A SURVEY OF THE LITERATURE DEALING WITH THE
CALCIUM-PHOSPHORUS METABOLISM OF
NORMAL CHILDREN

by

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A Thesis Submitted to the Graduate
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MASTER OF SCIENCE

Major Subject: Child Nutrition

* The average child is taken as normal
The writer wishes to express her gratitude to Mrs. Christine B. Clayton, Dean of the School of Home Economics and Professor of Foods and Nutrition at the Utah State Agricultural College, for her patient and competent guidance in this work.
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Chapter I

Introduction

Purpose of the Study

The purpose of this study is to collect and organize all data available to the investigator on the subject of calcium and phosphorus requirements for normal children. Since it is the business of nutrition to maintain health and prevent disorders, leaving the cure of disorders to the medical profession, this study deals with the calcium and phosphorus metabolism of normal children and avoids going into the pathological phases, taking up rickets and tetany only in so far as prevention is concerned.

If this study has any value it lies in the fact that the findings of investigators seem to be scattered throughout a great many books and scientific journals, and it was thought that the collection and organization of these findings would serve as useful purpose in making this research more readily available to nutrition students. The bibliography for the study was made up from references given by such recognized authorities and sources as Sherman, McLester, Starling, Lusk, Van Slyke and Peters, Bogert, Rose, Child Development Abstracts, British Nutrition Abstracts, and Chemical Abstracts. From this bibliography were chosen those books and articles which seemed to the writer to be most promising as to reliability, amount of information, and variety of information. Part of the work has of necessity been adapted to children from experiments on adults.

The importance of calcium and phosphorus in the diet of little children is emphasized by Sherman as follows: "The effect of an insufficient intake of calcium is naturally more serious with growing than with full grown animals. The young need more calcium because during growth and development the body in increasing not only the amount but the percentage
of calcium which it contains. *** Growing children whose height, weight, and appearance are normal may have a calcium-poor condition of the body. *** Since this is largely a matter of the deposition of calcium phosphate in the developing bones, the phosphorus content of the body tends to remain low when the calcium is low and to rise to normal with the calcium when the calcium content of the food is increased."

**Forward**

It has been very difficult to determine when calcium and phosphorus metabolism was first recognized or studied. Hess (44) gives a discussion of the earliest findings on rickets, which may be taken as an index of the beginning of such investigations. He states that Soranus, in the first and second centuries after Christ, referred to the symptoms of rickets. Galen, a contemporary, also referred to the disorder. Barth Reusner, is said by some, though this questions, to have written a paper or book describing what is now known as rickets. Dutch and German paintings of about that period show children with the deformities attributed to rickets. In 1609 two French writers mentioned the deformities but attributed them to too tight clothing or to wrong ways of carrying children. In 1645 Whistler of England wrote a doctor's dissertation on the disorder. At that time the word rickets was first used. There seem to be two conflicting stories as to the origin of the name. One is "ricket" meaning "to breathe with difficulty". The other is "wrick" used as follows: "To wrick one's ankle." In the 19th century the knowledge of rickets advanced rapidly. In the latter part of the 19th century chemistry was first applied to such a disease.

Judging from the dates of reports on the subject investigated by the

44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
writer, it seems that calcium and phosphorus metabolism has been studied
(or at least studied with satisfactory results) only since the beginning
of the 20th century, with very little being done even in the first decade
or in this our current century. Osborne and Mendel (75) in writing of
"Feeding Experiments with Isolated Foodstuffs" 1911 do not give special
place to inorganic foodstuffs although theymention that certain minerals
seem to be necessary and therefore vegetables and milk are important
in the diet. Mendel's book "Nutrition: The Chemistry of Life" (69) written in
1923 was a decided expansion of his work on minerals. However, he was pre-
ceeded by several groups of workers who made definite progress in the field
of calcium and phosphorus metabolism. The first milestone of importance
discovered in this investigation of literature was the work done by Forbes
(52-53) and his co-workers in 1914, at which time they carried on experiments
and also reviewed and compiled literature on the phosphorus compounds of the
animal body. Another definite forward step was the work done by Sherman and
Hawley (89) in 1922, on the calcium and phosphorus requirements of normal
children from 6 to 15 years of age. At about the same time Bogert (15, 14,
15, 16) and her associates were experimenting on the various factors influ-
encing calcium and phosphorus assimilation. Hill(49) and his assistants,
working during the decade 1920 to 1930, discovered an important role of
phosphagen in muscle metabolism that had been previously been obscure. It
was from 1926 on that Mellanby and assistants (67,68) working in London, and
Lewis et al (61,63) working at the Merrill-Palmer school in Detroit have
contributed their important studies on dentition. There have been other
important findings too numerous to mention, but those mentioned above are
enough to show the trend in the study of these minerals.

89. Sherman and Hawley - JBC 55: 575; 1922
69. Mendel - Nutrition: The Chemistry of Life - 1923
Osborne and Mendel - Feeding Experiments with Isolated Food Stuffs,
52. Forbes - Ohio Agric. Exp. Sta. Blt. 6 - 55, with Keith in Blt. 5
49. Hill, A. V. - Physiol. Rev. 5:225; 1933
Chapter II

Functions of Calcium

Skeletal Formation and Growth

Bones. That calcium is very necessary to growth is shown by Sherman and McLeod (91) in an experiment with rats in which growth stopped when the diet, though adequate in other respects, was low in calcium.

1. 5% of the human body (by weight) is composed of calcium. All writers on the subject, (13, 91, 104, 25) seem to agree that 95% of this amount is found in the skeleton of the adult. Stearns (94) states that from 97 to 98% of the total calcium retained by infants and children is used in the formation of bone. She says also that "for practical purposes the retention of calcium can thus be used as an index of the rate of bone growth."

The percent of the calcium in the ash of the body increases with age (while the percent of phosphorus decreases). This change in opposite directions, according to Hammett (39) indicates that there is a change in the type of calcium-phosphorus complex laid down. In the further study (40) the same writer shows that the percent of water decreases with age, due to ash deposition.

The calcium needed for prenatal growth is presented best by Michel (64) in tabular form, in which the author shows that a fetus adds .41 grams of calcium per week at the 16th week, and 2.09 grams per week from the 23th to the 40th week. He suggests cow's milk as the best means of obtaining the necessary increase of calcium needed during these important last ten weeks of pregnancy. Hoffstrom (64) shows that during the last 25 weeks of pregnancy the mother retains a total of 34.31 grams of calcium, 50.12 grams of which goes to the fetus. Besides the increase in retention by the growing organism, there is a decrease in fecal

91 - Sherman, H. C. and McLeod, A. L. - J.B.C. 54:429; 1925
13 - Bogert, L. J. - Nutrition and Physical Fitness
104 - Van Slyke and Peters - Quantitative Clinical Analysis
25 - Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
96 - Stearns, G. - J.B.C. 42(2):749; 1931
39 - Hammett, F. S. - J.B.C. 64:693; 1925
40 - Hammett, F. S. - J.B.C. 64:409; 1925
64 - Lusk, G - The Science of Nutrition - 1926
excretion of calcium by the mother. Van Slyke and Peters (104) state that "in growing children with calcium deficiency, increased absorption means increased retention".

Sherman (90) observes that "although the body is gaining calcium and is growing in height and weight, the rate of gaining calcium may not be enough for bone development".

Henderson and Weakley (42) made a study of the bones of animals fed varying amounts of calcium and phosphorus. They found that the bones of animals fed less than .55% calcium were 1. low in ash and 2. high in moisture and extractable material. The groups were classed as follows:

1. sufficient calcium and phosphorus
2. low calcium
3. low phosphorus
4. low in both

Group 4 grew as well for some time but not over the two-year-period. Group 5 grew as well over the two-year-period.

The calcium content of the blood of normal children seems of importance here because blood is the carrier of minerals to the bone (106). Briggs (23) gives the average calcium content of blood as 9.6 grams per liter. There should be .098 grams calcium per liter for an equilibrium normality as .004.9.

Cantarow (25) summarizes the findings of investigators on blood calcium as follows:

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Ages Studied</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jansen</td>
<td>7 wks. - 16 yrs.</td>
<td>13.5-20.7 mg./100 cc</td>
</tr>
<tr>
<td>Jones</td>
<td>4 hours - 12 days</td>
<td>12.5</td>
</tr>
<tr>
<td>Mayer</td>
<td>infants - children</td>
<td>11.25</td>
</tr>
<tr>
<td></td>
<td>4-10 years</td>
<td>11.55</td>
</tr>
<tr>
<td>Nobler</td>
<td>newborn infants</td>
<td>12.65</td>
</tr>
<tr>
<td>Leicher</td>
<td>up to 20 years</td>
<td>11.6</td>
</tr>
</tbody>
</table>

90. Sherman, H.C. – The Chemistry of Food and Nutrition – 1952
25. Cantarow, A. – Calcium Metabolism and Calcium Therapy – 1961
all of these experimenters indicate that the blood calcium level decreases with age.

Of this total calcium in blood, various experiments (25) give figures for the diffusible fraction as from 50 to 75% with an average of 62%.

Calcium forms 24-48% of the composition of bone (64) and is formed in the following distribution:

1. According to Van Slyke and Peters (104)
   as phosphate 84-85%
   as carbonate in adults 15-16%
   as carbonate in newborn 9-10%

2. According to Cantarow (25)
   as phosphate 85-90%
   as carbonate 9-13%

3. According to Holt (49)
   as carbonate 14%

Ca₃(PO₄)₂ is found (49) to compose 75% of the total ash of the body. The majority of experimenters find calcium as both CaCO₃ and Ca₃(PO₄)₂ in bone, although some find just the latter and some find still a third. Table I is a resume of the experimenters' findings. Hammett (39) believes there is a change with age, calcium increasing while phosphorus decreases. Henderson and Weakley (42) believe the proportion of calcium and phosphorus in the ash of bones remained the same regardless of whether the ration is low in calcium or phosphorus or both or contained sufficient of both.

