when the first indicator tube has turned dark red, showing that the sample is past the end of the induction period. In some cases the second tube will show a color change depending upon the speed with which the sample oxidizes. In any case the samples should be removed before the third indicator tube begins to change color.

The following data on samples of butterfat will serve to illustrate the correlation between the peroxide number and the color change in the indicator tubes:

Sample	Hours	Color of Indicator	Peroxide Number	Stability Value
I.	40½	Red	17.5	
	39½	Reddish Brown	9.5	40½
	38½	Yellow	3.9	
II.	38	Red	16.1	
	37	Yellow	2.7	38
	36	Yellow	2.4	
III.	21½	Red	37.0	
	20½	Red	11.5	20½
	19½	Yellow	2.6	

This method has also been used to a limited extent with lard, olive oil, and corn oil with equal success. The amount of alkali used in the case of butterfat seems to be quite satisfactoy in the case of lard where a peroxide value of 20 is taken as the end point.

In the case of a fat which has developed hydrolytic rancidity the color change may occur within a few minutes after the sample has been started. In the case of butterfat it has been found satisfactory to remove the indicator tubes at the end of the first hour and substitute new tubes with a fresh alkaline solution. The development of an acid reaction in the latter tubes denotes the end of the induction period.

This method of approximating the end of the induction period has the advantage of permitting the operator to check on the samples with a glance at the indicator tubes rather than smelling of the exhaust air from the individual samples. This is especially desirable in cases where the samples of fat vary a great deal in the length of their induction periods or where the odors of the fat tend to mask the odor due to oxidation. It was also found that some experience had to be gained in order to determine the point at which butterfat samples should be removed when judged solely by the sense of smell. This method has the further advantage of promptly indicating any plugged capillary.

BIBLIOGRAPHY

1. King, A. E., Roschen, H. L. and Irwin, W. H.—Oil and Soap, 10: 105 (1933).
2. Greenbank, G. R. and Holm, G. E.—Journal of Industrial and Engineering Chemistry, 16: 598 (1924).
3. Briggs, L. H.—Journal of Dairy Research, 3: 71 (1932).
4. Powick, Wilmer C.—Journal of Agricultural Research, 26: 323 (1923).
5. Powick, Wilmer C.—Journal of Oil and Fat Industries, 1: 63 (1924).

FACTORS THAT INFLUENCE THE ANTIRACHITIC VALUE OF MILK FOR INFANT FEEDING

(A REVIEW)

By ARTHUR D. HOLMES and MADELINE G. PIGOTT

Research Laboratories, The E. L. Patch Company, Boston, Mass.

ORDINARILY milk constitutes the sole food for infants during the first few months of life. Accordingly it would seem that milk should contain all the constituents necessary to adequately meet the nutritive requirements of an infant. It was formerly believed that breast milk, the natural food for the infant, was the ideal baby food and the results of numerous clinical studies show that its nutritive value is superior to that of foods which have been devised to supplant it. However, when breast milk is not available, reliance must be placed upon some substitute and cow's milk is quite generally employed for this purpose. Unfortunately the composition of cow's milk is not identical with that of human milk. Consequently many procedures have been developed for modifying milk so that it will approximate the composition of breast milk. Nevertheless, in spite of the noteworthy advances that have been made in infant nutrition artificial feeding frequently fails to produce optimum results.

At times artificial feeding is attended by excessive mortality but, even when mortality is not excessive, the growth and physical development of infants may not be completely satisfactory. As a consequence numerous clinical studies and nutritional investigations have been conducted to determine the causes of various types of malnutrition which result from improper feeding. These studies and investigations have shown that rickets is one of the most prevalent forms of malnutrition that result from inadequate infant nutrition. Eliot[1] reports that approximately 86% of babies in a typical American city developed rickets. According to Hess[2] the occurrence of rickets during infancy and early childhood is general in most civilized countries. He reports that in Norway from 32% to 75% of children under two years have rickets. Thirty-five per cent of the breast-fed and 75% of the bottle-fed babies develop rickets in the Faroe Isles. The incidence of rickets varied from 15% to 95% in Russia. It is quite prevalent in Newfoundland, Switzerland, Italy, Sicily, West Indies, China, India, Australia, and it is also not uncommon in Greece, Turkey, Palestine, the Canal Zone, Mexico, South America, Africa and New Zealand.

It has long been recognized that rickets is prone to develop at periods of most active growth; namely, during the first months of an infant's life. Premature, very fat, and large, rapidly growing infants very frequently develop rickets coincident with their active growth.

Rickets is characterized by a disturbance in the equilibrium of the calcium and phosphorus of the circulating fluids, particularly the blood. A diminution of either inorganic phosphorus or calcium content of the blood is probably the first clinical sign of rickets. Hence it is generally believed that of the many factors that may contribute to the development of infantile rickets the amount and proportion of calcium and phosphorus and the antirachitic vitamin in the diet are of major importance. The data that were obtained from a survey of the literature relative to the calcium and phosphorus content of cows and human milk are summarized in Table I and Table II.

According to these data the calcium content of cow's milk may vary from 0.91% to 0.166%, a variation of 80%, and the phosphorus content may vary from 0.040% to 0.124%, a variation of 200%. The variation in calcium content of human milk was from 0.014% to 0.057%, a variation of 300%, and the variation in phosphorus content was from 0.010% to 0.031%, a variation of 200%. Since human or cow's milk constitutes the principal if not the entire source of calcium and phosphorus during infancy and early childhood, when rickets is prone to develop, such decided variation in the supply of these elements is of interest to the pediatrician and others responsible for infants' and children's dietaries. It has been frequently noted that in general cow's milk contains four times as much calcium and phosphorus as human milk, and yet the literature reports rickets to be much more common among artificially than breast-fed infants.

