reproduced to illustrate the irregularity and uncertainty in the occurrence of infections rather than to compare their incidence among the children in the "aseptic ward" and those in an ordinary ward. It shows that among the latter there was an epidemic of respiratory infections during the month of November, whereas among the former there was a violent outbreak in March. The diet of both groups was not only the same, but unchanged throughout the period. The occurrence of "grippe" was not due to dietary deficiency but to some fortuitous occurrence, probably to the chance introduction of a highly infective agent.

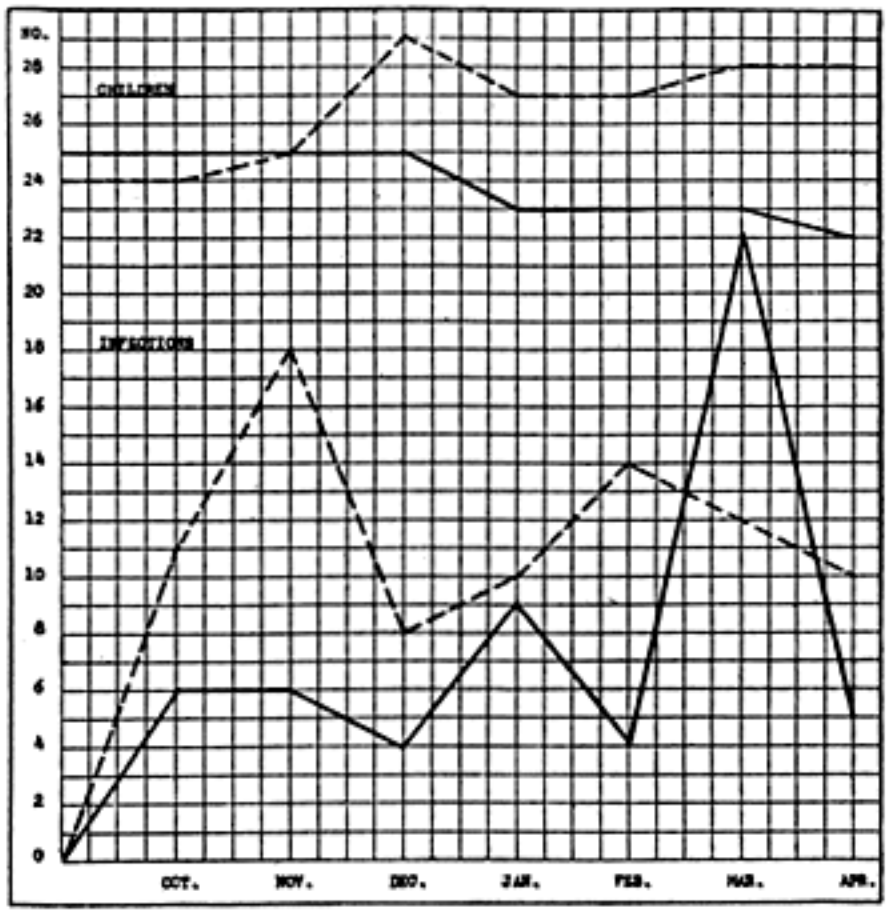

CHART 1. Outbreak of Infection in protected ward (broken line) in November. Outbreak in control ward (solid line) in March.

These and similar experiences have led, in the first place, to the conclusion that mild rickets does not predispose to infection and that antirachitics—ultraviolet irradiation or cod liver oil—do not lessen their incidence. Severe rickets probably does entail increased susceptibility, but the rickets to which we have reference is the prevalent type throughout the community that is manifested by beading of the ribs, occasional craniotabes, diminution of the inorganic phosphorus in the blood and, in about one-third of the cases, slight roentgenologic changes at the epiphyses. Not only is there no disposition to infection in this type of rachitic child, but infections have shown no tendency to be unduly severe. In a tabulation of the incidence of pneumonia of 114 mildly rachitic infants and of 102 non-rachitic infants, who had been protected by means of cod liver oil or ultraviolet irradiation, the superiority happened to be with the mildly rachitic group which did not receive oil.

What was found to be true of mild rickets held likewise for general nutrition, as judged by weight; this factor bore no relationship to the occurrence or to the fatality of pneumonia, with the possible exception of infants under six months of age.

Of late, *vitamin A* has been accorded the greatest credit in warding off infection, and a deficiency of this factor in increasing susceptibility. In fact vitamin A is at times termed the "anti-infectious vitamin". This designation has tended to replace the term "growth vitamin" since it has been realized that neither this nutritional factor nor any other has been entrusted with the control of the growth of the body. All who have carried out investigations in this field have found that growth is affected adversely by a deficiency of any one of many food constituents, for example, lack of an inorganic salt. However, the rôle of this vitamin in protecting the body against infection, more especially against invasions of the respiratory tract, has gained an increasingly strong foothold. Since the classic publication of Bloch[4] in 1917 there can be no doubt that a lack of vitamin A may induce a heightened susceptibility to respiratory infections. But, it should be borne in mind that the infants that formed the basis of Bloch's report suffered from malnutrition and had been subjected to a marked deficiency of this vitamin. For us, the important question is whether the ordinary diet of infants, children and adults, includes an

adequate quantity of this nutritional factor and, in turn, whether under prevailing dietary conditions, a deficiency of this vitamin can be held accountable for the high incidence of respiratory infections throughout the community. Although it may be stated at the outset that it is not possible at present to give a categorical answer to this question, there are sufficient clinical data to render a discussion of this important question quite worthwhile.

In the first place let me call to mind again the experience of 1929, in which the addition of cod liver oil to a liberal dietary failed to prevent explosive outbreaks of "grippe" in November and in March. During the winter of 1930-31 a very painstaking investigation of this problem which was carried out in my clinic by Barenberg and Lewis[5], led to similar failure. Without reciting the details of this study, which will be found in the original communication, it may be stated that a large series of infants was given a diet especially rich in vitamin A—including not only milk, but butter as well as vegetables, and that in the course of an observational period varying from four months to a year, all of these infants developed one or more infections. Furthermore, it proved to be immaterial whether the infants received still greater amounts of this vitamin, for respiratory infections were not diminished in number or in severity among a large group which was given the customary amounts of cod liver oil, nor even among a smaller group which received double the usual quantity.