Holt, LaMer, and Chown (49) (confirmed by Bassett and by Wendt and Clarke) think that CaHPO₄ is first precipitated as an intermediary product. All three groups of experimenters agree that it is transitory, but they have different ideas as to just what happens to it. Bassett (49) believes that "the more slowly precipitating Ca₃(PO₄)₂, or a more basic salt, forms a

39. Hammett, F. S. - JBC 64: 695; 1925
   CDA 6 (4): 351; 1932
49. Holt, LaMer, Chown - JBC 64: 509, 567, 579; 1925
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1951
49. Holt, LaMer, Chown - JBC 64: 509, 567, 579; 1925
64. Lusk, G. - The Science of Nutrition - 1928
Table I

Compounds Believed or Found to be Present in Bones

<table>
<thead>
<tr>
<th>Experimenters</th>
<th>Ca CO₃</th>
<th>Ca₃(PO₄)₂</th>
<th>CaCO₃-nCa₃(PO₄)₂</th>
<th>CaHPO₄</th>
<th>Ca(OH)₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sherman (90)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taylor &amp; Sheard (90, 104)</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rosberry, Hastings, Morse (104)</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Slyke and Peters (104)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shear and Kramer (104)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sjollema (93)</td>
<td>X</td>
<td>X</td>
<td>possibly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holt, Lamer, Chown (49)</td>
<td>X</td>
<td>X</td>
<td>transitory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bassett (49)</td>
<td></td>
<td>X</td>
<td>transitory</td>
<td>X (?)</td>
<td></td>
</tr>
<tr>
<td>Wendt &amp; Clark (49)</td>
<td></td>
<td>X</td>
<td>transitory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruendenberg &amp; Gyorgy (25)</td>
<td></td>
<td></td>
<td>X with protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gassman (25)</td>
<td></td>
<td></td>
<td>X closed ring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronson (25)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A crystal substance as in rocks; n = greater than 2 but less than 3

25. Bronson, B. S. - Nutrition and Food Chemistry - 1930
90. Sherman, H. C. - The Chemistry of Food and Nutrition - 1932
104. Van Slyke and Peters - Quantitative Clinical Analysis - 1951
93. Sjollema, B. - JBC 57: 255; 1923
49. Holt, Lamer, Chown - JBC 64: 509, 567, 579; 1925
gelatinous layer about the crystals of CaHPO₄, preventing free diffusion and thus impeding equilibrium formation. The resulting solid phase is then a mixture of the two and perhaps three salts indicated in the table. Wendt and Clarke (49), although they do not present analysis to support their conclusions, believe that CaHPO₄ is precipitated first but that it is unstable and decomposes as follows:

\[ 4 \text{CaHPO}_4 \rightarrow \text{Ca(H}_2\text{PO}_4)_2 \text{(soluble)} + \text{Ca}_3\text{(PO}_4)_2 \downarrow \]

Holt et al believe in a "transitory existence of CaHPO₄ in bones as follows:

1. \[ \text{Ca}^{xx} + \text{HPO}_4 \rightarrow \text{CaHPO}_4 \downarrow \]
2. \[ 3 \text{Ca}^{xx} + 2 \text{PO}_4 \rightarrow \text{Ca}_3\text{(PO}_4)_2 \downarrow \]

These two reactions start simultaneously, according to them, but the former proceeds faster so that CaHPO₄ is precipitated first. They give the cause for this as the relative number of molecule collisions necessary (two in the first, five in the second). The solution then becomes more alkaline than as though reaction 1. were not taking place. The reaction for CaHPO₄ reduces the number of PO₄ ions available for the Ca₃(PO₄)₂ reaction, so the tertiary phosphate is delayed still more. As the CaHPO₄ reaction nears completion the second reaction exceeds it and thus PO₄ ions are being removed more rapidly than HPO₄ ions. This causes the HPO₄ to dissociate into H⁺ and PO₄⁻³ to maintain the value of K₅. This is naturally accompanied by an increase in acidity. When a certain amount of HPO₄ ions have been used up the \[ \text{Ca}^{xx} \text{X} \text{HPO}_4^- \] falls below the solubility product of CaHPO₄ and this solid salt dissolves, thus assisting the precipitation of \[ \text{Ca}_3\text{(PO}_4)_2 \downarrow \]. Equilibrium cannot be reached until all the CaHPO₄ is dissolved.

104. Van Slyke and Peters - Quantitative Clinical Analysis, 1931
It will be seen from this discussion that if, as these experimentors believe, CaHPO$_4$ is a preliminary stage it's precipitation is quicker than and delays precipitation of Ca$_3$(PO$_4$)$_2$ because of the following factors: (49)

1. Most substances dissolve more slowly than they precipitate.
2. If Bassett is right there is an added delay due to the gelatinous covering around the CaHPO$_4$.
3. Part of slowness is probably due to its being fifth order reaction.

The investigator thinks that Van Slyke and Peters (104) seem to give the best summary of the manner in which calcification of bone takes place, and of the factors upon which it depends.

The first theory mentioned is that calcification depends upon the degree of saturation of blood plasma with Ca$_3$(PO$_4$)$_2$. In other words it is dependent upon the solubility of the calcium salts which are brought to the bone by the blood in which such salts circulate. There appears to be a characteristic supersaturation (with CaCO$_3$ and Ca$_3$(PO$_4$)$_2$) of the solution and because of this, much of the serum calcium remains in solution. The presence of Ca$_3$(PO$_4$)$_2$ causes a precipitation of Ca as CaCO$_3$. The Ca and PO$_4$ ions act in a reciprocal manner. If one increases the other decreases thus since serum is normally saturated with Ca$_3$(PO$_4$)$_2$ an increase of either ion causes a removal of the other by excretion or, more favorably, by precipitation in bone. It is thought by some, although not agreed to by all, that if the serum and fluids circulating around bone were not saturated, bone would dissolve. The writers felt that "the higher inorganic phosphate content of infants' blood may indicate that in the active bone forming period either the solubility of calcium and phosphate in serum is greater or the serum is normally more saturated with these substances".

The second theory mentioned is that calcification depends upon some vital property of osteod tissue. Proof given for this theory is that calcification is prevented by protoplastic poisons.

104. Van Slyke and Peters - Quantitative Clinical Analysis, 1931
27. Demuth, F. - Monatschr., Kinderheilk 31(3/4); 252; 1925 & 26
CDA 4(5) 501; 1980
The third theory given is known as the Robinson theory. Robinson, a British worker, ascribes to actively growing bone and cartilage an enzyme, called phosphoricesterase which he considers essential in bone formation. It, he thinks, increases the phosphate concentration sufficiently to cause the calcium X phosphate to exceed the effective solubility product so that Ca₃(PO₄)₂ is precipitated. In other words by adding PO₄ to the already supersaturated solution, it causes precipitation. This theory is not, up to the present, confirmed. Demuth (27) demonstrates such a phosphatase and describes it further as having a pH optima of from pH 5.5 to pH 7.0, according to the source. He states that in normal serum it shows relatively weak activity at a wide pH range.

Watt (109) states that "evidence seems to point to the fact that calcium deposition is dependent upon definite cellular activity." He seems to look upon this deposition in the bone matrix as a secretion by the osteoblasts rather than as a mere precipitation. He states that in cartilage, calcium salts are deposited as distinct granules which become densely packed but do not fuse. They are seen first around the blood vessels. In bone the fine granules do fuse and are seen first around osteoblasts. Watt says there are three stages of bone formation as follows: cartilage, calcification of cartilage, bone.

Holt, (49) gives a fourth and fifth theory of calcification somewhat similar to Watt's interpretation of the Robinson theory. He states that "the osteoblasts may be considered as resting in tissue spaces which are in contact with the amorphous bone matrix on the one hand, and with the walls of blood vessels on the other." This matrix he says consists of a protein substance called osssein or collagen. He attributes one-third of mass of

49. Holt, LaMer, and Chown - JBC 64: 509, 587, 579; 1925
bone to the matrix, while two-thirds is said to be of calcium and phosphorus in the proportions needed for Ca₃(PO₄)₂, and small amounts of other salts, including magnesium. The theories he presents are as follows:

1. Both collagen and lime salts are secreted by the osteoblasts.
2. Lime salts are laid down in matrix, separately or as double salts, by simple precipitation.

In either case the inorganic salts must be derived from the blood stream.

Holt favors the first but thinks the second may yet be proven.

It will be seen that although the theories vary considerably, they are not in absolute contradiction. Writers, in explaining what calcium salts do for bones, all agree on one or more of the following functions:

Sherman (90) ---------------------------------- rigidity permanence

Van Slyke and Peters (104) ------------------ formation of rigid supporting structure of all osseous tissue.

MoLester (65) ------------------ building and repair

There are a great many factors affecting various phases of Calcium and Phosphorus metabolism which will be discussed in Chapter IV, but there are several factors that especially affect Calcium deposition which seem to be of importance at this part of the survey. Summarized in table form they are as follows:

<table>
<thead>
<tr>
<th>Factors favoring Calcification</th>
<th>Experimenters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irradiated ergosterol</td>
<td>Hume (51)</td>
</tr>
<tr>
<td>Ca:P ratio</td>
<td>(Stearns (96)*</td>
</tr>
<tr>
<td></td>
<td>(Hess (44))</td>
</tr>
<tr>
<td></td>
<td>(McCullum et al (64))</td>
</tr>
<tr>
<td>God liver oil</td>
<td>(Hess (44))</td>
</tr>
<tr>
<td>Ultra violet lamp treatment of food</td>
<td>Penn State College (78)</td>
</tr>
<tr>
<td>Parathyroid hormones (if there is sufficient Ca</td>
<td>Van Slyke &amp; Peters (104) **</td>
</tr>
<tr>
<td>in blood)</td>
<td></td>
</tr>
<tr>
<td>High Ca diet</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>High P diet</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Van Slyke &amp; Peters (104) **</td>
</tr>
<tr>
<td></td>
<td>(McCullum et al (64))</td>
</tr>
<tr>
<td></td>
<td>(Hess &amp; Weinstock (47))</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Park (65) ***</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>(Hess &amp; Weinstock (47))</td>
</tr>
<tr>
<td></td>
<td>(McCullum et al (64))</td>
</tr>
<tr>
<td>Vitamin C (possibly)</td>
<td>(Howe (50))</td>
</tr>
<tr>
<td></td>
<td>(McCullum et al (64))</td>
</tr>
</tbody>
</table>
Searns gives figures from several experimenters (Schabal; Howland, Marrot, Kramer; Kramer and Shear) on the retention ratio of normal infants. They range from 1.85:1 to 2.19:1. She concludes that the expected ratio during infancy is more than 1.5:1 but less than 2.1:1. A ratio above 2.1:1 indicates a shortage of phosphorus, whereas a ratio less than 1.5:1 indicates a deficiency of calcium retention. Muscles form approximately one-fourth of the body weight at birth and according to Scammon (quoted by Searns) do not grow as rapidly as the rest of the body during infancy (shown by the ratio of 2:1). Searns gives the optimum retention in childhood as 1.5:1 or 1.7:1. This, she says indicates an equal growth of bones and other tissues. She states that "the rapid growth of muscles during childhood necessitates a slower growth of other soft tissues, since the skeleton remains the same percent of body weight". She says the ratio may be lower than 1.5:1, though if less than 1:1 it shows that bone growth is only half as fast as soft tissues containing phosphorus. If it approaches 2:1 it shows more rapid growth of bone than soft tissues as in infancy. For a detailed report of the findings of many investigators, see Table 2, quoted from four tables given by Searns.