TABLE II—CALCIUM AND PHOSPHORUS CONTENT OF HUMAN MILK

Investigator	Year	No. of Samples	Calcium* Percent	Phosphorus* Percent
Korenchevsky[17]	1922	86[a]	(0.021–0.046)	
Korenchevsky[17]	1922	26[b]	0.032 (0.014–0.033)	
Burhans et al.[18]	1923	55[c]	0.028 (0.015–0.040)	0.017 (0.010–0.031)
De Buys et al.[19]	1924	19[d]	0.033 (0.024–0.040)	
De Buys et al.[19]	1924	51[e]	0.028 (0.018–0.040)	
Sherman[6]	1927	..	0.034	0.015
Lowenfeld et al.[20]	1927	21[f]	0.033 (0.025–0.039)	
Widdows et al.[21]	1930	103[g]	(0.032–0.034)	(0.017–0.017)
Donelson et al.[22]	1931	15[h]	0.031 (0.026–0.039)	0.014 (0.011–0.017)
Macy et al.[23]	1931	16[i]	0.034 (0.030–0.038)	0.014 (0.012–0.016)
Macy et al.[23]	1931	16[j]	0.034 (0.031–0.039)	0.015 (0.013–0.017)
White House[14]	1932	..	0.034	0.015
Nims et al.[24]	1932	35[k]	0.031 (0.014–0.057)	0.016 (0.012–0.029)

Footnotes for Table II

*Average values—figures within the parenthesis are the minimum and maximum percent reported.

[a]Milk from mothers of normal infants.

[b]Milk from mothers of rachitic infants.

[c]The samples were from colored, Jewish, Italian, American and Slavish mothers from 17 to 38 years, from 1–5 parity and at 4–52 weeks postpartum.

[d]Milk from 19 mothers of normal infants taken at 14 days to 14 months postpartum.

[e]Milk from 51 mothers of rachitic infants taken at 2 to 14 months postpartum.

[f]Samples from 4 mothers, 3 of whom were primiparae, at 2 to 13 days postpartum.

[g]The calcium figures are from 103 samples taken at intervals from 1 week to 10 months postpartum. The phosphorus figures are from 68 samples taken over the same period. In both instances the minimum figures are for the beginning and the maximum figures are for the end of lactation.

[h]Samples from 3 mothers at 25–35 years, 2 to 4 parity and 7–65 weeks postpartum.

[i]Sixteen samples of milk taken during first half of lactation period.

[j]Sixteen samples of milk taken during last half of lactation period.

[k]Samples from 12 mothers at 1–60 weeks postpartum.

A number of investigators have studied the cause for rickets being far less frequent among breast-fed than bottle-fed babies, in spite of human milk being only about one-fourth as rich in calcium and phosphorus as cow's milk. Wang, Witt and Felcher,[25] in a comparison of the metabolism of cow's and breast milk, found that the same infant utilized 55.50% to 82.40% (average 63.04%) of calcium of breast milk and only 35.09% to 64.95% (average 47.51%) of the calcium in cow's milk. Nevertheless, the daily retention of calcium from breast milk was 0.45 grams as compared with 0.8 grams from cow's milk. Telfer[26] obtained similar results in metabolism experiments with four infants that were changed from breast milk to cow's milk. Swanson[27] and Witt[28] also found that the calcium and phosphorus retention was higher in the artificially fed than in the breast-fed baby. According to Bosworth[29] human milk, unlike cow's milk, contains no insoluble phosphates—no dicalcium phosphate.

The method employed in preparing milk for infant or child feeding apparently influences the extent to which its calcium content is utilized. In studies of the utilization of milk by growing pigs Washburn and Jones[30] found the breaking strength of pig's femur was greatest for raw milk and decreasingly less for evaporated and condensed milks. Magee and Harvey[31] in later studies with pigs obtained better utilization of both calcium and phosphorus with fresh than pasteurized milk. Daniels and Loughlin[32] observed that young rats fed long heat-treated milks, evaporated, condensed and pasteurized by the "hold" method failed to grow normally but, if the precipitated calcium salts were incorporated into the various milks, growth was normal. Bosworth[33] has referred to the variation in the solubility of calcium and phosphorus in cow's milk dried by different methods. Later Daniels and Stearns[34] reported that calcium and phosphorus retention in infants was considerably greater for quickly boiled milk mixtures than for pasteurized milk; that the longer heat treatment decreases the availability of calcium and phosphorus, and that a baby fed pasteurized milk for a long pe-

TABLE I—CALCIUM AND PHOSPHORUS CONTENT OF COWS MILK

Investigator	Year	No. of Samples	Calcium* Percent	Phosphorus* Percent
Sherman et al.[3]	1910	2	0.120 (0.117–0.124)	0.040 (0.040–0.040)
Sommer et al[4]	1919	30	0.125 (0.095–0.150)	0.107 (0.082–0.126)
Rothwell[5]	1925	4	0.129 (0.120–0.137)	
Sherman[6]	1927	..	0.120	0.093
Storms[7]	1927	11[a]	0.126 (0.117–0.134)	
Rogers[8]	1928	..	(0.095–0.150)	
Hart et al.[9]	1929	3	0.107 (0.100–0.110)	
Supplee[10]	1930	12[b]	0.122 (0.121–0.123)	0.089 (0.083–0.092)
Supplee[10]	1930	12[c]	0.122 (0.118–0.126)	0.092 (0.084–0.094)
Sanders[11]	1931	2	0.127 (0.126–0.128)	
Sanders[11]	1931	1[d]	0.115	
Sanders[11]	1931	1[e]	0.136	
Fleming[12]	1932	1	0.121	0.092
McHargue[13]	1932	1	0.130	0.098
McHargue[13]	1934	9[f]	0.149 (0.129–0.176)	0.112 (0.097–0.118)
McHargue[13]	1934	11[g]	0.123 (0.111–0.147)	0.100 (0.060–0.116)
White House[14]	1932	..	0.124	0.092
Lythgoe[15]	1932	1[h]	0.125	
Lythgoe[15]	1932	2[h]	0.124 (0.0122–0.125)	
Lythgoe[15]	1932	1[h]	0.116	
Lythgoe[15]	1932	1[h]	0.118	
Lythgoe[15]	1932	2[h]	0.125 (0.123–0.126)	
Lythgoe[15]	1932	1[h]	0.109	
Lythgoe[15]	1932	5[h]	0.122 (0.103–0.130)	
Lythgoe[15]	1932	4[h]	0.128 (0.123–0.134)	
Lythgoe[15]	1932	9[i]	0.118 (0.091–0.134)	
Holm et al.[16]	1932	9[j]	0.122 (0.110–0.166)	0.092 (0.084–0.106)
Holm et al.[16]	1932	10[j]	0.138 (0.132–0.146)	0.119 (0.116–0.124)
Holm et al.[16]	1932	10[j]	0.107 (0.096–0.126)	0.081 (0.078–0.086)
Holm et al.[16]	1932	10[j]	0.112 (0.105–0.131)	0.092 (0.080–0.098)

Footnotes for Table I

*Average values—figures within the parenthesis are the minimum and maximum percent reported.