Our experience during the past winter has served only to strengthen the impression gained during previous years. In the course of a test of the antirachitic potency of several dietaries, one series of infants was given a certified raw milk which was assayed and found to be rich in vitamin A, another series the same kind of milk which had been enhanced in its vitamin D content by feeding the cows irradiated yeast ("vitamin D milk") and a third series was fed pasteurized milk and in addition received three teaspoonfuls of cod liver oil daily. The other constituents of the diet were much the same as outlined in connection with the test of 1930-31. Although the investigation was undertaken primarily in connection with rickets, it serves as a gauge of the efficacy of vitamin A as "the anti-infectious vitamin". In regard to the incidence of infection, the results of this study were similar to those of former years. In other words, no difference was noted in the number or in the severity of respiratory infections among the members of the different groups, notwithstanding the fact that one group was given the benefit of a large addition of vitamin A by supplementing the dietary with cod liver oil. These infants were about three to six months of age at the outset and were under close observation for a half year or more. It is not so much that no distinction, in regard to infection, could be drawn between the members of these groups, but that the absolute number of infections was unusually high in all three. By infections I have in mind respiratory disturbances which are manifested by catarrhal symptoms and a rise in temperature to 100° F. or above. Indeed, in spite of the liberal diet and of the fact that they were cared for in individual cubicles and that the hygienic surroundings were unexcelled, every infant developed almost one infection a month. Major respiratory diseases were few in number; but whether or not pneumonia, empyema, otitis media or mastoid disease develops is merely a matter of chance, depending on the nature of the infective agent and, probably, on other factors with which we are as yet insufficiently informed. That such is the case we have been forced to conclude as the result of a prolonged experience, during the course of which we have at times been led to believe, perhaps for a period of five years or more, that we had gained mastery over severe infections, only to be disillusioned by a subsequent year*.

In connection with this consideration of the value of vitamin A in protecting infants against respiratory disorders, it seemed worthwhile to consult the records of a group of children which manifested "carotinemia" some years ago. This name was given in 1919, by Hess and Myers[6], to a clinical condition in which the skin became yellow and carotin was found in high concentration in the blood; it came about as the result of feeding a diet which contained a large amount of carrots and spinach. As has been recently shown, by v. Euler and others, carotin must be regarded as the "provitamin" of vitamin A, capable of transformation into the specific vitamin within the animal body. It is true that this chemical metamorphosis has not been definitely proved in regard to man. On consulting the histories of these cases it was found that infections were by no means infrequent during this period, in fact that in some cases "grippe" had been noted every few weeks. If carotin can be transmuted into vitamin A, these infants must have been thoroughly saturated with this nutritional factor. In this connection it should be mentioned that carotinemia is found most commonly in persons suffering from diabetes, due to their consumption of exceptionally large amounts of vegetables rich in carotin. Nevertheless, as is generally accepted, diabetics are prone rather than immune to infection.

*It may be added, that we have attempted to cure vaginitis, gingivitis and stomatitis, infections which involve ectodermal tissues, by means of feeding large amounts of vitamin in the form of cod liver oil, but have not found this therapy of benefit. Furthermore, infectious diseases such as measles, when occasionally they have broken through quarantine and gained access to the wards, attacked the children indiscriminately, quite independent of whether they were getting a diet enriched with cod liver oil. Measles is singled out because it must be regarded as a respiratory disease from a pathogenetic point of view. The same indiscriminate distribution is true of chickenpox, which is still more infectious and can only occasionally be limited by isolating infants in cubicles. More infectious, in our experience, than either of these highly communicable disorders is the common "grippe" of winter and early spring.

In the course of these various studies it has become increasingly evident that during infancy, even during the first year of life, *age* plays an important rôle in determining whether infection comes about. That such is the case was clearly brought out some years ago in a tabulation which showed, for a period of ten years, the incidence of pneumonia in the institution in relation to the age distribution of the children. As will be seen (Table 1), among some 1,200 infants under one year of age, the incidence was three times as great in those six to twelve months as in those under six months of age. The fatality rate, however, was higher in the younger group. Curiously enough the importance of the factor of age was lost sight of until last year when it was again brought to our attention by a striking incident. For many years we had made use of a cubicle system for quarantining infants during the first few weeks of their stay in the institution. On account of the good results obtained with this method, a large cubicle system was recently constructed for the permanent care of infants. On the first floor those under six months were placed, and on the second floor those about six to twelve months of age. It became increasingly evident that the number of infections among the younger infants on the ground floor was decidedly fewer than among those on the second floor. The usual explanations were thought of, such as defects in nursing technic or some unknown carrier of infection. In order to gain additional information in regard to this divergence, a few of the younger infants were transferred to the second floor and a few of the older ones to the ground floor. The result of this change demonstrated that the difference in incidence of infections did not depend on the character of the nursing or the situation of the cubicles but was inherent in the age of the infants—those under six months of age being definitely less subject to respiratory infections than those between six and twelve months. I emphasize this clinical phenomenon in the first place, because it has not been given significance in computing morbidity statistics in institutions or in communities. It indicates that, during the first months of life, in regard to immunity from infection, the infant is still leading a somewhat parasitic existence, depending largely on the protective substances carried over from the mother. I wish to emphasize especially in this connection, however, that this immunity cannot be attributed to vitamin A. Just as infants do not come into the world with a large store of the antirachitic factor, as a biologic assay by Miss Weinstock and me showed, so it has recently been demonstrated that the store of vitamin A is insignificant at birth. Wolff[7] found that the livers of 62 per cent of newborn infants in Amsterdam contained none of this vitamin whatsoever and that those who had a store at the time of birth, contained this factor in but small amount. It is evident that the outstanding immunity of the very young infant to respiratory infections cannot be ascribed to an exceptional supply of vitamin A.