90. Sherman, H. C. - The Chemistry of Food and Nutrition - 1932
104. Van Slyke and Peters - Quantitative Clinical Analysis - 1931
65. McLester, J. S. - Nutrition and Diet in Health and Disease - 1931
50. Howe, P. C. - Jr. Am. Dental Assn. 15(9); 1926
51. Huse, E. W. and Smith, H. H.
96. Searns, G. - JBC 42(2); 749; 1931
44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
54. Lusk, G. - The Science of Nutrition - 1929
76. Penn, State College Dept. Agric. Blt., 250; 22; 1928
47. Hess & Weinstock - A. J. D. 24; 865; 1927
102. Todd, T. Wingate - Child Devol. 2(1); 49; 1931
90. Sherman, H. C. - Chemistry of Food and Nutrition - 1932
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
50. Howe, P. R. - Jr. Am. Dental Assn. 15(3); --; 1926
### Table II

Retention Ratios of Calcium and Phosphorus
Reported by Stearn (16)

<table>
<thead>
<tr>
<th>Writer</th>
<th>Age</th>
<th>Conditions</th>
<th>Retention/Kg B.W./Da</th>
<th>Retention Ratio Ca/P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sherman &amp; Hawley (JBC 53)</td>
<td>3-15 years</td>
<td>Healthy children receiving Liberal Ca &amp; P</td>
<td>0.018</td>
<td>0.010</td>
</tr>
<tr>
<td>Willard &amp; Blunt (JBC 75)</td>
<td>3-4</td>
<td>&quot; &quot;</td>
<td>0.011</td>
<td>0.011</td>
</tr>
<tr>
<td>Kramer, Latgke, Shaw (JBC 73)</td>
<td>7-12</td>
<td>&quot; &quot;</td>
<td>0.018</td>
<td>0.010</td>
</tr>
<tr>
<td>Wang, Kern, Kaucher (AJDC 59)</td>
<td>6-12</td>
<td>&quot; &quot;</td>
<td>0.012</td>
<td>0.009</td>
</tr>
<tr>
<td>Burton (JBC 85)</td>
<td>3-5</td>
<td>&quot; &quot;</td>
<td>0.042</td>
<td>0.032</td>
</tr>
<tr>
<td>Stearns (unpublished)</td>
<td>6-12</td>
<td>&quot; &quot;</td>
<td>0.021</td>
<td>0.019</td>
</tr>
<tr>
<td>Willard &amp; Blunt (JBC 75)</td>
<td>8</td>
<td>Previous Diets Deficient in Ca</td>
<td>0.028</td>
<td>0.015</td>
</tr>
<tr>
<td>Stearn (unpublished)</td>
<td>10</td>
<td>&quot; &quot;</td>
<td>0.017</td>
<td>0.009</td>
</tr>
<tr>
<td>Sherman &amp; Hawley (JBC 53)</td>
<td>4-12</td>
<td>Diet Deficient in Ca due to Experiments</td>
<td>0.009</td>
<td>0.009</td>
</tr>
<tr>
<td>Cheaney &amp; Blunt (JBC 86)</td>
<td>10-11</td>
<td>&quot; &quot;</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Burton (JBC 85)</td>
<td>12-13</td>
<td>&quot; &quot;</td>
<td>0.005</td>
<td>0.013</td>
</tr>
<tr>
<td>Wang, Kern, Kaucher (AJDC 59)</td>
<td>4-12</td>
<td>&quot; &quot;</td>
<td>0.008</td>
<td>0.005</td>
</tr>
<tr>
<td>Stearn (unpublished)</td>
<td>6-12</td>
<td>&quot; &quot;</td>
<td>0.009</td>
<td>0.006</td>
</tr>
<tr>
<td>Nelson (unpublished)</td>
<td>Months</td>
<td>Artificially fed infants</td>
<td>0.057</td>
<td>0.034</td>
</tr>
<tr>
<td>Jeens, Stearn et al (unpublished)</td>
<td>2-5</td>
<td>&quot; &quot;</td>
<td>0.067</td>
<td>0.039</td>
</tr>
<tr>
<td>Daniels, Hearn, Hutton (AJDC 57)</td>
<td>3-6</td>
<td>&quot; &quot;</td>
<td>0.028</td>
<td>0.022</td>
</tr>
<tr>
<td>Telfer (Quarterly J. Med. 16)</td>
<td>7-12</td>
<td>&quot; &quot;</td>
<td>0.061</td>
<td>0.055</td>
</tr>
</tbody>
</table>
** From the discussion it appears according to experiments performed by Allbright et al and from others by Van Slyke and Peters, that the primary action of the parathyroid hormone is to protect against tetany. Therefore, if blood calcium is low the parathyroid hormone increases it even though it must decalcify bone to do so, but if the blood calcium is sufficiently high the parathyroid hormone favors the precipitation of calcium salts in bone.

*** The effect of Vitamin D upon calcium and phosphorus is, according to the discussion by Van Slyke and Peters, limited to that associated to the growth. This is understandable when it is seen that one of the four effects of vitamin D (discussed in Chapter IV) is to increase calcium solubility in serum. (An overdose results in hypercalcification.)

**** Park calls the effect of vitamin D upon bone metabolism "stimulating and regulatory". Hess thinks that Cod Liver oil favors the calcification of epiphyses "probably by direct chemical action on bone and cartilage."

### Factors Hinderiing Calcification

<table>
<thead>
<tr>
<th>Factor</th>
<th>Experimenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological conditions</td>
<td>Todd (102)</td>
</tr>
<tr>
<td>Race</td>
<td>Todd (102)</td>
</tr>
<tr>
<td>Low Ca Diet</td>
<td>Sheridan (90)</td>
</tr>
<tr>
<td>Low P Diet</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Excess of other inorganic elements, especially P</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Acidifying measures</td>
<td>Cantarow (25)</td>
</tr>
<tr>
<td>Alkalizing measures</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Incomplete intestinal absorption of fat</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Starvation</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Parathyroid extract (if blood calcium is low)</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Cantarow (25)</td>
</tr>
<tr>
<td>Vitamin D Deficiency</td>
<td>Van Slyke &amp; Peters (104)</td>
</tr>
<tr>
<td>Vitamin A Deficiency</td>
<td>Cantarow (25)</td>
</tr>
<tr>
<td></td>
<td>Howe (50)</td>
</tr>
</tbody>
</table>

102. Todd, T. Wingate - Child Devel. 2(1): 49; 1951
90. Sheridan, H. C. - Chemistry of Food and Nutrition - 1932
104. Van Slyke and Peters - Quantitative Clinical Analysis - 1931
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
50. Howe, P. R. - Jr. Am. Dental Assn. 15(9): --; 1928
Todd found that "negroes were more susceptible to disorders which
derange skeletal maturation". He also found that Italians were not as tall
nor as heavy (age for age in six months periods) as Americans, but as there
was no clear distinction in skeletal differentiation he doubts any specific
relation of race to it.

In further discussing skeletal differentiation, Todd says that the
"order and date of epiphyscal differentiation and union is constant; it
follows a human pattern which is not obscured by sex modification. The
progressive uniformity in the general bodily development of boys and girls
during infancy continues until six years. The undoubted earlier appearance
in general of bony deposition in cartilage of the female is not at all re-
lated to the ultimate progress of skeletal differentiation and epiphyscal
union".

He mentions further that "age indications of the several skeletal
areas in a single child may be moderately discordant, usually as a result
of a disturbance in the growth pattern".

As a means of classifying children's skeletal records, a figure three
times the standard deviation is taken as a class line. Thus a child whose
skeletal record is nine months ahead or behind the mode is classed as ac-
celerated or repressed, respectively, no matter what his height or weight.

Sherman, in giving low calcium as hindering calcification, speaks
of "muscles competing with bone for the available calcium. Howe (50) brings
out an interesting paint connected with calcification. According to him,
Vitamin A affects the place of bone formation. In a deficiency of vitamin
A there are no bone changes, but rather an area of bone in the teeth ( in
place of dentin). This will be discussed under the work on teeth.

Teeth

Moore (76) says, "An adult's teeth are largely made or ruined in
infancy". She goes on to state that "teeth share prominently in the early
demand for good building material because:

1. the deciduous teeth are formed and enamelling is begun before birth.
2. the permanent teeth have the enamelling begun soon after birth.

The crowns of teeth are formed early, and when the crowns and enamel are once done they cannot be redone. Toverud and Toverud (104) found that when a mother has a negative calcium balance during pregnancy and lactation her child is more susceptible to dental caries. Mellanby (67) states that "the resistance of teeth to caries and attrition can be influenced by diet, independent of structure. McCollum and Simmonds (66) state that "small jaws and crowding of teeth in children is almost certainly the result of the faulty skeletal development of rickets and any dietary errors that might interfere with the calcium and phosphorus metabolism of children." Rogers (85) found that there is no dental caries among animals and certain races of men, thus proving that caries is not a necessary evil. He gives as proof that poor teeth are not hereditary, the fact that there was a time when caries did not exist, and that caries are not an aid to the survival of the fittest.