[a]New Zealand milk.

[b]Monthly samples of milk produced in New York State teritory.

[c]Monthly samples of milk produced in Wisconsin territory.

[d]Holstein milk.

[e]Jersey milk.

[f]Monthly samples for a single cow (Jersey) taken throughout period of lactation.

[g]Monthly samples for a single cow (Holstein) taken throughout period of lactation.

[h]Milk sold August, 1932, by dealers supplying Boston.

[i]Samples taken same day from Registered Holstein cows of same herd, feed, etc., but of unknown period of lactation.

[j]Monthly samples for a single cow taken throughout period of lactation.

riod probably receives too little calcium for growth needs. Willard and Blunt,[35] in metabolism studies with children 3 to 12 years of age, found that calcium utilization was somewhat higher for evaporated than for pasteurized milk. Kramer, Latzke, and Shaw[36] found in studies with five children, of 7 to 12 years, that the child retains more calcium from fresh milk than from equivalent amounts of dried milk.

A number of investigators have shown that calcium is best utilized from milk which is slightly acid. Jones[37] produced experimental rickets in puppies by making their food alkaline and cured the rickets by adding hydrochloric acid to their ration. Irving and Ferguson[38] studied calcium absorption by means of blood calcium determinations and found that more calcium was absorbed from an acid than from an alkaline or neutral medium. Flood,[39] in studies of the nutritive value of acid milks, found that the addition of hydrochloric acid to milk increased the amount of calcium retained by rachitic babies. On the other hand Wills and coworkers[40] were unable to increase calcium retention by feeding infants milk acidified with hydrochloric acid.

It appears that the utilization of calcium by artificially fed babies may be influenced by the kind of carbohydrate added to the formula. Since lactose is a constituent of human milk, it has been used extensively in the preparation of formulas for infant feeding. According to Underhill[41] and Inouye[42] lactose will increase the blood calcium and relieve tetany in certain experimental calcium deficiency conditions. In a comparison of the effectiveness of various sugars for increasing calcium absorption Bergeim[43] found lactose far superior to glucose, sucrose, maltose, or dextrin which are also used in infant feeding.

Since water is used as a diluent for cow's milk in the preparation of a substitute for breast milk, and since it is also used as a beverage for both breast and bottle-fed babies, it may contribute to an infant's calcium intake. However, little evidence is available concerning the influence of calcareous waters on the prevalence of rickets. One might anticipate some correlation for, according to Hess,[2] "from what we know of the effect of lime in the intestinal tract it would seem quite possible that its presence in high degree in drinking water might tend to the development of rickets by precipitating the phosphates in the canal." A large amount of information[44] is available as to the chemical composition of the drinking water used in the United States. The calcium in the water supplies[45] of the larger cities in the United States in 1921 ranged from about one part per million in Pensacola, Florida, and Asheville, N. C., to over 200 parts per million in Aberdeen, S. D. Many large supplies, like the Metropolitan District Supply for Boston and the Catskill Supply of New York, have less than five parts per million of calcium. The supplies of cities on the Great Lakes, except Lake Superior, such as Chicago, Detroit, or Cleveland, have about 35 parts per million of calcium. Many ground water supplies in Ohio, Indiana, and Illinois, have about 70 or 80 parts per million of calcium. The average for the supplies most widely used is from 4 to 80 milligrams of calcium per day as Ca or 10 to 200 milligrams of calcium calculated as $CaCO_3$. There is no reason to believe that the general composition of the water supplies in other countries is very different from those of the United States, but the complexity of the problem makes it extremely difficult if not actually impossible to correlate cases of rickets with the content of calcium in the water.

The extent to which ingested calcium is utilized is influenced by factors that cause increased elimination of calcium from the body. Sisson and Denis[46] have noted the important role of minerals in infant nutrition and conclude that shortage or improper relation of minerals may influence some nutritional disorders of infants. In this connection Bosworth[47] says "The influence of the salts on the mechanical condition of the milk after it reaches the stomach, on the digestibility of the food components of the milk, after digestion, and on the utilization of the vitamins of the milk, are pertinent questions." Cantarow[48] has pointed out that, while the metabolic relationship between calcium, magnesium, sodium, and potassium is yet poorly understood, these elements influence calcification and decalcification of bone and an excess of these elements prevents normal calcification. Greenwald and Gross[49], Jeppsson[50], Whelan,[51] Miller,[52] Mendel and Benedict,[53] Malcolm,[54], Bogert and McKitterick,[55] Hart and Steenbock,[56] Palmer, Eckles and Schutte,[57] Elliot, Crichton and Orr,[58] and Orr and Holt[59] have administered magnesium, sodium, potassium or phosphorus compounds in varying amounts and under different conditions and produced increased calcium excretion. Hess[2] noted the large consumption of sodium chloride by the New York negroes. He was of the opinion that salt may influence the high incidence of infantile rickets among them but he was unable to confirm this opinion by animal experiments or clinical observations.