TABLE 1

AGE DISTRIBUTION OF CHILDREN IN INSTITUTION (1916-1927) AND OF THOSE WITH PNEUMONIA

Age	Population, 1916-1927	Per Cent of Total	Cases of Pneumonia, 1916-1927	Case Rate per Age Group. Per Cent
0 to 6 months	505	7.3	22	4.3
6 months to 1 year	739	10.7	106	13.0
1 year to 2 years	1,392	20.2	214	15.4
2 to 3 years	1,318	19.1	105	8.0
3 to 4 years	1,317	19.1	41	3.1
4 to 5 years	1,623	23.6	17	1.0
Totals	6,894	100.0	505	7.3

TABLE 2

NUMBER OF INFECTIONS IN RELATION TO AGE AMONG INFANTS RECEIVING COD LIVER OIL OR VIOSTEROL (1926, 1929, 1930)

Age (Mos.)	Number of Infants		Average Period of Therapy (Months)		Number of Infections		Infection per Infant per Month	
	Cod Liver Oil	Viosterol	Cod Liver Oil	Viosterol	Cod Liver Oil	Viosterol	Cod Liver Oil	Viosterol
0-3	27	47	2.0	1.7	8	7	0.14	0.08
3-6	61	75	2.4	2.5	29	21	0.19	0.11
6-9	64	88	2.6	2.8	56	56	0.33	0.22
9-12	57	78	2.7	2.8	59	58	0.38	0.26
12-15	48	65	2.7	2.5	31	33	0.24	0.20
15-18	37	43	2.5	2.1	16	19	0.17	0.21

I do not believe that the dietary which the children in my institution receive can be poor in vitamin A in view of its content of 24 to 32 ounces (750 to 1000 cc.) of milk, of vegetables and even of butter, and certainly that it cannot remain deficient in this particular after it is supplemented by liberal amounts of cod liver oil. In my opinion, the everyday infections which sometimes prove so serious have little or nothing to do with this deficiency, although there is no doubt that a decided or long-standing deficiency may bring about increased susceptibility. Spence[8] of Newcastle, who has carried out careful studies of this nutritional condition, has failed to note an increase of infections even among a group of children suffering from xerophthalmia and night-blindness. He found them subject merely to an increase in infections of the skin, such as impetigo and boils. Perhaps the diarrhea which has been reported in connection with fat-soluble A deficiency and which indeed is the outstanding symptom of

"hikan", a disorder reported by Mori[9], is another manifestation of infection of the surface of the body.

As is well known, Mellanby and Green[10] have stated recently that a lack of vitamin A in the diet is responsible for puerperal sepsis, and are of the opinion that they were able to prevent this serious condition by giving a vitamin A concentrate. I am not in a position to cite cases of this description from actual experience, but the distribution of puerperal sepsis throughout various countries of the world does not seem to bear out this contention. As is well known, the incidence of puerperal sepsis in the United States is very high compared with European countries. For example, the mortality is stated to be more than twice as high in this country as in towns in the European part of the Soviet Union, as reported in 1926, on the basis of over one-half million confinements[11]. It is difficult to square these statistics and those of a similar nature with the vitamin A intake and economic status of the peoples of Europe and of the United States*. Aykroyd[13] tells us that on the coast of Newfoundland, night-blindness, a symptom of vitamin A deficiency, occurs in women usually in association with pregnancy, but he adds that puerperal sepsis is not common in Newfoundland.

In connection with a consideration of infection it should be mentioned that *intestinal parasitism* has been noted by many observers in association with vitamin A deficiency. Gamboa[14] has referred to ascariasis, and Mori to the frequency of anchylostoma in the mother. Most observers attribute the vitamin deficiency to the intestinal infestation rather than that the parasitism has resulted from the food deficiency, which to my mind is the true sequence of events. In 1921, Pappenheimer, McCann and I[15], in the course of a study of diets deficient in vitamin A, pointed to the fact that infestation with cestodes was extremely common. Orr[16] has recently emphasized the close relationship between intestinal parasitism among African tribes and deficiencies in diet. It is quite possible that the notable frequency of intestinal parasitism in the Far East, in Porto Rico and elsewhere may be ascribable to one or more deficiencies in the diet. In this connection it may be of interest to cite the following comment of Hegner[17], "There is an interesting relation between these intestinal protozoa and the character of our diet. Meat-eating animals are not ordinarily infected with them, but vegetarians are very highly parasitized. Casein seems to be the best of the proteins. A diet consisting largely of casein soon brings about a decrease in the number of certain organisms and often leads to their total elimination."

The stumbling block in this entire question is to determine what constitutes an adequate amount of vitamin A in the dietary. In the rat a lack of this factor leads to a cessation of *growth* as soon as the body store of the vitamin has been used up. In fact, cessation of growth, together with xerophthalmia, is used as the criteria in assaying products for this vitamin. In infants, however, the relationship between growth and deficiency is not so intimate or reliable; otherwise we should have at hand a valuable means and measure for gauging the adequacy of vitamin A. In a study of the "clinical rôle of the fat-soluble vitamin", carried out with Unger[19] in 1920 in which a few infants were closely observed who had received a minimal quota of this vitamin for periods of some months, it was remarked that "their growth in length has been normal and their growth in weight slightly below normal". In fact, adding an increased amount of cereal, which contained practically none of the deficient vitamin, brought about a gain in weight. The experience of the past few years has served to strengthen my opinion that failure to gain in weight should not be attributed to lack of vitamin A. If we use growth as a criterion of adequacy of this vitamin, we must conclude that our infants are receiving sufficient, for on adding cod liver oil to the dietary we have not been able as a rule to bring about a gain. With this point in mind, we have recently reviewed a large number of weight charts, and have found more instances in which a failure to gain followed giving cod liver oil, than cases in which an increase in weight was brought about. In his recent study, Spence also emphasizes the fact that the growth of the children which developed xerophthalmia was but little inhibited and that their nutrition did not suffer. On the other hand, in Blegvad's cases, which advanced to the stage of keratomalacia, there was loss of weight for two or three months before the signs developed. Cases of keratomalacia are of no value in a consideration of the question of adequacy of the diet or of signs of early deficiency.