The importance of doing what can be done to assist dental calcification is further shown by the incidence of caries. Mellanby (66) found only 14.5% perfect and 21% nearly perfect teeth among 1,036 deciduous teeth examined. Of 354 children, Hellman (quoted by Lewis (61)) found only 3% had normal occlusion.

The manner of calcification is not much discussed. Watt (109) classed ameloblasts (in tooth enamel) and odontoblasts (in dentine) as among the types of cells that can secrete or lay down calcium salts. Sherman (90) records finding the complicated structure Ca$_3$O$_7$·$n$ Ca$_5$(PO$_4$)$_2$ in teeth as in bones. On the other hand, Howe (50) speaks of the area of bone caused in

78. Moore, C. U. - Nutrition of Mother and Child, 1924
104. Toverud, K. U. & Toverud, G. - CDA 6(6): 496; 1932
67. Mellanby, M. - British Dental Jr., 1928
66. McCollum and Simmonds - Newer Knowledge of Nutrition
63. Lewis and Lehman - Dental Cosmos - May 1929
teeth by a deficiency of vitamin A (see page 15) as less dense and resistant, thus suggesting its abnormality. The only other consideration of the manner of calcification of teeth given in references is the time that process occurs. Besides what has already been discussed, the following copy of an illustration given by Rogers (83) shows the age range:

In this connection Mellanby (67) state that the earlier the calcification takes place the better.

Calcification of the teeth are in general affected by the things that affect calcium and phosphorus metabolism in any way (discussed in Chapter IV). There are, however, a few factors that especially affect dentition. One of the most important of these is artificial feeding of infants. Moore (78) reports a group of figures from a dentist (confirmed by another dentists' findings) as follows: There were 78 patients from 3 to 10 years of age; of these 78 only 4 had been breast fed. Moore attributes part of the advantage of breast-fed babies over the artificially fed group to the fact that the process of breast-feeding is a better suckling mechanism and gives more strength. Lewis (61) reported a study by Hallman of 554 children,

100. Watt, J. C. - CDA 4 (6): 685; 1930
90. Sherman, H. C. - Chemistry of Foods and Nutrition
50. Howe, P. R. - Journal Am. Dental Assn. 15 (9): 1928
67. Mellanby, M. - British Dental Jr. 1928
78. Moore, C. U. - Nutrition of Mother and Child - 1924
80% were at least mostly bottle fed, and there was but 3% normal occlusion. Rogers (85) reports that in a group of Seattle children from 2 to 7 years of age, those who had been fed sweetened condensed milk the first month had twice as many caries as those who had been fed mother's milk or modified cow's milk. Howe (50) states that artificial feeding of infants is a cause for malocclusion. These writers, especially Moore, are most emphatic in urging mother's milk. Mellenby (67) stresses abundant calcium during pregnancy and lactation, stating that a deficiency is shown in offspring by:

1. small interglobular spaces in dentine.
2. defectively calcified enamel.

Although most experimenters give vitamin C credit for assisting dentition, Mellenby (67) says there is an evidence that either B or C affect dentition. Howe (50) states that a deficiency of the antiscorbutic vitamin (commonly called C) causes the body to cease forming intercellular material. Thus in the teeth there is a cessation of the formation of dentine, and pulp shrinks away from the already formed dentine. Howe further advocates breast-feeding because of the abundance of vitamin C of human milk.

Vitamin A is shown by Howe (50) to affect teeth in a peculiar way. He states that a deficiency of this vitamin causes the osteoblasts to lay down bone instead of dentine. This, he says, indicates that the osteoblast is merely a special type of bone cell called odontoblasts. Mellenby (67) found that puppies with a deficiency of vitamin A had irregular arrangements of teeth, delayed and retarded eruption of permanent teeth, and thick, poorly calcified jaw bones.

87. Mellenby, M. – Brit. Dental Jr. 1928
76. Moore, C. U. – Nutrition of Mother and Child – 1924
Vitamin D of course affects teeth as it affects bone and will as such be discussed later. However, one or two points are of interest at this point. Mellenby (67) says that vitamin D enables ameloblasts and odontoblasts to make use of the circulating calcium and phosphorus and other salts and to incorporate them in developing enamel and dentine.

Mellenby and Pattison (68) have done an interesting and accepted experiment on the effect of a substance which seems to hinder calcification. This substance is found in cereals, especially oatmeal. Their experiment was on children, 6 to 12 years of age, having bone Tuberculosis and extensive caries. They were divided into three groups as follows:

A. Large amount of calcifying vitamin
B. Some calcifying vitamin, moderate amount of oatmeal
C. Intermediate in calcifying influence between A and B, no oatmeal.

Table III
Results of the Mellenby and Pattison Experiment

<table>
<thead>
<tr>
<th>Diet</th>
<th>No. of Children</th>
<th>Time in Weeks</th>
<th>Caries at beginning of Exp.</th>
<th>No. Teeth per child with new caries</th>
<th>No. Teeth per child &quot;in which spread old caries&quot;</th>
<th>Total No. teeth per child &quot;in which extended caries&quot;</th>
<th>Increased &quot;de-&quot;ing of carious areas per child</th>
<th>Hardening of carious areas per child</th>
<th>Softening of carious areas per child</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>23</td>
<td>28</td>
<td>9.50</td>
<td>0.47</td>
<td>1.31</td>
<td>1.77</td>
<td>2.05</td>
<td>2.00</td>
<td>1.54</td>
</tr>
<tr>
<td>B</td>
<td>24</td>
<td>25</td>
<td>5.55</td>
<td>2.38</td>
<td>5.38</td>
<td>5.78</td>
<td>6.66</td>
<td>0.04</td>
<td>1.54</td>
</tr>
<tr>
<td>C</td>
<td>24</td>
<td>28</td>
<td>8.75</td>
<td>0.63</td>
<td>2.40</td>
<td>3.05</td>
<td>4.05</td>
<td>1.17</td>
<td>1.12</td>
</tr>
</tbody>
</table>

Note: There seems to be a slight discrepancy in some of the figures in this table. The direction of results was not, however, affected.

Although in diet B, there was less time and fewer caries to start, this diet had the most new caries, spread of old, extended caries, degree of caries, softening of carious areas, and the least hardening of carious areas.

Hair

There seems to be little direct reference to the function of calcium in growth of hair. Since the various endocrine glands influence calcium and phosphorus it may be interesting to note the following influences of glands upon growth and distribution of hair.

According to Cooper (26) "reduced parathyroid activity is associated with scanty growth of hair". Reduced pituitary activity, according to the same writer, is usually associated with loss of hair everywhere except scalp, while hyperpituitism brings increased thickness as well as an increased area of distribution of hair.

Brown (24) states that in rabbits light in the environment affects the proliferative activity of hair follicles.

Blood Coagulation

Bogert (15), Van Slyke and Peters (106), Starling (95), Bronson (25), Cantarow (25), and Sanford (87) all give some attention, in their discussion of calcium metabolism, to its function in normal blood coagulation. Van Slyke and Peters bring out the fact that this does not refer to hemophilia, which is due to factors other than calcium.

There seems to be some discussion as to what part of the coagulation process calcium is associated with Cantarow (25) states that, according to Howell and Morawitz, Fuld, and Spiegs, "probably the action of calcium is exerted with that of thrombodinase upon the activation of prothrombin". Kausawa (106) thinks it is also necessary "for the subsequent change of fibrinogen to fibrin". Van Slyke and Peters themselves (106) say that calcium is necessary for the formation of the fibrin clot in shed blood.

15, Bogert, L. J. - Nutrition and Physical Fitness
106, Van Slyke and Peters - Quantitative Clinical Analysis
95, Starling, E. H. - Human Physiology - 1930
25, Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
87, Sanford, H. N. - CDA 6(4): 338; 1932
25, Bronson, B. S. - Nutrition and Food Chemistry - 1930
Bogert (15) suggests that the calcium is combined with fibrinogen as it functions in coagulation. Starling (35) states that the calcium must be in the ionic state to be of value in coagulation.

Bogert (15) indicates that the calcium value for serum is higher in infants' blood than in their mothers'. This is explained by the fact that there is less fibrinogen in infants' blood and therefore less calcium combined with it, so more calcium remains in serum. The calcium value for whole blood is the same for infants' as for the mothers'.

Cantarow (25) and Starling (35) state that calcium can be replaced, though less efficiently, in the blood clotting function by strontium, magnesium, or barium. Starling further indicates that although strontium can take the place of calcium in clotting, magnesium and barium cannot take the place of calcium in starting a clot.

Van Slyke and Peters (106) state that "oral administration of calcium has no effect on the coagulation time." Sanford, (67) states that "short exposure of new born infants to ultra-violet light has no effect on the coagulation time although it increases the bleeding time and can thus be used as a therapeutic measure for infants with delayed bleeding time."

Cell Processes

McLester (65) states that "every element which finds a place in the structure of the cell is essential to life". McLester thinks minerals are a part of the cell structure, but advances the two theories as follows:

1. (favored) Everything going into the cell becomes an integral part of it and as such is concerned in energy exchange.

2. The cell is an unchanging structure and other substances coming in are dissolved or suspended in the mesh between.
Starling (25) says that Ca is built up into organic compounds in plants only as salts of proteins and thus they enter into the physical chemistry of cell protoplasm. They are then taken up by the animal as salts and executed as such.

Cantarow (25) states that calcium in affecting the colloid of the cell membrane itself, inhibits cell permeability, while sodium fosters it.

Cantarow also tells of the Ringer experiments in which the latter found that normal cell function and heart action are both dependent upon the presence of certain electrolytes, especially calcium, sodium, and potassium in balanced proportions. Bronson (25) states that "mineral salts are essential to the proper functioning of the cell". He calls it a "peculiar and essential role".

Zondek (8) thinks that the nerves control the distribution of ions within the cells and cell membranes.