The fat content of the diet may also influence the excretion of calcium. The amount of fat ingested by artificially fed babies varies with the nature of the formula employed. According to Macy[60] the fat content of human milk is variable. Papers by Givens,[61] Lindberg,[62] Steinitz,[63] Sawyer, Bauman and Stevens,[64] Bowditch and Bosworth,[65] and Telfer[66] indicate that an excess of fat causes increased mineral elimination but Meyer and Cohn[67] are not in agreement with this conclusion. They contend that an increase in the amount of fat ingested causes increased mineral retention and McCollum, Simmonds, Shipley and Park,[68] Husband, Godden, and Richards,[69] Harvey,[70] Hart, Steenbock, Kletzien and Scott,[71] and others have shown that cod liver oil stimulates calcium and phosphorus assimilation; but Hart, Steenbock, Teut and Humphrey,[9] who fed eight ounces of cod liver oil daily to liberally milking cows, obtained no favorable influence upon calcium assimilation.

Relatively few studies have been made of the Vitamin D content of human milk. However the studies reported in the literature, though few in number, were conducted under sufficiently varied conditions as to yield definite data. The results of observations by Hess and Unger,[72] Lesné and Vagliano,[73] Kennedy and Palmer,[74] Hess,[75] Gerstenberger,[76] Hess, Weinstock and Sherman,[77] Outhouse, Macy and Brekke,[78] Eufinger, Wiesbader, and Focsaneanu,[79] and Macy,[60] show that the Vitamin D content of human milk is low and far from uniform. The reports by Hess and Weinstock[80] that 20 to 25 cc. of human milk fed daily to rats showed "no protective influence," by Outhouse and associates[78] that "40 cc. daily contains no antirachitic factor," and by Gerstenberger[76] "That human milk does not contain enough of the antirachitic factor to cure rickets nor to prevent it" indicate quite conclusively that the Vitamin D content of human milk is very low. Yet Kennedy and Palmer[74] state "We have found that it may be strongly antirachitic."

A number of investigators have attempted to increase the antirachitic potency of human milk. Hess[81] irradiated a lactating woman with ultra-violet rays on alternate days for a month and found that the antirachitic activity of her milk had been significantly enhanced. Bunker, Harris and Eustis[82] have reported that the antirachitic potency of human milk can be increased by adding Vitamin D milk to the diet of a lactating woman. McBeath and McMahon[83] found a lower incidence of rickets in babies of mothers that received Vitamin D milk (yeast) from the sixth month of pregnancy to the sixth month of lactation than in a control group of babies. On the other hand Lewis[84] states that the administration of Vitamin D milk to lactating women may not increase the antirachitic potency of the breast milk sufficiently to protect the infants against rickets. Also Barnes and associates[85] found that the breast milk of a woman who received a superior diet supplemented with two quarts daily of cow's milk containing 300 units of a Vitamin D concentrate of cod liver oil did not heal rickets in three colored breast-fed babies or in experimental rachitic rats (her own breast-fed infant showed no signs of rickets). The extensive use of cow's milk in the diet of infants and young children has suggested the need for definite data concerning its Vitamin D potency. Studies conducted by Hess[86], Hess and Unger[87], Bethke, Steenbock and Nelson,[88] Hess and Weinstock,[89] Steenbock, Hart, Hoppert and Black,[90] Daniels, Pyle and Brooks,[91] Supplee and Dow,[92] Sherman and Stiebeling,[93] Honeywell, Dutcher and Dahle,[94] and Hess, Lewis, MacLeod and Thomas[95] show that the Vitamin D content of cow's milk is quite variable. Bethke[88] and associates reported that 1 cc. of whole milk per rat per day produced normal calcification and Steenbock[90] and co-workers produced healing in rachitic rats with 8 to 12 cc. of fresh milk daily. On the other hand Honeywell, Dutcher, and Dahle[96] "found that 12 cc. of raw milk were required to prevent a decrease in the ash content of femur bones." Supplee and Dow[97] prevented any symptoms of rickets by feeding their rats 15 cc. of milk daily; but Outhouse, Macy and Brekke[78] found it necessary to feed 30 c. of milk per rat per day to protect their animals against rickets. Also Hess and Unger[98] observed severe rickets in an infant that had received a liter of milk and 30 grams of spinach daily for a long time. Possibly the observations reported by Kon and Booth[99] concerning the variable Vitamin D content of butter may have some bearing upon the variable results, noted above, for the antirachitic value of milk. In a study of the antirachitic potency of butter produced by (a) cows on summer pasture, (b) cows fed irradiated yeast, (c) cows fed cod liver oil, and (d) irradiated winter butter, Kon and Booth found that the labile and stable antirachitic factors of butter varied with the type of butter studied.

As data accumulated showing the low and variable Vitamin D content of milk a question naturally arose concerning the possibility of increasing its Vitamin D potency. The need for improving the antirachitic activity of cow's milk is particularly apparent during the winter and early spring when the infant's greatest need coincides with the lowest ebb of this factor in cow's milk. The antirachitic activity of milk may be enhanced by modifying the diet or environment of the lactating animal, or by subjecting the excreted milk to chemical or physical treatment. In the early attempts to enhance the vitamin content of milk, cod liver oil, which has been shown[100–108] to be efficacious in the prevention and cure of rickets, was administered during lactation. Drummond, Coward, Golding, Mackintosh and Zilva[109] found that the administration of 2 to 4 ounces of cod liver oil daily to milch cows increased the Vitamin A (in 1921 these authors did not recognize Vitamin D as a separate vitamin) content of their milk four-fold. Korenchevsky[17] also concluded that cod liver oil confers antirachitic value when given to the mother during lactation —however his experiments are not entirely conclusive. Golding, Soames, and Zilva[110] report "The inclusion of cod liver oil in the winter ration of the cow raises the Vitamin A and the Vitamin D content of the milk." Subsequently Sheehy and Senior[111] stated "The increase in the Vitamin D content of cow's milk effected by the feeding of cod liver oil is well recognized and can be demonstrated by experiments on rats." In a later study Golding and Zilva[112] found the daily addition of two ounces of cod liver oil to a winter ration did not raise the Vitamin D content of the butter to any appreciable extent and Hess, Weinstock and Tolstoi[113] report that the antirachitic content of cod liver oil fed to lactating rats is not transmitted through the mother's milk in sufficient quantity to afford protection to the young. In later experiments Hess and Weinstock[114] confirm this conclusion and Gerstenberger[76] found that breast milk from women receiving one tablespoon of cod liver oil daily did not contain enough antirachitic factor to prevent rickets.