Without doubt infants are more susceptible than adults, which is true in respect to all the vitamins. Furthermore, it can be stated that there is unanimity that the first year of life is the period of greatest susceptibility. Thalberg[20], in his early description of cases from St. Petersburg, reported that most of his cases were breast-fed infants whose mothers had fasted for a considerable period. Among Bloch's 86 cases, 47 developed the disorder during the first year of life and 20 of these in the course of the first six months. Of Blegvad's 430 cases of keratomalacia, in other words of advanced deficiency, 368 occurred during the first year, the majority

*Macy and her coworkers[18] write as follows: "Milk from women on the average American dietary is apparently a relatively rich source of vitamin A, since 2.5 to 3 cc. of the mixed milk from a group of wet nurses in various stages of lactation were sufficient to satisfy the nutritive demands for this factor during growth and reproduction of the rat. Further evidence of the potency of breast milk is illustrated in the children's clinics, where ophthalmia is rarely, if ever, observed in suckling infants."

in the second quarter; 62 were seen during the second year of life[21]. The curve of incidence which he publishes reminds one of the age-incidence of infantile scurvy. The mortality likewise was greatest in the second quarter of the first year and comprised 90 deaths.

It is evident, therefore, that infants must be considered quite apart from older children or adults. This is true likewise from a symptomatic standpoint as the earliest sign of vitamin A deficiency differs in the two groups. In infants the earliest sign of deprivation is xerosis of the cornea, which is a stage antecedent to xerophthalmia, in older children and adults the earliest symptom is purely subjective and consists of night-blindness.

The data in relation to infants are less numerous and detailed than that for adults. In general it may be stated that no case of xerophthalmia has been reported which developed on whole milk, irrespective of quantity, nor in an infant that was receiving cod liver oil. From the point of view of vitamin A, these agents seem to represent adequacy, coupled with a factor of safety. Furthermore, all active cases seem to have responded promptly to milk or to cod liver oil. In regard to the oil the customary dose has been about three teaspoonfuls daily, in other words the amount which the children in my institution received and which failed to protect them against frequent respiratory infections. Mori noted a marked improvement as early as one-half day after giving cod liver oil. Monrad[22] writes that 10 gm. of whole milk brought about a prompt subsidence of xerosis in cases occasioned by a diet of milk which had been not only skimmed by centrifugation but doubly heated. If we can draw any conclusion from this and other experiences it would seem that an allowance of 24 ounces (750 cc.) or more of milk, which is the usual quota for our infants, should amply cover requirements. It may be added that Blegvad found that boiled milk was just as effective a curative agent as raw milk.

As stated, older children and adults must be considered as a group separate from infants because they manifest night-blindness or nyctalopia. This is often the first symptom noted by the Russian peasants following the Lenten fast. It is intensified by sunlight, probably owing to the fact that the rays use up the visual purple in the background of the eye. It is likewise the first symptom of improvement in this deficiency disorder. Spence tells us that 10 cc. of cod liver oil cured the condition rapidly, doing away with night-blindness in older children within a period of from three to five days. Aykroyd remarks that it is the rule that the vision is normal 12 to 24 hours after liver or liver oil is given; the dose of the liver oil was usually about two tablespoonfuls. The rapidity in the disappearance of symptoms reminds us of the magic cures of polyneuritis in pigeons, brought about by feeding rice polishings or yeast. Aykroyd's note to the effect that the vision is kept normal by giving about an ounce of cod liver oil every four or five days throughout the summer is particularly interesting as it furnishes some measure of the demands and the utilization of this vitamin under extreme conditions*.

The significance of night-blindness in connection with our study is that this defect in vision is a rare clinical condition in this country and, therefore, it may be inferred that a lack of vitamin A in older children and in adults is exceptional. The Quarterly Index for 1931 does not refer to a single clinical paper from the United States on the subject. It should be mentioned, however, that night-blindness seems to be increasing in England, as Spence observed 17 cases in the course of a year in Newcastle. It is quite possible that if economic stress should be prolonged and should increase in this country, similar cases will be noted here. At present, however, the rarity of night-blindness must lead us to conclude that it is rare for the dietary of older children and adults to be deficient in this factor.

In passing, I should like to draw attention to a cheap and effective source of vitamin A which, with advantage, could be added to the human dietary, especially when a deficiency of this vitamin is suspected. As is well known, *alfalfa* is one of the richest sources of vitamin A, the only vegetable which contains a comparable amount being spinach. Like spinach, it is also rich in iron and other mineral salts. This legume is also used as a source of high-grade protein for animals. In regard to vitamin A, it is the equivalent of butter, one teaspoonful containing approximately the same number of units as a teaspoonful of average dairy butter. Biological assay shows it to have about one-half the potency of cod liver oil, but, it should be added, a level teaspoonful of alfalfa weighs only one-third as much as the oil. Having these qualities in mind we have recently incorporated alfalfa in the dietary of our children†. The simplest method was found to be to add one or more teaspoonfuls to the six-ounce portion of broth which they regularly obtain. This forms a palatable soup, having a taste similar to pea soup, and is liked by infants and young children. It has been incorporated also in the cereal immediately after cooking; one teaspoonful is added. It would seem that alfalfa could be introduced in the dietary with notable effect in Russia, China and the Far East where A avitaminosis is most common. It is at one and the same time a food which is inexpensive and

*He writes, interestingly, that after two men had been complaining for some days, one of the crew shot a sea gull and the sufferers ate half of its liver, uncooked, apiece. Their vision returned to normal in 24 hours.