Nerve and Muscle Action

That calcium is essential to nerve irritability and to passage of nerve impulses seems unquestioned, but the manner of affecting these actions seems somewhat obscure. Cantarow (25) says that calcium is probably associated with the autonomic nerves and sympathetic activity. Van Slyke and Peters (106) state that "calcium has a peculiar influence on the excitability of the motor system". Bogert (13) mentions the function of calcium in the irritability of nerves. Hooker (25) states that "calcium increases vascular tone". Locke (25) attributes to calcium a role in nerve impulses. Overton (25) goes a bit further and states that calcium is necessary for the transmission of the excitatory process across the synapses. Cantarow (25) finds information to the

65. McLeester, J. S. - Nutrition and Diet in Health and Disease - 1951
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1951
25. Bronson, E. S. - Nutrition and Food Chemistry - 1950
90. Sherman, H. C. - Chemistry of Foods and Nutrition - 1932
effect that calcium is necessary also for the passage of nerve impulses from
the nerves to muscles across the myoneural junctions. McLester (65) states
that calcium is necessary for nerve conductivity. Berg, Hess, and Sherman (8)
found (by sectioning the sympathetic and vagus nerves) that there is a re-
ciprocal between nerves and the inorganic salts of the body. They also quote
Zondek, and Zondek and Kraus. The latter experimenters state that "nerves
exert their special function by means of various ions. The sympathetic sys-
tem has an activity similar to calcium or to an artificial excess of cal-
cium." The former shows that "the stimulation of vagus nerves results in a
preponderance of potassium in the blood stream, whereas the stimulation of
sympathetic nerves results in a preponderance of calcium".

Bogert (15), Cantarow (25), Sherman (90), Starling (95), Bronson (28),
McLester (65) and Haury (43) give some consideration to the function of cal-
cium in muscle contractability. Haury states that normal muscle contains
74.0 milligrams of calcium per 100 grams of dry muscle, and further states
that this amount is 50% above the rachitic level of 41.6 grams. Sherman (90)
states the muscle contains more Mg than Ca, whereas blood contains more
calium than magnesium. Cantarow states that "the antagonistic effect of

\[
\text{Na vs. K increases muscle irritability} \\
\text{Ca vs. Mg decreases muscle irritability.}
\]

Starling reports an experiment in which a frog's leg contracted in a solu-
tion containing 0.5% NaCl, 0.2% Na$_2$HPO$_4$, 0.04% Na$_2$CO$_3$, and distilled water.
Tap water, containing slight traces of calcium neutralized the contraction.
Starling goes on to say that probably molecular changes are associated with
excitation. Howell, quoted by Bronson, "the ions of calcium salts, when in
quantities above normal, or when in a proportional excess over the sodium
and potassium ion, they cause a condition of tonic contraction that has been

95. Starling, E. H. - Human Physiology - 1930
106. Van Slyke and Peters - Quantitative Clinical Analysis -
15. Bogert, L. J. - Nutrition and Physical Fitness
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
25. Bronson, B. S. - Nutrition and Food Calcium - 1950
designated as calcium rigor. McLester states the calcium is probably involved in the energy exchange of muscle contractibility. Cantarow says that calcium is necessary in cardiac, skeletal, and striated muscle.

The function of calcium in heart action besides being mentioned by Cantarow is also spoken of by Sherman (90) and Bronson (25). Both of these latter state that rhythmic heart beat is due to the balance between calcium and sodium or potassium.

Iron-Sparing Action of Calcium on the Intestines

Van Slyke and Peters (106), Sherman (90), Bronson (24), McLester (85), mention the iron-sparing action of calcium in the intestine, giving proof for their statements, but none of the references studied or searched for seem to explain this action. The most clear-cut evidence is an experiment by Von Wendt, quoted by Sherman, in which the iron requirements ranged from .008 to .016 grams / day, the largest amount being required in a case of calcium deficiencies; figures for the experiment are as follows:

<table>
<thead>
<tr>
<th>Diet</th>
<th>Amount in Food</th>
<th>In Feces</th>
<th>In Urine</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron (Bread and Milk)</td>
<td>.0057</td>
<td>.0053</td>
<td>.0002</td>
<td>+.0002</td>
</tr>
<tr>
<td>(Bread and Egg)</td>
<td>.0085</td>
<td>.00852</td>
<td>0.002</td>
<td>--.0022</td>
</tr>
<tr>
<td>Calcium (Bread and Milk)</td>
<td>1.69</td>
<td>1.34</td>
<td>.15</td>
<td>+.10</td>
</tr>
<tr>
<td>(Bread and Egg)</td>
<td>.10</td>
<td>.34</td>
<td>.07</td>
<td>--.61</td>
</tr>
</tbody>
</table>

He states that the results may not be due alone to the calcium, but to —

1. The superior nutritive value of the iron compounds found in milk.
2. General conditions of digestion and nutrition, which are better when milk is included in the diet.

Bronson reports a similar experiment in which several diets resulted in

49. Haury, V. G. - JBC 89:467; 1930
65. McLester, J. S. - Nutrition and Diet in Health and Disease - 1951
106. Van Slyke and Peters - Quantitative Clinical Analysis, 1951
90. Sherman, J. S. - Nutrition and Food Chemistry, 1952
positive iron balance and several in negative iron balance. Bronson states that "calcium was also deficient in the latter experiments, and the fact that the iron balance was negative here seems to depend quite as much on the low intake of calcium as upon the low intake of iron. The metabolism of iron appears therefore to be bound up rather closely with that of calcium".

McLester speaks of the phenomena as the synergistic effect of calcium and iron. He quotes from Meltzerander: "With an abundant intake of calcium the organism can maintain equilibrium on an appreciably smaller supply of iron." McLester goes on to say that "the beneficial influence is manifold". Van Slyke and Peters give statements that are more elusive, but nevertheless definitely point to the act that a relationship exists between Ca and Fe. They state that the admission of enough parathyroid extract to produce a high degree of hypercalcification causes an increase of water withdrawal from the blood and a higher concentration of red blood cells and hemoglobin.

**Miscellaneous functions of Calcium**

Two experimenters show evidence that points to a relationship between calcium and phosphorus metabolism and allergic disorders. Sterling (36) states that "the mineral deficiency in asthma, hay fever, and allied diseases may be the missing link which makes the allergic differ from the normal". He thinks the addition of Ca, P, Fe, Hc, and K is a possible cause of the favorable results obtained in the experiment, and that these results are true whether sensitivity can be proved or not. Van Slyke and Peters show that there is a moderate hypocalcemia in hay fever, asthma, and hyperesthetic rhinitis, and that this hypocalcemia is favorably affected.

106. Van Slyke and Peters - Quantitative Clinical Analysis - 1931
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy - 1931
by ultra violet light though not by calcium administration alone.

Cantarow (25) shows that inorganic elements are important in the water balance, and states that "the effect of calcium is probably exerted upon

1. the permeability of the capillaries
2. the hydration capacity of the colloids."

Cantarow indicates two other functions of calcium as follows:

"Calcium facilitates the process of activation of certain enzymes (as trypsinogenase)."

"Calcium is important in the physiological response to certain drugs."

25. Cantarow, A. — Calcium Metabolism and Calcium Therapy — 1931
Chapter III

Functions of Phosphorus in Normal Nutrition

Note: It is impossible to separate the discussion of calcium and phosphorus entirely, therefore much of the work on phosphorus has been taken up in the preceding chapter, and this one presents just such phases of phosphorus metabolism as are rather distinct and separate from calcium.

Skeletal Formation and Growth

The function of phosphorus in skeletal formation and growth has been amply discussed in connection with the function of calcium in bones, teeth, and hair in Chapter II, except for the percent of the total body phosphorus that is found in the skeleton.

MoLester (65) states that "phosphorus is the most widely distributed of any inorganic material in the body." Phosphorus composes about 1% of the entire weight of the body, (23) (90). Hammett (39) shows that while calcium increases with age, phosphorus decreases with age. He also found the percent of phosphorus in the ash of the body to be greater in males than in females. The figures for the percent of this amount that is in the skeleton varies from 66 2/5 % to 90% (13). The figures given by Sherman (90) and Van Slyke and Peters (106) are as follows:

<table>
<thead>
<tr>
<th>(Adults)</th>
<th>Sherman</th>
<th>Van Slyke and Peters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeleton</td>
<td>600 grams</td>
<td>600 grams</td>
</tr>
<tr>
<td>Muscle</td>
<td>50 &quot;</td>
<td>57 &quot;</td>
</tr>
<tr>
<td>Brain</td>
<td>5 &quot;</td>
<td>5 &quot;</td>
</tr>
<tr>
<td>Blood</td>
<td>2 &quot;</td>
<td></td>
</tr>
</tbody>
</table>

106. Van Slyke and Peters - Quantitative Clinical Analysis, 1951
15. Bogert, J. - Nutrition and Physical Fitness
90. Sherman, F. S. - Chemistry of Foods and Nutrition
39. Hammett, F. S. - JBC 64:695; 1925
23. Bronson, E. S. - Nutrition and Food Chemistry - 1930
Of the total phosphorus in bones, 84% is found to be the tertiary calcium phosphate, \( \text{Ca}_3(\text{PO}_4)_2 \), and 12% is found to be tertiary magnesium phosphate, \( \text{Mg}_3(\text{PO}_4)_2 \), according to Bronson (25). Henderson and Weakley (42) found from an experiment on calves that the food must contain 0.2% of phosphorus or the bones are low in ash and high in moisture and extractable material. The amount of phosphorus needed for fetal growth is shown by Hoffstrom and by Michel (quoted by Lusk (64)) as follows:

1. Hoffstrom found that at the 16th week of pregnancy the fetus contained 0.67 grams of phosphorus and that during the last 25 weeks there was the following retention:

   total ----- 55.83 grams
   for mother -- 54.00 "
   for fetus -- 1.83 "

2. Michel's figures are as follows:

<table>
<thead>
<tr>
<th>Week</th>
<th>( P_4 ) content of Ovum</th>
<th>Added per week</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>0.67</td>
<td>0.20</td>
</tr>
<tr>
<td>20</td>
<td>1.47</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>2.58</td>
<td>0.25</td>
</tr>
<tr>
<td>28</td>
<td>3.58</td>
<td>1.28</td>
</tr>
<tr>
<td>29</td>
<td>4.58</td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>13.93</td>
<td>1.28</td>
</tr>
</tbody>
</table>

Since supersaturation of blood with phosphorus is necessary for normal bone formation, the investigator thinks a discussion of blood content is not amiss at this point. It seems evident from all contributions on the subject that the blood of children contains 2 to 3 times as much phosphorus as the blood of adults. Briggs (22) and Tolstoi (105) state that normal adult blood contains 2.5 to 3.5 mgms. phosphorus 100 cc of blood. Tolstoi quotes Hess and Gutman as giving 4 mgms./100 cc as normal for infants' blood, and Von Heysenburg as giving 5 mgms./100 cc. for the same.