In a study of the factors which influence the antirachitic value of milk Luce[115] subjected a cow to various rations and intensities of light. She concluded that sunlight is a contributing factor. This conclusion has been confirmed by Chick and Roscoe[116] and Steenbock, Hart, Hoppert, and Black.[90] The latter authors found artificial irradiation particularly effective—they say "The time is probably not far distant when every producer of high-grade milk will find it necessary to irradiate his cows artificially." Supplee and Dow[97] report that summer milk has greater antirachitic potency than winter milk due, they believe "to the greater degree of solar radiation prevailing in the summer months." Yet Steenbock and co-workers[117] say "Daily exposure of cows to sunlight or artificially generated ultra-violet radiations has little if any effect on the antirachitic potency of milk."

In view of the prevalence of rickets among breast-fed babies Hess[77] and associates investigated the value of light for the nursing mother and found that "ultra-violet irradiation of a nursing woman brought about a marked increase in the antirachitic potency of her milk." Gerstenberger, Hartman, and Smith[118] have also reported that the antirachitic content of human milk can be increased by irradiating the nursing mother.

During the progress of numerous investigations, conducted to determine the extent to which the antirachitic potency of various food materials could be increased by ultra-violet irradiation, studies were made with milk. Steenbock and Daniels[119] were able to increase the antirachitic activity of milk and such other diverse materials as wheat, Indian corn, yeast, rolled oats, cornstarch, meat, egg-yolk, butter and liver by irradiation. Soon after Steenbock and Black[120] reported that they had increased the antirachitic potency of whole milk and egg yolk 15 to 20-fold by subjecting these materials to the action of ultra-violet light. Hess and Weinstock[121] found that dry milk as well as whole milk could be rendered antirachitic by irradiation with a mercury vapor lamp. In a later study Steenbock, Hart, Hoppert and Black,[90] using a quartz mercury lamp, increased the antirachitic activity of cow's milk eight or more times; whereas, under the same conditions, they increased the activity of goat's milk twenty-four times. Supplee and Dow[97] tested the antirachitic potency of summer and winter-produced dry milk—the summer-produced milk was superior, due probably to solar irradiation of the cows. However, when both milks were irradiated with a Hanovia mercury lamp, both became more highly antirachitic but the increase was greatest for the winter-produced milk.

Subsequently Supplee and Dow[92] studied the irradiation of dry milk on a commercial scale, with a view to eliminating the "disagreeable flavor and odor commonly found in milk products that are exposed to the ultra-violet rays for long period of time"—under some conditions irradiation[122] imparted a "fishy odor resembling that of cod liver oil." They were successful in this and minimized the destruction of Vitamins A and C. Supplee, Flanigan, Kahlenberg and Hess[123] report that whole milk, irradiated in fluid form and subsequently dried, possesses marked antirachitic activity—the amount of activity being determined by the fat content and period of exposure. Anderson and Triebold[124] made a biochemical study of milk irradiated with carbon arc light. Their analyses showed no significant difference in the milk and butter fat before and after irradiation. They conclude that such irradiation causes no change in composition or digestibility of milk.

The increase in the calcifying activity of milk resulting from ultra-violet irradiation has been demonstrated by several investigators both experimentally and clinically. Hess[125] fed irradiated milk to rachitic infants and obtained improvement or cures. Kramer[126] administered irradiated milk to eight patients with active rickets. The milk induced a marked retention of both calcium and phosphorus and produced a healing in every case. MacKay and Shaw[127] also fed irradiated milk, with gratifying success, to four patients, three cases of rickets and one of tetany. They report that irradiated milk should be particularly beneficial for premature infants. Daniels, Stearns and Hutton[128] in a study of calcium and phosphorus metabolism in artificially fed infants found that irradiated milk materially increased the retention of both elements.

In studies of the effect of irradiating a large number of naturally occurring materials with ultraviolet light Steenbock, Black, Nelson, Nelson and Hoppert[129] found that yeast acquired high antirachitic potency. Later Hess[122] irradiated dried yeast for one-half hour at a distance of one foot and found that 5 to 10 milligrams caused calcification of the epiphysis of rats and 0.5 to 1.0 grams daily produced definite cure of rachitis in infants. Kon and Mayzner[130] administered to six rachitic infants 0.75 grams daily of irradiated yeast suspended in milk. They report a disappearance of symptoms in six to eight weeks.

While irradiated yeast suspended in milk was shown to be effective in the treatment of human rickets it appeared preferable to rely on milk of high antirachitic potency. The irradiation of milch cows in commercial herds is inconvenient and relatively expensive. Accordingly studies were conducted to determine the value of feeding yeast to milch cows for enhancing the antirachitic value of their milk. Wachtel[131] has reported that the antirachitic value of milk may be increased several times by feeding irradiated yeast to cows. Hart, Steenbock, Kline and Humphrey[132] fed 200 grams of irradiated dried brewer's yeast daily to Holstein cows and materially increased the Vitamin D content of their milk. In a later test Steenbock, Hart, Hanning and Humphrey[133] found that as little as 50 grams of irradiated yeast fed daily to cows increased the antirachitic value of the milk. Thomas and MacLeod[134] were able to increase the Vitamin D potency of cow's milk sixteen-fold by feeding irradiated yeast. Hess, Lewis, MacLeod and Thomas[95] report that milk from cows fed irradiated yeast would prevent human rickets and, in cases in which rickets had already developed, the milk brought about calcification within a month. Wyman and Butler[135] administered irradiated milk to infants and young children diagnosed as having active rickets and obtained healing. The milk was still antirachitic after five minutes boiling.