†Edible alfalfa is in the form of a very fine flour and contains about seven times the vitamin A units of ordinary alfalfa, owing to the fact that it has been dried rapidly by a mechanical process rather than allowed to dry slowly in the sun (Russell).

contains a specific vitamin in exceptional concentration. It is sad to contemplate that this source of vitamin A could well have been at the disposal of Denmark during and immediately after the War period and could have averted the many cases of blindness which resulted from a deficiency of this specific factor. A similar comment is pertinent in regard to the bone disorders which occurred in Germany, Austria and Poland during the War which could have been prevented had the specific properties of solar and artificial ultraviolet rays been appreciated at that time.

In regard to *vitamin C*, I shall refer only to the bearing of this vitamin on infections, more particularly of the respiratory tract. In 1917, in a paper on the pathogenesis of infantile scurvy, I emphasized the fact that a lack of the antiscorbutic factor which leads to scurvy, at the same time predisposes to infections[23]. This enhanced susceptibility has been confirmed by Abels, Ludwig Meyer and many others. It exists even before the scorbutic signs are manifest in the stage which is better termed "latent scurvy" than "Praeskorbutus" as the abnormal scorbutic state already exists. Similar susceptibility to infections goes hand in hand with adult scurvy. This was pointed out years ago by Lind and others in connection with scurvy in the mercantile marine and among the soldiers in times of war, for example, in our Civil War and in the Crimean War.

But I wish to emphasize quite another aspect of infection in connection with infantile scurvy. In 1917, and again in 1920, I called attention to the "widespread occurrence of nasal diphtheria in infantile scurvy", remarking that "we have encountered nasal diphtheria—with typical bloody mucus discharge—so frequently in connection with scurvy that where this local infection occurs among a group of infants they should be carefully examined for latent or mild scurvy"[24]. At the same time I drew attention to the fact that "clinical tests showed that the blood contains sufficient antitoxin (diphtheria) to afford protection." These were the days previous to the use of toxin-antitoxin*. Much to our surprise, some of these cases gave a negative Schick test in spite of the definite clinical signs of nasal diphtheria. In two instances the diphtheria bacilli were tested on guinea pigs and found to be virulent. Not long after these observations an infant died from diphtheria of the larynx which developed although the Schick test was negative. At postmortem a typical membrane was found on the larynx.

Since this time, there has been little opportunity to investigate this subject, as diphtheria has been banished from our institution by the routine use of toxin-antitoxin. Recently, however, we have met with three cases of nasal diphtheria which developed soon after their admission to the institution. These cases were characterized by the typical bloody nasal discharge. In two instances the cultures showed avirulent bacilli, in one which was obtained in December, 1930, the bacilli from the nose were virulent. In spite of this fact, not only was the Schick test negative, but tests carried out in February, 1931, with increasing doses of toxin 1/50-1/40-1/30-1/20-1/10-1/5 M.L.D. all failed to induce a skin reaction. As the result of these experiences we infer that a lack of the antiscorbutic vitamin exerts a local effect on the mucous membrane which diminishes its immunity, but at the same time may not be accompanied by a lowering of systemic immunity. It is probable that a similar phenomenon holds true in connection with a deficiency of vitamin A and that the marked changes in the epithelium, described by Wolbach, bring about a local diminution in resistance. Susceptibility to infections of the skin and of the respiratory tract which occur when this deficiency is marked may be largely a manifestation of a local pathological change.

*The runabout children had a habit of pulling off the buttons of their shoes and pushing them into their nostrils where they remained until they were removed some time later with forceps. This condition led to a bloody nasal discharge which on cultivation often showed diphtheria bacilli.

CONCLUSIONS

The antirachitic factor, whether given as ultraviolet irradiation, as irradiated ergosterol, or as cod liver oil does not increase the immunity of infants to respiratory infections.

Respiratory infections are not due to a lack of vitamin A and generally cannot be lessened by giving a diet rich in this factor even when supplemented with cod liver oil.

The average infant seems to receive an adequate amount of vitamin A in its milk, judging by the fact that xerosis of the eyes is exceedingly rare, and that no gain in weight or increase in immunity is brought about by adding vitamin to the diet. The same seems to hold true for older children and adults, in view of the infrequency of night-blindness, the first sign of this deficiency.

A lack of vitamin C may induce heightened susceptibility to infection of the respiratory tract. It may, however, induce merely local susceptibility without appreciable loss of systemic immunity. This peculiar phenomenon is manifested by the occurrence of typical nasal diphtheria, associated with virulent diphtheria bacilli, but a Schick reaction negative to highly potent solutions of toxin.

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Discussion

Dr. Hill: We have heard from Dr. Hess what I thought we would hear—a brilliant, intensely interesting paper.

The second part of the program departs from the traditional method of conducting a medical meeting. We have four pediatricians here, Dr. Utter, Dr. Garland, Dr. Percy and Dr. Romberg, whose experience, reputation and ability is such that what they have to say should carry with it considerable weight. Each one of these gentlemen will be asked four questions which he will endeavor to answer to the best of his ability from the background of his clinical experience.

The first question is as follows: From your clinical experience do you believe that cod liver oil does good to children over two years old who are free from active rickets and who are already taking a reasonable diet? If so, what good?

I will call first on Dr. Garland of Boston to answer that question.

Dr. Joseph Garland, Boston: I was hoping to be able to hear what my colleagues had to say before I was called on. Two or three years ago Dr. Holmes, who is the director of the laboratory of the E. L. Patch Company, published a paper on the use of cod liver oil among the employees of that company and demonstrated that those who took cod liver oil had fewer colds and also suffered less from dysmenorrhea. That was statistical. We do not have statistics and have to deal with our impressions. My experience is that I have never seen any value from cod liver oil in older children.

Dr. Karlton G. Percy, Boston: We are sacrificial lambs, and I think we have been goats. It comes down to the subject of what my opinion is. I believe that the medical profession is undoubtedly in the hands of the houses that are selling cod liver oil. We have it crowded down our throats or rammed underneath our skins so that we are led to believe that it is an absolute necessity. Practically speaking, when you have passed the infant age and a child is able to get a mixed diet, a normal child is in my opinion never in need of cod liver oil if he has a rational diet, I believe, however, that after infections, especially long drawn out infections, it does help a child to recover faster, and that it also helps perhaps during the winter months. My impression is that older children are perhaps less susceptible to infection, but that is only an impression.