25. Bronson, B. S. - Nutrition and Food Chemistry
42. Henderson and Weakley - W. Va. Agric. Exp. Sta. Blt. 231; 56; 1930
64. Lusk, G. - The Science of Nutrition - 1923
22. Briggs, S. P. - JBC 57; 351; 1923
105. Tolstoi, E - JBC 55; 157; 1923
Van Slyke and Peters (106) give the phosphorus content of infants' blood as 2 - 5 mgm./100 cc as compared to 4 - 7 in adults' blood. These figures according to Van Slyke and Peters, represent the inorganic portion. They give the total phosphorus content of blood as follows:

<table>
<thead>
<tr>
<th></th>
<th>Cells</th>
<th>Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>47-114</td>
<td>5-18</td>
</tr>
<tr>
<td>Infants</td>
<td>49-90</td>
<td>5-14</td>
</tr>
</tbody>
</table>

Fedoroo (51) makes the subject a bit more clear by stating that "the total phosphorus content of the blood of adults and children is about the same", but that "the difference comes in the proportion". He thinks there is relationship between the inorganic phosphorus of blood and the intensity of oxidative processes, both of which are greater in children than adults. He finds no sex differences in his study of children from 7 to 15 years of age. His figures are as follows:

- Inorganic phosphorus in blood of young children ——— 4.2 - 5.2 mg/100 cc
- Inorganic phosphorus in blood of boys and girls ——— 5.87 mg/100 cc
- Organic Phosphorus in blood of boys and girls ——— 6.02 mg/100 cc
- Total Organic Phosphorus and Inorganic Phosphorus in children — 10.00 mg/100 cc

**Cell Processes**

Nucleic acids and nucleoproteids, of which phosphorus is a constituent, are found according to all writers on the subject, in all cells of the body. Van Slyke and Peters (106) give typical formula for a nucleic acid as 4 hexose radicles linked with 4 phosphoric acid groups, as found in the thymus gland. Starling (95) gives the structure and degradation of typical nucleic acids as follows:

4 mononucleotides which 4 mononucleotides are linked together as follows:

106. Van Slyke and Peters - Quantitative Clinical Analysis
51. Fedoroo - CDA 5(4): 514; 1951
95. Starling, E. H. - Human Physiology - 1930
Phosphoric acid → Hexose → Guanine

Phosphoric acid → Hexose → Cytosine

Phosphoric acid–Hexose → Thymine

Phosphorus acid – Hexose → Adenine

Degradation of Nucleoproteins:

Nucleoprotein

Nuclein and protein

Nucleic acid and protein

4 mononucleotides

4 nucleosides → 4 phosphoric acid

The following functions are given by various experimenters for the nucleic acids or nucleoproteins:

Van Slyke and Peters (106) components of cells and glands of body; food for the growing embryo (eggs, milk). In the latter connection he says they may or may not be present in the adult body.

Starling (95): important in cell nuclei and especially spermatogon 

Bronson (25): cell structure; egg and milk formation

106. Van Slyke and Peters – Quantitative Clinical Analysis
95. Starling, E. H. – Human Physiology – 1930
Forbes and Keith (33) reviewing literature, quote:

Kossel: great importance in the heart and activity of every cell.

Gustav Mann in 1906: probably the agencies by which amino acids are built up into cell plasm.

Herlitzka and Borrino in 1902 and 2: catalytic actions (affected by (nucleohistones of cell nuclei)
(nucleoprotein of cell cytoplasm)

Several experimenters in the 1930's: fibrin ferment and blood coagulation action (by nucleoproteins and nucleohistones of blood and of muscles)

Several experimenters in 1912 and 1915: anti-coagulating effects. Doyan and Servonat in 1915 decided that orthophosphates do not have this power but that meta and pyro-phosphates do.

Organic phosphates also act as non-diffusible anions in the cells and as such are buffers (106). Each organic phosphate has at least one free hydrogen ion for combination with the alkaline salts of cells. Nucleic acids have the power of combining with 4 equilibriums of alkalie each. There is 110 millimols of organic phosphates per kilo of cell water, and it is capable of binding over half the total base found in cells. The organic phosphates are said (106) to find more alkalie than Cl does and possibly more than proteins do. Phosphocreatine, discussed under intermediary metabolism, has the power of combining with 2 molecules of base, and is also a buffer against lactic acid.

Phosphatides are another type very important in cell processes, but will be more fully discussed under intermediary metabolism. Starling (95) gives special attention to the importance of lecithin in the peculiar permeability, the osmotic relations, and the surface conditions of cells.

33. Forbes and Keith - Ohio Exp. Sta. Tech. Bt., No. 5 - 1914
106. Van Slyke and Peters - Quantitative Clinical Analysis
95. Starling, E. H. - Human Physiology - 1920
Intermediate Metabolism

Phosphorus plays a very important part in muscle metabolism. Late in 1930, Dr. A. V. Hill (48) and his associates discovered, after much study, that the breakdown of phosphagen (creatine-phosphoric acid) supplies the heat for muscle activity, and that the formation of lactic acid from glucose supplies the heat for the resynthesis of phosphagen. Van Slyke and Peters (106) give the following equation for the breakdown of creatin-phosphoric acid:

\[
\begin{align*}
\text{HN} & \equiv \text{NH}_2\text{PO}(-\text{OH})_2 \\
\text{HN} & = \text{N} \quad \text{CH}_2\text{CH}_2\text{COOH} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O} \\
\text{HN} & = \text{O}
\end{align*}
\]

This combination of reactions prevents, according to Van Slyke and Peters, an extreme change in the acidity of the internal environment of the muscle cell. One molecule of phosphoric-creatine is capable of nullifying the acidifying effects of the liberation of 0.88 molecules of lactic acid.

Muscle, according to Sterling (95) contains as 1 to 1.5% of its ash, K, HgPO₄, and traces of Ca and Mg. "Most or all of the HgPO₄ is in organic combination as phosphagen, hexose-phosphates, lecithin, and there are possibly pyrophosphates present." The action of the salts has been discussed under the effect of calcium in muscle metabolism. Bronson (23) confirms the abundance of di-K-phosphate in muscle, but states that "phosphorus probably is not a part of the striped muscle of internal organs." Lusk (64)

48. Hill, A. V. - Physiol. Rev. 5:225; 1932
106. Van Slyke and Peters - Quantitative Clinical Analysis
95. Sterling, E. H. - Human Physiology - 1930
23. Bronson, E. S. - Nutrition and Food Chemistry
64. Lusk, G. - The Science of Nutrition
finds that there is 0.075 g/2a. % of Ca and 4.88 g/2a. % of P2O5 in fresh muscles (suicidal human case).

** The role of phosphorus in carbohydrate metabolism is mentioned by McLester (65) who says that "the starch molecule is said to contain small amounts of phosphorus," and by Bollinger and Hartman (19) who says that "glucose is better utilized in the presence of excess phosphates, and "vice versa", but the investigator finds that Van Slyke and Peters (106) have the most comprehensive discussion of it. They find that there are combinations of glycerin and H2PO4 and of hexoses and H3PO in the process of carbohydrate metabolism. They have found experimental evidence of the occurence, simultaneously of reducing substances or lactic acid (or both) and inorganic phosphates following the breakdown of the acid-soluble organic phosphates of blood. This has been found to be a reciprocal reaction. Proof of the latter is found in an experiment by Irving and Bastedo (quoted by Van Slyke and Peters) who demonstrated that the amount of organic phosphate that was broken down to inorganic phosphorus during muscular exercise was too great to have come entirely from phospho-creatine. Other evidence given is that when glucose is rapidly removed from the blood, the inorganic phosphate content of blood and excretion is decreased. The hexose-phosphates have not yet been isolated and therefore their nature and function is quite obscure. It is thought (106) that there may be the following:

Hexose diphosphate C6H10O4(P04H2)2
Hexose monophosphate (C6H10O5P04H2)
Glycerophosphates

65. McLester — Nutrition and Diet in Health and Disease
106. Van Slyke and Peters — Quantitative Clinical Analysis
Forbes (32) in an experiment on pigs, found that animals receiving glycerophosphates showed the best bones, flesh, muscle, brains, and gain in weight. Van Slyke and Peters (106) conclude that hexose-phosphate is necessary for:

1. the intermediary product in anaerobic decomposition and aerobic restoration of glycogen (as discussed under creatin-phosphoric acid).
2. maintenance of the normal reaction of blood. Embden, quoted in (106) concludes that the inorganic phosphate of the blood is involved in the process by means of which sugar is removed from the blood, probably because the phosphate combines with glucose.

Van Slyke and Peters (106) give three classes of fats as belonging to the phosphatide (or phospholipid) group. They are as follows:

1. Sphingomyelin, important in brain and nerve tissue, will be discussed later.

\[
\begin{align*}
\text{H} & \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \text{H} \\
\text{H} & \quad \text{C} & \quad \text{C} & \quad \text{O} & \quad \text{P} & \quad \text{O} & \quad \text{C} & \quad \text{H} & \quad \text{N} & \quad (\text{CH}_2)
\end{align*}
\]

\text{sphingosin} \\
\text{choline}

2. Cephalin, which is important in blood coagulation as well as in cell processes:

\[
\begin{align*}
\text{H} & \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \text{H} \\
\text{H} & \quad \text{C} & \quad \text{C} & \quad \text{O} & \quad \text{P} & \quad \text{O} & \quad \text{C} & \quad \text{C} & \quad \text{NH}_2 \\
\text{O} & \quad \text{O} & \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \text{H} \\
\text{R}_1 & \quad \text{R}_2
\end{align*}
\]

amino-ethanol
(a base replaces its methylated derivative choline.)