The Vitamin D value of milk may be increased by adding Vitamin D to it. This is most generally accomplished by means of a cod liver oil concentrate (Zucker). The data concerning the efficacy of this procedure are much more limited than the data concerning enhancing the antirachitic potency of milk by modifying the diet or environment of the lactating animal. Barnes[136] reports protecting normal infants against rickets during winter months and gradually healing rickets by the administration of milk (Zucker) containing 50 Vitamin D units. On the other hand, Wilson[137] was unable to protect infants against rickets by feeding milk (Zucker) containing 150 Steenbock units.

Clinical studies have been made of the relative antirachitic value of irradiated milk and milk from cows fed irradiated yeast. Hess and Lewis[138] report that the "efficacy ratio" of irradiated milk required about half as many units to produce similar degrees of healing. On the other hand, Wyman and co-workers[139] found no indication of any difference between the two milks, unit for unit, in respect to their clincal antirachitic effectiveness. Kramer and Gittleman[140] who fed irradiated and yeast milk at two levels obtained similar results. They found the milks to be equally effective, even if fed at levels which provided as little as 40 Steenbock units per day. These results were duplicated by Gerstenberger and associates[141] who concluded that, for rachitic infants, there was no practical difference in antirachitic efficacy of cow's milk made antirachitic by irradiation or by feeding cows irradiated yeast.

SUMMARY

It is quite evident from the foregoing that both breast milk and cow's milk contain variable amounts of calcium, phosphorus and Vitamin D. Since these factors are of primary importance for promoting satisfactory bone growth it is apparent that neither breast milk nor cow's milk can always be depended upon to protect infants against rickets. Hence it has become a quite general practice to supplement breast milk with orange juice and cod liver oil or other sources of the necessary vitamins, and modify cow's milk by adding materials which supply the desired minerals, vitamins and calories. According-

ly the need for careful supervision of the diet of the infant has become very generally accepted, particularly as the infant's dietary is very restricted and its margin of safety as regards its nutritive requirements is lower than during later life.

REFERENCES

[1]Eliot, M. M.: J. A. M. A. **85,** 656 (1925).

[2]Hess, A. F.: Rickets, Osteomalacia and Tetany, Lea and Febiger, Philadelphia, 1929.

[3]Sherman, H. C.; Metler, A. J., and Sinclair, J. E.: Office of Expt. Stations, U. S. Dept. of Agri., Bul. 227 (1910).

[4]Sommer, H. H., and Hart, E. B.: J. Biol. Chem. **40,** 137 (1919).

[5]Rothwell, C.: J. Biol. Chem., **65,** 129 (1925).

[6]Sherman, H. C.: Chemistry of Food and Nutrition, Third Ed., Macmillan Co., New York (1927).

[7]Storms, L. B.: Trans. N. Z. Institute **58,** 277 (1927).

[8]Rogers, L. A.: Fundamentals of Dairy Science, Amer. Chem. Soc. Monograph (1928).

[9]Hart, E. B.; Steenbock, H. Teut, E. C., and Humphrey, G. C.: J. Biol. Chem. **84,** 359 (1929).

[10]Supplee, G. C.: J. Dairy Sci. **13,** 522 (1930).

[11]Sanders, G. P.: J. Biol. Chem. **90,** 747 (1931).

[12]Fleming, R. S.: Borden Co., Syracuse, N. Y., Personal Communication.

[13]McHargue, J. S.: Univ. of Kentucky, Lexington, Ky., Personal Communication.

[14]White House Conference, Section 1, Medical Service, Growth and Development of the Child, Part 3, Nutrition, The Century Co., New York (1932).

[15]Lythgoe, H. C.: Mass. Dept. Public Health, Personal Communication.

[16]Holm, G. E.; Webb, B. H., and Deysher, E. F.; J. Dairy Sci. **15,** 331 (1932).

[17]Korenchevsky, V.: Med. Research Council, Special Rpt. 71 (1922).

[18]Burhans, C. W., and Smith, D. N.: Am. J. Dis. Child. **26,** 303 (1923).

[19]De Buys, L. R., and Von Meysenbug, L.: Am. J. Dis. Child. **27,** 438 (1924).

[20]Lowenfeld, M. F.; Widdows, S. T.; Bond, M., and Taylor, E. I.: Biochem. J. **21,** 1 (1927).

[21]Widdows, S. T.; Lowenfeld, M. F.; Bond, M., and Taylor, E. I.: Biochem. J. **24,** 327 (1930).

[22]Donelson, E.; Nims, B.; Hunscher, H. A., and Macy, I. G.: J. Biol. Chem. **91,** 675 (1931).

[23]Macy, I. G.; Nims, B.; Brown, M., and Hunscher, H. A.: Am. J. Dis. Child. **42,** 569 (1931).

[24]Nims, B.; Macy, I. G.; Hunscher, H. A., and Brown, M.: Am. J. Dis. Child. **43,** 1062 (1932).

[25]Wang, C. C.; Witt, D. B., and Felcher, A. R.: Am. J. Dis. Child. **27,** 352 (1924).

[26]Telfer, S. V.: Glasgow Med. J. **114,** 265 (1930).

[27]Swanson, W. W.: Am. J. Dis. Child. **43,** 10 (1932).

[28]Witt, D. B.: Am. J. Dis. Child. **43,** 306 (1932).

[29]Bosworth, A. W.: J. Biol. Chem. **20,** 707 (1915).

[30]Washburn, R. M., and Jones, C. H.: Vermont Agri. Exp. Sta. Bul. 195 (1916).

[31]Magee, H. C., and Harvey, D.: Biochem. J. **20,** 885 (1926).

[32]Daniels, A. L., and Loughlin, R.: J. Biol. Chem. **44,** 381 (1920).

[33]Bosworth, A. W.: Am. J. Dis. Child. **22,** 455 (1921).

[34]Daniels, A. L., and Stearns, G.: J. Biol. Chem. **61,** 225 (1924).

[35]Willard, A. C., and Blunt, K.: J. Biol. Chem. **75,** 251 (1927).

[36]Kramer, M. M.; Latzke, E., and Shaw, M. M.: J. Biol. Chem. **79,** 283 (1928).