Dr. Eli C. Romberg, Boston: It is difficult to tell when active rickets ceases. Empirically we say it ceases at about two or three years of age. Actually we are unable to determine when it does stop, however, unless we see the character of the epiphyses by x-ray.

Provided that the diet is adequate, I think that cod liver oil is unnecessary in the treatment of a child over two years of age. In certain cases, particularly after prostrating illness where the child has lost a lot of weight and is washed out, cod liver oil seems to do some good. I do not believe it helps because of its antirachitic value, but rather perhaps, because of the high caloric fat value contained in cod liver oil. The same results could probably be achieved by giving the child olive oil or some other fat product.

I believe that when children have teeth of poor quality, where decay is present and the color is poor, the administration of cod liver oil should be somewhat extended.

Dr. Henry E. Utter, Providence: I believe in the use of cod liver oil for children who are taking a reasonable diet. It increases the weight if the child is not gaining and certainly lessens the nervous irritability, which is an important factor in its use.

I do not believe that cod liver oil will prevent respiratory infections, but that the susceptibility to these infections is considerably lessened. Cod liver oil in addition to the regular diet is an important factor in preventing dental caries.

Dr. Hill: The second question is as follows: Do you believe in routine sunbaths, with the body completely exposed, for normal infants? If so, why? If not, why not?

DR. GARLAND: My answer to the question "If so, why?" is, I believe that the routine sunbath is of some value and advise my patients to adopt it; the reason why is because all the literature emphasizes its value.

DR. PERCY: If this refers to routine sunbaths, I should say "no" because sunbaths are baths offered by mothers at any time. I think the danger of sunbaths when there is no sun, which is the routine sunbath to the mother, is a definite danger; but there is no doubt that the child who basks in the summer sun, who has had a summer with very few clothes on, the infant especially, is in far better condition than the one who is kept under the sheets and who does not get the effect of the summer sun. However, as a routine procedure I should say "no".

DR. ROMBERG: I am assuming that you allow the youngster to go out in the sun whether he is dressed or not. Except that a child looks healthier by being tanned, and his appearance attracts more favorable comment from the neighbors, I do not see the necessity of exposing the child's complete body to the sunlight. If the mother has not given the child any cod liver oil, or cannot afford vitamin milk or viosterol, or is prejudiced against giving cod liver oil in the summer because she believes it overheats the blood, I think in such cases perhaps an exposure of the body to the sunlight is beneficial.

I think the risk of over-exposure of the child to the sun, bringing about blistered skin or gastro-intestinal upsets, is too great. In general, therefore, I do not see the necessity of especially exposing the body to the summer's sun.

DR. UTTER: I believe in giving sunbaths to infants. If we accept craniotabes as an early manifestation of rickets, and I believe we should, it is remarkable to note with what rapidity this symptom disappears. I make it a practice to stop cod liver oil when sunbaths are instituted.

Under the use of sunbaths the children both eat and sleep better. The great danger of sunbaths is in overdoing the procedure. An exposure of ten minutes to the front and back daily is usually sufficient. If the skin becomes too pigmented we possibly produce a barrier to the entrance of the ultraviolet rays; if we can attain a general hyperemia, we are probably using a procedure of real value.

DR. HILL: The third question is as follows: Are you convinced that there is a detectable clinical syndrome prevalent in this country in young infants due to vitamin B deficiency? Have you seen any of the carbohydrates, with added vitamin B, do good to these infants or to any infants? If so, what good?

DR. GARLAND: I don't know how to answer that rather long question. I am open to conviction, but I am not convinced. I have not yet seen any sign of a detectable syndrome. If there is such a thing, I should be glad to know about it. I have seen no results from using preparations containing vitamin B, and I am not sure what they are.

DR. PERCY: Well, I think we have been sold by the pharmaceutical houses, first because of a very good piece of work by Dr. Dennett of New York, but thereafter taken up by wholesale houses. I am ashamed to say that I cannot see a syndrome which necessitates the use of vitamin B with cereal additions, though like the cases of difficult feeding in which the grandmother comes along and gives condensed milk and the baby does well, we do see infants do well with cereals. Whether it is due to the effect of vitamins or whether it is because of ignorance that it has been impossible for us to find the reason for it I don't know.

DR. ROMBERG: If we are to believe the investigations of the Toronto observers, there must be some such clinical syndrome as vitamin B deficiency. Up to this afternoon before I heard Dr. Blackfan's lecture about acrodynia which might possibly be traced to vitamin B deficiency, I interpreted the pallor and the loss of tone and the irritability and the crying as cramps and colic and teething, but now since I have heard this lecture I am going to be on the lookout for these vitamin B manifestations which so far we have not been able to recognize in the early form and which I personally have not seen. With the mixed diet that most of our patients are getting, it is hard to believe that a vitamin B deficiency could exist. I have tried the various dextri-vitavose preparations and I find that the children who do not take them get along as well as the children who do.

DR. UTTER: If vitamin B protects the nervous system there must be a great many children who show a deficiency of this vitamin, but so far I have been unable to recognize a distinct syndrome due to this deficiency.

I have but one observation to make in this respect. I use wheat flour in many formulae when a baby comes to me being fed on milk, water and sugar mixtures. There results a distinct lessening of nervous symptoms but it must not be forgotten that the mother or nurse is instructed in matters of routine, regularity of feeding hours, sunshine and sleep, all of which factors are important in making a baby happy. Under such circumstances it is hard to state just how much importance the addition of wheat has in the matter.

I have seen very little result in the feeding of preparations with addition of vitamin B not obtained by the use of other infant foods without this addition.

DR. HILL: The fourth question is as follows:

Do you think it rational to administer cod liver oil plus viosterol to normal infants? If so, why? If not, why not?

DR. GARLAND: I suppose sacrificial lambs should feel a sense of responsibility. Personally I can see no particular value in adding viosterol to potent cod liver oil. It may be a good thing, but I don't know.