3. Lecithin

\[
\begin{align*}
\text{H} & \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \text{H} \\
\text{H} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{O} & \quad \text{P} & \quad \text{O} & \quad \text{C} & \quad \text{C} & \quad \text{N} & \quad (\text{CH}_2)_3 \\
\text{O} & \quad \text{R}_1 & \quad \text{R}_2 & \quad \text{H} & \quad \text{O} & \quad \text{H} & \quad \text{OH}
\end{align*}
\]

fatty acids 1 saturated choline
1 unsaturated
Starling (95) comments on the universal distribution of lecithin, and says this indicates its importance in cellular activity and in the transportation of fat. This latter function is probably due to the fact that it has the capacity of colloidal solubility in water. Bronson (25) states that this phosphorized fat is present in all cells. He also states that there are probably many complex forms of phospholipids whose nature we do not yet know.

Nerve and Brain Tissue

Several different compounds have been thought components of brain and nerve tissue. Starling (95) thinks a glycolipide, more stable to oxygen than lecithin, is the phosphorus compound found in brain tissue. Van Slyke and Peters (106) name sphingomyelin as the main constituent of brain and nerve tissue. Bronson (25) says the compound found is "a phospholipin of the lecithin type". The metabolism of nerve and brain tissue is active (they need oxygenated blood and sugar) and the lecithin type of fatty acids contains an unsaturated group and is therefore also reactive and suited to the needs of an active tissue. Sugar, oxygenated blood and phospholipins are all necessary to consciousness. An increase in the content of these foods does not increase mentality, though a certain amount is necessary for optimum activity.

Blood Buffers

Starling (95) gives to phosphates the importance of a place equal to the CO2 system of buffering. He states that "acidity is determined by the ratio $\frac{NaH_2PO_4}{Na_2HPO_4}$", and that neutrality is affected when the ratio is 1:2.5.

95. Starling, E. H. - Human Physiology
106. Van Slyke and Peters - Quantitative Clinical Analysis
25. Bronson, B.D. - Nutrition and Food Chemistry
Van Slyke and Peters (106) rather contradict the importance of the PO₄ system by quoting from Henderson that although the inorganic phosphates may act as excellent buffers they are in such small quantities that they have little effect in comparison to the carbonates. Van Slyke and Peters state that "for every molecule of phosphate that is changed from an alkaline to an acid salt in excretion, one equivalent of base is conserved (as HCO₃) for the organism". The process by means of which this happens is still a question but two possibilities are named:

1. Selective (excretion of B₃H₂PO₄)
   (retention of B₃H₂PO₄)
2. Either during or after secretion into the kidneys the following reaction takes place:
   \[ \text{Na}_2\text{HPO}_4 \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{NaH}_2\text{PO}_4 \rightarrow \text{NaHCO}_3 \]
   The latter product is retained or reabsorbed by the blood.

**Miscellaneous Functions of Phosphorus**

Van Slyke and Peters state that cephalin is essential for the formation of the thrombin of blood coagulation.

McLester (64) states that phosphorus is an essential to other body fluids as well as to blood.

McLester also says that phosphorus like calcium aids in the work of the glands, as sex and milk glands.

106. Van Slyke and Peters - Quantitative Clinical Analysis
64. McLester, - Nutrition and Diet in Health and Disease
Chapter IV
Factors Affecting the Calcium-Phosphorus Equilibrium

Percent of Possible Sunlight

There are several conditions which affect the percent of possible sunlight. These are well described by Hess (44) in his discussion of the incidence of rickets. He reports that in London, rickets is twice as prevalent as in New York, due to differences in the amount of time the sun shines in the two places. However, he and Frawley (34) both find that the latitude seems to make no difference. (Hess reports the difference between New Orleans and New York; Frawley, the different parts of California.) Frawley claims that local climatic conditions affect the percent of ultra violet rays in the visible light rays and heat in sunshine. He considers it "inadvantageous in extremely hot climates to depend on" sun baths "for prevention and treatment of rickets". Thus, although Mellanby (67) thought tropical groups were relatively free from dental caries, because of the sunlight, she also says that the Eskimos were relatively free because of a diet rich in fish and meat having a large amount of Vitamin D carrying fat. Thus, the consensus of opinion seems to be that distance from the equator has little effect.

In reporting the effect of winter sunshine, Lewis et al. (62) state that there is no marked effect in the antirachitic effect of winter and summer sunshine. They attribute this similarity to:

1. the high percentage of winter sunshine
2. the low humidity
3. the small amount of smoke in the atmosphere

44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
34. Frawley, J. M. - A.J.D.C. 41:751; 1931
62. Lewis et al. - A. J. D. C. 41:71; 1931
Wilder (110) and Wyman et al. (112) indicate rather different thoughts about winter sunshine in Boston (which is of approximately the same latitude though different altitude as Utah.) Wilder says there is some curative effect in the sunlight late in February, with a marked increase in March. Wyman et al, on the other hand, concluded that infants could be cured of rickets by exposure to sunlight from November to March, though they became tanned more quickly after March 1st. The writers found a deposition of calcium immediately following exposure after the first two weeks.

Although Fedorov (51) found no seasonal tide of phosphates, Bronson (25) states that there are seasonal variations, with the tide from June to August and the ebb from January to March.

Hess (44) reports studies on Denver, Colorado and Ogden, Utah. In Denver, Forbes and Green (quoted by Hess) found about one-third of the children with rickets, and in Ogden, Smith found about 13% of the children affected. Both investigators attribute the comparative freedom from rickets to the altitude.

In discussing the purity of the atmosphere (from smoke), Hess states that "besides the actual hours of sunlight, certain important qualifying factors must be considered. The most important of these is the degree of congestion of the population. *** Industrialism plays an important role in the distribution of rickets." Bronson speaks of the purity of the atmosphere from clouds, fog, and smoke as very important. She also mentions skyshine as a reflector.

110. Wilder and Vark - CDA 6 1932
112. Wyman et al - CDA 6 1932
44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
51. Fedorov, P. - CDA 5 (4): 514; 1951
25. Bronson, B. S. - Nutrition and Food Chemistry - 1931
A study of rickets in the Alps by Fee is reported in the same reference (44). The investigator finds that rickets occur in the same degree in spite of the fact that the drinking water of mountainous districts is rich in lime. He suggests that it may be due to the precipitation of phosphates in the intestines caused by an excess of calcium. It is not ascertained in his study whether tetany occurs less frequently.

Use of Ultra-Violet Light

That calcium and phosphorus metabolism is aided by ultra-violet light is an undisputed fact. The role of ultra-violet light may be spoken of differently by several investigators although there seems to be no special contradiction. Increased absorption of calcium and phosphorus is reported by Hess (44) and Orr et al (quoted by Lusk (64)) whose figures are as follows:

- before irradiation: negative balance of 0.1 gm. Ca, 0.01 gm. P
- after irradiation: positive balance of 2.31 gm. Ca, 1.73 gm. P

This latter figure represents a retention of 50%. Hess (44) reports also a change in the path of excretion from feces to urine. Howland and Kramer (quoted by Lusk (64)) found an increase of the inorganic phosphorus in serum while Cantarow (25) quotes Clark as finding an increase in the percent of diffusible calcium following irradiation. Sanford (87) found that short exposure of new born infants could be used as a therapeutic measure to increase the bleeding time, though it did not affect coagulation.

Hess says that ultra-violet light activates the ergosterol near the skin and sets it into circulation. Jones (55) states that the excess

44. Hess, A. P. - Rickets, Osteomalacia, and Tetany - 1929
45. Orr et al 64. Lusk G. - The Science of Nutrition
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy
87. Sanford, H. N. - CDA 6(4): 333; 1932
55. Jones, H. J. - JBO 89: 647; 1930
calcium caused by irradiated ergosterol comes from food and not from body tissues. McLeaster (65) says that the increased retention of calcium and phosphorus after injection of irradiated ergosterol may be brought about by increased absorption making it more easily accessible to circulating blood or some other improvement of metabolism.

The manner of irradiation is divided into two types, food and individual. The individual may be irradiated by artificial ultra-violet lamp (quoted from Hess and Unger (64)), exposure to sun (64) which is more effective if there is "skysline" as a reflector (82) and by irradiation of a nursing woman so that her milk will have antirachitic value.

Foods that can be effectively irradiated are:

1. Cholesterol (64) (ergosterol portion)

McLeaster (65) showed that a maximum potency (250 times the value of cod liver oil) is obtained with 15 minutes of irradiation, $\frac{1}{20,000}$ mgm. or less is the daily dose to cure rickets. The advantages of irradiated ergosterol are that it is reliable and acts rapidly. The disadvantage is that enormous amounts cause calcification of tissues other than bone, as blood vessels.

2. Cottonseed oil)
   Linseed oil) effective if irradiated (64)
3. Wheat (64)
4. Milk (64) and (1)

Vitamins (Luak (64) suggests "food hormone" as a better name)

Park (quoted by Roberts (31)) says "If pregnant women received ample well balanced diet in which green vegetables were abundantly supplied and cow's milk was taken regularly, and kept a sufficient part of their time in the open air and sun, and if their infants were placed in the direct rays
of the sun for a part of each day and were fed cod liver oil for the first two or three years of life, more could be accomplished in regard to the irradiation of caries of the teeth than all other ways put together, and rickets would be abolished from the earth." Park later states that Vitamin D has a stimulating and regulating effect on calcification. Roberts says that "artificially fed babies, especially, need cod liver oil or sunlight early and continuously."