[37]Jones, M. R.: J. A. M. A. **82,** 439 (1924).

[38]Irving, L., and Ferguson, J.: Proc. Soc. Exper. Biol. and Med. **22,** 527 (1925).

[39]Flood, R. G.: Am. J. Dis. Child. **32,** 550 (1926).

[40]Wills, L.; Sanderson, P., and Paterson, D.: Arch. Dis. Childhood **1,** 245 (1926).

[41]Underhill, F. P., reported by Irving, L.: J. Biol. Chem. **68,** 513 (1926).

[42]Inouye, T.: Am. J. Physiol. **70,** 524 (1924).

[43]Bergeim, O.: J. Biol. Chem. **70,** 35 (1926).

[44]Collins, W. D., and Howard, C. S.: Index of analyses of natural waters in the United States: U. S. Geol. Survey Water-Supply Papers 560–C and 659–C.

[45]Collins, W. D., The industrial utility of public water supplies in the United States: U. S. Geol. Survey Water-Supply Paper 496.

[46]Sisson, W. R., and Denis, W.: J. A. M. A. **75,** 601 (1920).

[47]Bosworth, A. W.: Am. J. Dis. Child. **22,** 193 (1921).

[48]Cantarow, A.: Calcium Metabolism and Calcium Therapy, Lea and Febiger, Philadelphia (1931).

[49]Greenwald, I., and Gross, J.: J. Biol. Chem. **66,** 201 (1925).

[50]Jeppsson, K.: Reported by Greenwald and Gross, Reference No. 49.

[51]Whelan, M.: J. Biol. Chem. **63,** 585 (1925).

[52]Miller, H. G.: J. Biol. Chem. **67,** 71 (1926).

[53]Mendel, L. B., and Benedict, S. R.: Am. J. Physiol. **25,** 23 (1909–10).

[54]Malcolm, J.: J. Physiol. **32,** 183 (1904–05).

[55]Bogert, L. J., and McKittrick, E. J.: J. Biol. Chem. **54,** 63 (1922).

[56]Hart, E. B., and Steenbock, H.: J. Biol. Chem. **64,** 75 (1925).

[57]Palmer, L. S.; Eckles, C. H., and Schutte, D. J.: Proc. Soc. Exper. Biol. and Med. **26,** 58 (1928).

[58]Elliot, W. E.; Crichton, A., and Orr, J. B.: British J. Exper. Path. **3,** 10 (1922).

[59]Orr, W. J., and Holt, L. E., Jr.: Am. J. Dis. Child. **28,** 574 (1924).

[60]Macy, I. G.: Yale J. Biol. and Med. **4,** 451 (1932).

[61]Givens, M. H.: J. Biol. Chem. **34,** 119 (1918).

[62]Lindberg, G.: Reported by The White House Conference—Growth and Development of the Child, Part III, Nutrition, The Century Co., New York (1932).

[63]Steinitz, F.: Reference same as No. 62.

[64]Sawyer, M.; Bauman, L., and Stevens, F.: J. Biol. Chem. **33,** 103 (1918).

[65]Bowditch, H. J., and Bosworth, A. W.: Am. J. Dis. Child. **6,** 394 (1913).

[66]Telfer, S. V.: Quart. J. Med. **20,** 7 (1926–27).

[67]Meyer, L. F., and Cohn, S.: Reference same as No. 62.

[68]McCollum, E. V.; Simonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **50,** 5 (1922).

[69]Husband, A. D.; Godden, W., and Richards, M. B.: Biochem. J. **17,** 707 (1923).

[70]Harvey, D.: Biochem. J. **21,** 1268 (1927).

[71]Hart, E. B.; Steenbock, H.; Kletzien, S. W., and Scott, H.: J. Biol. Chem. **71,** 271 (1927).

[72]Hess, A. F., and Unger, L. J.: Am. J. Dis. Child. **24,** 327 (1922).

[73]Lesné, E., and Vagliano, M.: Compt. rend. Soc. Biol. **91,** 143 (1924).

[74]Kennedy, C., and Palmer, L. S.: Proc. Soc. Exper. Biol. and Med. **23,** 230 (1925).

[75]Hess, A. F.: Am. J. Dis. Child. **32,** 458 (1926).

[76]Gerstenberger, H. J.: Am. J. Dis. Child. **32,** 461 (1926).

[77]Hess, A. F.; Weinstock, M., and Sherman, E.: J. A. M. A. **88,** 24 (1927).

[78]Outhouse, J.; Macy, I. G., and Brekke, V.: J. Biol. Chem. **78.** 129 (1928).

[79]Eufinger, H.; Wiesbader, H., and Focsaneanu, L.: Klin. Woch. **8,** 826 (1929); Chem. Abs. **23,** 3955 (1929).

[80]Hess, A. F., and Weinstock, M.: Am. J. Dis. Child. **34,** 845 (1927).

[81]Hess, A. F.: J. A. M. A. **88,** 24 (1927).

[82]Bunker, J. W. M.; Harris, R. S., and Eustis, R. S.: N. E. J. Med. **208,** 313 (1933).

[83]McBeath, N. E., and McMahon, H. O.: Wis. M. J. **32,** 385 (1933).

[84]Lewis, J. M.: N. Y. State J. Med. **34,** 685 (1934).

[85]Barnes, D. J.; Cope, F.; Hunscher, H. A., and Macy, I. G.: J. Nutrition **8,** 647 (1934).

[86]Hess, A. F.: J. A. M. A. **76,** 693 (1921).

[87]Hess, A. F., and Unger, L. J.: Am. J. Dis. Child. **22,** 186 (1921).

[88]Bethke, R. M.; Steenbock, H., and Nelson, M. T.: J. Biol. Chem. **58,** 71 (1923).

[89]Hess, A. F., and Weinstock, M.: J. Biol. Chem. **63,** 297 (1925).

[90]Steenbock, H.; Hart, E. B.; Hoppert, C. A., and Black, A.: J. Biol. Chem. **66,** 441 (1925).