DR. PERCY: At dinner we heard Dr. Hess speak about the unpopularity of cod liver oil, how little was taken because the baby didn't like the smell or because it was unpleasant for the mothers. Statistically he tried to show that about one-third of the cod liver oil ordered by milk stations was never given. And then he said that there was probably enough of the vitamins in milk if they were absorbed, to protect most children against rickets and vitamin deficiency. However, knowing the improvement that has occurred in the children of the United States in the last 25 years with the decrease of mortality and the increase in knowledge of the giving of cod liver oil, it does seem wise and just that every child should be ordered the proper amount of cod liver oil.

Now if human nature is such that what is ordered is not given in the proper amount, I have felt that if you can bolster up your cod liver oil with viosterol, you are going to get in a small dose which is going to be the necessary amount of vitamin a day, and I can say I have been using more viosterol with cod liver oil.

DR. ROMBERG: Ordinarily in normal infants the administration of a reliable plain cod liver oil is sufficient to take care of all the child's needs. However, when one realizes that so many of the cod liver oils on the market are poorly assayed or unstable or impotent, I believe that most of us feel more happy or assured if we can give the children cod liver oil supported by viosterol. Nowadays, however, it is hard to ask families to give their children viosterol and cod liver oil, with the prices that are being asked for such products.

DR. UTTER: I have never been quite convinced in the matter of using viosterol alone. To mix viosterol with cod liver oil does not seem a fair experiment for we never know which gives the desired result.

In 1929 I tried several experiments to satisfy myself in regard to the clinical value of viosterol and other antirachitics. Using craniotabes as the test, I gave one group of infants viosterol, another cod liver oil and still another cod liver oil with phosphorus. In the viosterol group it seemed to me that about as many developed craniotabes as I was accustomed to find in babies who had not received any antirachitic agent. In the cod liver oil group a smaller number developed craniotabes, while the group taking cod liver oil and phosphorus did not develop craniotabes at all. I have always believed that cod liver oil with phosphorus was the best antirachitic.

DR. HILL: We will now have a general discussion of the subject.

DR. RICHARD M. SMITH, Boston: After listening to the lambs I think we might go back to some of the ideas which Dr. Hess has been discussing. I am sure we have all of us been much interested in his presentation of the subject. There are two questions which constantly occur in the minds of us who are dealing with children and which are hard to answer. I can only ask them, as they are perplexing, though I have been considering them for years. These questions have been touched upon, but I think there are matters in doubt in relation to both of these questions.

The first has to do with the quantitative measurements of vitamins. We have been observing children for years before and since the addition of vitamins as such to the diet, though we all gave vitamins before we called them by that name. The question arises whether we have been treating our children with insufficient amounts of vitamins. If that is so, we ought to have seen and be seeing still a large number of children presenting evidences of vitamin deficiency.

It is true that scurvy is less common than it used to be, and we are all giving the children enough vitamin C to prevent scurvy. Yet with relation to the other vitamin I am not so sure, and I should like to have Dr. Hess say something about the quantitative measurements of vitamins from the clinical point of view.

The second question is closely related to that, and has been touched upon. We ought to know more about it namely, the possibility of our recognizing vitamin deficiencies in the early stages. It is easy to recognize a well-developed but not a latent case of scorbutus; and the same is true with relation to the other deficiency diseases. We recognize that night-blindness is an early symptom of vitamin A deficiency, but are there not other signs which are as recognizable as this and have a real significance? If we were properly informed and sufficiently alert, might we not detect some of these deficiency diseases before serious damage had been done?

I think that the discussion in relation to acrodynia is timely. It is true that we make the diagnosis more commonly than we used to do; probably this is because we now recognize the mild cases of the disease which were formerly undiagnosed. May it not be true also that there are children with vitamin deficiencies in small degrees or with slight manifestations, in which, if we knew more about the conditions, we might prevent more serious manifestations?

DR. EDWIN T. WYMAN, Boston: From what Dr. Hess has told us, it seems to me that the way to keep our children's resistance to infection as high as possible is to keep them in the best possible condition by feeding them a proper diet and giving them sufficient Vitamin A, C and D.

Not so many years ago it was thought that if we fed fat, carbohydrates and protein in quantities suited to the individual child together with mineral salts contained in the food, that this was sufficient to supply all the needs for nutrition and development.

A few nights ago I heard Dr. E. V. McCollum speak and he said that there are 37 elements and chemical compounds all of which are necessary in the diet to promote proper growth and development.

After the second year if a child gets an ordinary American diet without too much sugar or wheat flour which would naturally replace other foods containing more of these necessary compounds, I believe one need think very little of vitamins or these various necessary chemicals. On the other hand, before a baby is two years old one has to think of vitamins, especially A, C and D. Before this last year I have thought that the possible lack of vitamin A in an infant's diet was of little consequence. However, Dr. Blackfan's cases at the Infant's Hospital this year have made me vitamin A conscious. One of the babies was fed on an adequate diet except that two ounces of cream were removed from the milk because of fat intolerance. This baby developed a respiratory infection and the autopsy showed a definite vitamin A deficiency. I think we should keep vitamin A in mind especially with babies who have a low fat tolerance and be sure that they get sufficient cod liver oil.

Vitamin C. I advise patients to get the best milk they can afford for their babies, certified milk if possible, and then either pasteurize or boil it for babies up to one year old. Of course this makes it necessary to consider vitamin C and see that they get sufficient orange juice or tomato juice to supply their vitamin C requirements.

In regard to vitamin D it seems to me that babies under two years of age should have vitamin D in addition to the vitamin D contained in their diet. There is no definite dose of cod liver oil, as babies' requirements vary according to the individual. As a general rule I think it is necessary to give two or three teaspoonfuls a day during the winter months and one to two teaspoonfuls during the summer months, depending in the summer on the amount of sunshine the baby gets. This amount of cod liver oil, however, isn't sufficient in all cases to prevent the occurrence of rickets and in some cases it is sometimes impossible to get the baby to take sufficient cod liver oil to prevent rickets. This is especially true in some very rapidly growing infants, babies born in the fall, twins and premature infants. In these babies the cod liver oil would have to be supplemented by viosterol, "Haliver" oil or sunlight. I believe the ideal food for a baby at the present time is vitamin D milk with sufficient cod liver oil added to take care of any possible vitamin A deficiency and orange juice to supply vitamin C.

I think that sunbaths are a good thing for all animals, if not overdone, and I believe the time will come when ultraviolet transmitting windows will be more generally used in nurseries, especially for babies born in the fall, premature babies and twins. Here the baby can have a sunbath in a warm room without the disadvantage of possible exposure to cold and I believe a half hour sunbath during the winter months gives the baby something he would not receive from cod liver oil or viosterol and would probably prove useful in maintaining his resistance against infections so common during the winter.

I would like to ask Dr. Hess if the cows fed on alfalfa give a milk more potent in vitamin A than do cows fed on ordinary hay.

DR. JOHN L. MORSE, Boston: I feel thoroughly incompetent to discuss this question. There are undoubtedly such things as vitamins. I think what has been learned regarding the vitamins during the last decade has been one of the greatest advances in medicine for many years.

There is no question but that the vitamins are necessary for the well-being of infants and children. I suppose that this is true also in the case of adults. Personally I never worry about them. On the other hand, I am thoroughly convinced that an insufficiency of any or all of the vitamins in early life is much less common than is generally believed. I think that the frequency of an insufficiency of the vitamins has been exaggerated, probably largely because of the advertising of the commercial houses. In that connection we must be extremely skeptical about believing anything that we read either in the newspapers or in the medical journals and we must wait for work like that of Dr. Hess before we accept anything. Work like his we can believe, for it is founded on facts and observations. Most of the stuff that we read is simply hot air.

Another thing I think we should be very skeptical about is the application of the results of animal experiments to human beings. Do not misunderstand me when I say this. I thoroughly believe in animal experimentation, and we would not know what we do about vitamins now if it had not been for animal experimentation; and a great deal of what we will know in the future will be learned from animal experimentation. Nevertheless, we must be careful as to how we apply those results to infants as Dr. Hess has

said. As I see it, what is most needed at present is an exact knowledge of how much of each vitamin is needed, and what the early symptoms of a slight deficiency of each of the vitamins are.

DR. ALFRED HESS (closing): The first question is as to the quantitative requirement of vitamins clinically. In regard to vitamin A I should think that most children, really almost all children, are getting enough. About the only way you can feed an infant is by giving milk which contains about 2,000 units to a quart. That ought to be enough.

There may be conditions where vitamins are not utilized; for instance, we do not know the relation of fever to their utilization. It may be that if a child has fever, it consumes a great deal of vitamin. It is quite possible that if the child vomits or has bowel disturbance it may not get the requisite amount of vitamins and one might have to increase the quota during an attack of this kind.

Again if the milk isn't pasteurized sufficiently, the vitamin A may be lost because of its susceptibility to oxidation; prolonged oxidation may destroy the vitamin. There is a method of homogenizing milk by beating it up and aerating it. That is a dangerous procedure from the standpoint of vitamins, both A and C. In Switzerland they had almost no scurvy until they introduced this method of mixing the milk.

In regard to the vitamin B, I think there is a sufficiency. I know of no symptoms due to a lack of vitamin B. I have tested various preparations and found them of no advantage. I tested vitavose and various extracts of wheat germ and potent extracts of yeast.

We see very little scurvy. I understand it is increasing somewhat, but I always believe that if we have a considerable number of any one of these deficiency diseases manifest, as well as latent cases, it must not be infrequent. It is hard to believe that there are latent cases of scurvy by the hundreds. The same is true of vitamin A. Xerosis of the eyes is rare and it is hard to believe that there are hundreds of latent cases. Wherever latent beriberi occurs, as in Japan, there is always a parallelism between manifest and latent cases.

In regard to vitamin D I do think we need a supplement, for milk has practically no vitamin D. The more milk you give, the less the scurvy, but the more you overfeed a child with milk, the more you get rickets; so there must be very little vitamin D in milk. Cod liver oil in three teaspoonful doses daily protects infants generally.

I do not quite agree with Dr. Utter in regard to craniotabes. This lesion is peculiar. Rickets is a lack of calcification of the cartilage; that is its main manifestation. The epiphyses do not ossify. Now the cranial bones do not contain cartilage, and we should not take a membranous bone as a criterion in considering rickets.

Premature babies must be regarded as entirely different animals. You may have an agent that will work beautifully on the normal infant but will not work on the premature.

I was asked about the milk of cows fed alfalfa. I don't know whether cows which get alfalfa have more vitamin A in their milk. Rapidly dried clover hay has a great deal more vitamin A than that slowly dried. You can't increase it beyond a certain amount. We gave yeast to cows, the yeast being rich in vitamin B, but in giving that amount of yeast which has vitamin G also, I found that neither had been increased, so that whether feeding alfalfa to the cows causes an increase in vitamin A remains to be proved.

In regard to animal experimentation, we have to be very careful. For example, one needs forty to fifty times more irradiated ergosterol for chickens than for rats in order to get the same result.

Another matter should be mentioned; you can't talk about units of cod liver oil and irradiated ergosterol and irradiated milk because they are different. You cannot compare irradiated ergosterol with irradiated milk. I have found that milk from cows fed with irradiated yeast has few "rat units". You have to give 800 units of irradiated ergosterol to protect an infant, and 160 units of cod liver oil and 160 units of this vitamin D milk, so that you can't speak in terms of units except for a particular preparation. This shows that they are utilized differently or bound differently chemically.

About the recognition of the early stages of deficiency-disorders; that is what we need in order to recognize them. The chemical test for rickets is lowered phosphorus in the blood. It is possible that we may find some chemical tests to recognize early deficiencies in relation to a lack of the other vitamins.