[91]Daniels, A. L.; Pyle, S. I., and Brooks, L.: Proc. Soc. Exper. Biol. and Med. **23,** 821 (1926).

[92]Supplee, G. C., and Dow, O. D.: Am. J. Dis. Child. **34,** 364 (1927).

[93]Sherman, H. C., and Stiebeling, H. K.: J. Biol. Chem. **83,** 497 (1929).

[94]Honeywell, H. E.; Dutcher, R. A., and Dahle, C. D.: J. Nutrition **2,** 251 (1930).

[95]Hess, A. F.; Lewis, J. M.; McLeod, F. L., and Thomas, B. H.: J. A. M. A. **97,** 370 (1931).

[96]Honeywell, H. E.; Dutcher, R. A., and Dahle, C. D.: J. Biol. Chem. **74,** lxxvii (1927).

[97]Supplee, G. C., and Dow, O. D.: J. Biol. Chem. **73,** 617 (1927).

[98]Hess, A. F., and Unger, L. J.: J. A. M. A. **74,** 217 (1920).

[99]Kon, S. K., and Booth, R. G.: Biochem. J. **23,** 111 (1934).

[100]McCollum, E. V.; Simmonds, N., and Becker, G. E.: J. Biol. Chem. **53,** 293 (1922).

[101]Shipley, P. G.; Park, E. A.; McCollum, E. V., and Simmonds, N.: Am. J. Hyg. **1,** 512 (1921).

[102]McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Proc. Soc. Exper. Biol. and Med. **18,** 275 (1921).

[103]McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **51,** 41 (1922).

[104]McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **50,** 5 (1922).

[105]Mellanby, M.: Lancet **1,** 856 (1920).

[106]Park, E. A.: Physiol. Reviews **3,** 106 1923.

[107]Park, E. A.; Guy, R. A., and Powers, G. F.: Am. J. Dis. Child. **26,** 103 (1923).

[108]Park, E. A., and Howland, J.: Bul. Johns Hopkins Hosp. **32,** 341 (1921).

[109]Drummond, J. C.; Coward, K. H.; Golding, J.; Mackintosh, J., and Zilva, S. S.: J. Agri. Sci. **13,** 144 (1923).

[110]Golding, J.; Soames, K. M., and Zilva, S. S.: Biochem. J. **20,** 1306 (1926).

[111]Sheehy, E. J., and Senior, B. J.: Biochem. J. **23,** 898 (1929).

[112]Golding, J., and Zilva, S. S.: Biochem. J. **22,** 173 (1928).

[113]Hess, A. F.; Weinstock, M., and Tolstoi, E.: J. Biol. Chem. **57,** 731 (1923).

[114]Hess, A. F., and Weinstock, M.: Am. J. Dis. Child. **27,** 1 (1924).

[115]Luce, E. M.: Biochem. J. **18,** 716 and 1279 (1924).

[116]Chick, H., and Roscoe, M. H.: Biochem. J. **20,** 632 (1926).

[117]Steenbock, H.; Hart, E. B.; Riising, B. M.; Hoppert, C. A.; Basherov, S., and Humphrey, G. C.: J. Biol. Chem. **87,** 103 (1930).

[118]Gerstenberger, J. H.; Hartman, J. I., and Smith, G. N.: Calif. and West. Med. **27,** 40 (1927).

[119]Steenbock, H., and Daniels, A. L.: J. A. M. A. **84,** 1093 (1925).

[120]Steenbock, H., and Black, A.: J. Biol. Chem. **64,** 263 (1925).

[121]Hess, A. F., and Weinstock, M.: Proc. Soc. Exper. Biol. and Med. **22,** 319 (1925).

[122]Hess, A. F.: J. A. M. A. **89,** 337 (1927).

[123]Supplee, G. C.; Flanigan, G. E.; Kahlenberg, O. J., and Hess, A. F.: J. Biol. Chem. **91,** 773 (1931).

[124]Anderson, A. K., and Triebold, H. O.: J. Dairy Sci. **15,** 469 (1932).

[125]Hess, A. F.: J. A. M. A. **84,** 1910 (1925).

[126]Kramer, B.: Am. J. Dis. Child. **30,** 195 (1925).

[127]MacKay, H. M. M., and Shaw, H. F.: Lancet **1,** 8 (1926).

[128]Daniels, A. L.; Stearns, G., and Hutton, M. K.: Am. J. Dis. Child. **37,** 296 (1929).

[129]Steenbock, H.; Black, A.; Nelson, E. M.; Nelson, M. T., and Hoppert, C. A.: J. Biol. Chem. **68,** XXV (1925).

[130]Kon, S. K., and Mayzner, M.: Lancet **1,** 794 (1930).

[131]Wachtel, M.: Munch. Med. Wochschi. **76,** 1513 (1929); Science **73,** 619 (1931).

[132]Hart, E. B.; Steenbock, H.; Kline, O. L., and Humphrey, G. C.: J. Biol. Chem. **86.** 145 (1930).

[133]Steenbock, H.; Hart, E. B.; Hanning, F., and Humphrey, G. C.: J. Biol. Chem. **88,** 197 (1930).

[134]Thomas, B. H., and MacLeod, F. L.: Science **73,** 618 (1931).

[135]Wyman, E. T., and Butler, A. M.: Am. J. Dis. Child. **43,** 1509 (1932).

[136]Barnes, D. J.: Proc. Soc. Exper. Biol. and Med. **31,** 1221 (1934).

[137]Wilson, W. R.: J. A. M. A. **102,** 1824 (1934).

[138]Hess, A. F., and Lewis, J. M.: J. A. M. A. **101,** 181 (1933).

[139]Wyman, E. T.; Eley, R. C.; Bunker, J. W. M., and Harris, R. S.: N. E. J. Med. **212,** 257 (1935).

[140]Kramer, B., and Gittleman, I. F.: N. E. J. Med. **209,** 906 (1933).

[141]Gerstenberger, H. J.; Horesh, A. J.; Van Horn, A. L.; Krauss, W. E., and Bethke, R. M.: J. A. M. A. **104,** 816 (1935).