What cod liver oil does for the body is summarized following:

1. Return of the normal excess in the % of phosphorus in the urine over that in feces (Sjollema (93) Hess (44).

2. Decreased total phosphorus excretion (44)

3. Improved calcium balance (44)

4. Increased absorption of phosphorus from intestines Van Slyke & Peters (106)

5. Decreased urinary calcium excretion (most important of all effects, according to Sjollema (95))

6. Increased creatine content of urine (due to added calcium) (95)

7. Decreased calcium in feces. Sjollema (95)

8. Decreased urinary phosphorus due to decreased total urine (95)

9. Increased diffusible fraction of serum Ca. Van Slyke and Peters

10. Increased solubility of calcium in serum Ca. Van Slyke and Peters

11. Prevents formation of soap stool. Hess (44)

12. Calcification favorably affected by direct action on bone and cartilage (questioned) Hess (44) Cantarow (25) Hume (51)


14. Increased calcium deposition. Lusk (64)

15. Increased inorganic phosphorus of serum. Quoted by Lusk (64)

44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1931
106. Van Slyke and Peters - Quantitative Clinical Analysis
93. Sjollema, B. - JBC 57: 255; 1922
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy
51. Hume and Smith - CDA 6:5: 205
64. Lusk, G. - The Science of Nutrition
Arthus and Jedrzejowska (2) found that vigantol, a concentrate of vitamin D, protected rabbits against parathyroid tetany and caused the decrease of blood calcium following parathyroidectomy to be much less.

Besides giving cod liver oil and vitamin D concentrates, egg yolk added to infants milk adds vitamin D (Hess and Matger, quoted by Lusk (64)). Park and Howland (also quoted by Lusk (84)) found that vitamin D administration shows favorable results as soon as from 2 to 3 weeks.

Bills (10) determined that vitamin D is destroyed readily by nitrous fumes, or slowly by heat or by mineral acids.

Sculling (86) and Bogert and Trail (15, 17) have done work on the effect of vitamin B upon calcium and phosphorus metabolism with varying results. Sculling concluded that vitamin B has no effect, but Bogert and Trail found that both yeast and butter fat favored the calcium and the phosphorus balances. In their experiment on vitamin B and calcium, (15) they conclude that the vitamin may either improve absorption or decrease excretion, and they suggest an influence upon calcium assimilation. In the other experiment (17) they say that "the effect of yeast and butter fat may be due to factors other than vitamins".

Vitamins A and C have been discussed under the functions of calcium in skeletal formation and growth.

Diet

In discussing diet as a means of getting a good start in calcium and

2. Arthus and Jedrzejowska - CDA 6(4); 239-1932
10. Bills, C. A. - JBC 64; 1; 1924
64. Lusk, G. - The Science of Nutrition
86. Schelling, V. - JBC 83; 575; 1930
15. Bogert and Trail - JBC 54; 837; 1922
17. Boldt et al - CDA 4 (5); 528; 1930
phosphorus metabolism, the greatest stress is placed on the superior value of breast milk over artificial. Moore (78) is one of the most emphatic writers on the subject and starts by stating "the mortality of artificially fed babies is 7 times that of breast fed".

Rominger and Meyer (34) found that artificially fed babies retained more Ca, but because there was not a corresponding retention of water, these writers conclude that the extra is in a biologically inactive form. Hess (44) states that about 70% of the Ca of human milk is retained, compared to 50% of cow's milk (acc. to Schabad, quoted by Hess).

A common disturbance noted in artificially fed babies is soap stool (70, 74) which results in a greater loss of Ca. Gelsner and Klinke (74) found that the insoluble soap stool could be changed to soluble by MgCO₃ or NaHCO₃.

The differences between cow's and woman's milk which affect calcium and phosphorus metabolism are found by different investigators to be as follows:

1. Human milk contains only a small amount of the antirachitic diet, so its greater value must come from other source (47, 44)

2. The value of human milk may be due to the favorable equilibrium of the different ions. (74)

3. Though phosphorus is 4 times as great in cow's as in human milk (46) Hess (44) finds it is not nearly as well retained.

4. There is a difference of from 7% lactose in human milk compared to 4% in cow's (47). The experimenters state that this lactose brings about an acid reaction in the intestinal tract which favors absorption of calcium. No other sugars added to make up the difference in amount, bring about this reaction.

5. Moore (70) states that since the amount of fat a child can have is limited, it should be of the right kind (found in human milk). If it is not, soap stool, causing loss of calcium results. Hess finds that woman's milk has the same fat content as cow's, but that 90-95% of the fat of human milk is absorbed.

78. Moore, C. U. - Nutrition of Mother and Child - 1924
34. Rominger and Meyer - CDA 4(2): 185; 1930
47. Hess and Weinstock - A.J.D.C 54: 845; 1927
46. Hess and Helman - JBC 64: 751; 1925
44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
All authors are agreed that the mother should be especially careful to supply herself with minerals and vitamins (see quotation at beginning of discussion on vitamins). Moore (70) further shows the importance of it as follows: "Any deficiency in the mineral and vitamin content of the mother's milk will result in the impaired development of the child such as can never be rectified even by an excess of these factors in later years."

There are several dietary factors which may affect the calcium and phosphorus metabolism of children after the nursing age. Details of the specific amounts of certain foods necessary or advised will be discussed in Chapter IV. However, relative amounts and kinds of certain food nutrients are best considered here.

High mineral content has been discussed by several experimenters, one of whom was Shohl (92). He studied the mineral content of the diet, feces, and urine of a group of children, then added twice the original amount of mineral and found that the children retained twice as much in the same proportions as before. Van Slyke and Peters (106) state that "in growing children increased absorption of Ca means increased retention." Boldt et al (13) fed infants high and low mineral as follows:

I. Human milk
II. Cow's milk, greater amount of Ca and P
III. Human milk.

The first period showed a greater percent of calcium and phosphorus retained, while the second period showed a greater total retention. In the last period the positive balance was less than the first but was thought to be still affected by period II. Henderson and Weakley (42) found that a group of pigs fed a diet with low mineral content grew as well for some time

70. Moore, C. U. - Nutrition of Mother and Child
106. Van Slyke and Peters - Quantitative Clinical Analysis
13. Bollinger and Hartman - JBC 64: 91; 1925
but not over a two-year period. The group receiving low phosphorus but sufficient calcium grew as well over the two-year period.

High phosphorus without correspondingly high calcium seems to have a deleterious effect on absorption (due to the formation of insoluble salts in the intestine), and therefore, on calcification Hess (44) reports that excess phosphorus increases mineral retention only if accompanied by cod liver oil. The optimal Ca:P retention ratio is from 1:1 to 1.5:1 with calcium somewhat higher than phosphorus (13, 36). A ratio of less than 1.5:1 shows that soft tissues are growing at a greater rate than bones. A ratio of less than 1:1 shows that bone is growing only half as fast as soft tissues.

There has been a bit of speculation on the effect, if any, of Mg salts on Ca or P metabolism. Elmslie (26) found that adding MgCl₂ to diets low in Ca slightly increases and MgCO₃ had no effect on the ash of bones though it was hard to ascertain due to the lack of appetite caused by Mg which made general conditions poor. Bogert and McKittrick (14) found that adding 6 gm. of Mg citrate to the diet caused an increase of calcium excretion.

A high carbohydrate diet seems to have an unfavorable effect on calcium and phosphorus. Rogers (33) reports that in New Zealand a group of children living near a candy store exhibit 25% more dental caries than those living at remote places. Hess (44) reports that children whose diets are rich in starches are prone to rickets. (He thinks this excess of starches may be the cause of the overweight associated with rickets.) Lactose (and possibly dextrin) seems to play apart in having a favorable rather than deleterious effect (44, 9, 19) due to the fact that lactose produces an acid medium in the intestine and this increases absorption. Bergelin (9)

44. Hess - Rickets, Osteomalacia, and Tetany
13. Bogert and McKittrick - JEC 54: 362; 1922
36. Stearns, C. - JEC 42: 749; 1931
9. Bergelin, C. - JEC 70: 51; 1926
found that when starch, glucose, fructose, or maltose comprised 50% of the diet, it slightly increased Ca and P absorption. (Though Bollinger and Hartman (19) do not specify lactose, they indicate that sugar ingestion sometimes increases and sometimes decreases the blood serum phosphorus. They further indicate that glucose definitely decreases serum phosphate and that phosphates are better utilized in the presence of glucose.) They state that sugar ingestion decreases the urinary phosphate.

Excessive or poorly utilized fat is found (42)(15, 44, 70) to have a deleterious effect on Ca absorption because of the formation of "soap stool", discussed earlier. Hess (46) believes that the effect of fat is an individual matter and that there are reciprocal factors such as the reaction within the bowels, constipation, and the kind of fat (as cod liver oil). He states that the addition of fat has an opposite effect on P as on Ca. The Ca soaps formed set free H₃PO₄ and allow it to be absorbed back by the intestine or to be excreted in the urine.

Certain phases of the effects of the acid-base equilibrium on calcium and phosphorus metabolism will be taken up in the miscellaneous portion of this chapter, but the effects of acid-forming and base-forming diets seem most appropriately discussed here. Bogert and Kirkpatrick (15) find that base-forming diets divert calcium from the urine to the feces, and vice versa. In 2/5 of the cases, acid-forming diets resulted in negative balances, and in all cases calcium excreted was increased. Samuel and Kugelmann (86) found that acid-forming diets lacking vitamin D produced rickets in young rats. Such diets decrease the serum phosphorus and alkaline

15. Bogert and Kirkpatrick - JBC; 397; 1922
36. Sanford, H. N. - CDA 6(4); 538; 1952
44. Hess, - Rickets, Osteomalacia, and Tetany.
reserve. Base-forming diets decrease the serum calcium somewhat. Acid-forming diets inhibit while base-forming diets accelerate the rate of growth, development, metabolism, and activity. On an acid-forming diet the muscles are flabby and the posture poor. Samuel and Kugelmass state that the growing organism needs both acid-forming and base-forming elements for growth and activity. The milk of very young children is base-forming and the "daily requirements of growth indicate a preponderance of base-forming elements." However, in actuality the diet just after weaning is apt to acid-forming and low in minerals, due to the large amount of cereals used. The early offering of orange juice and cod liver oil compensate by favoring retention of base-forming elements. A summary given by Samuel and Kugelmass follows:

Bartlett - addition of vegetables (base forming) favorably influence the metabolism of young infants.

Zucker - made a rickets producing diet antirachitic by decreasing the acid forming constituents.

McClendon - increased rickets by adding of alkalie.

Jones - cured a case of rickets by the adding of acid to diet.

Shelling - (Park's Lab.) acid forming diets produced a more severe degree of rickets than do base forming diets.

Chaney and Blunt - orange juice added to a diet increased the retention of Ca by an amount greater than that contained in the orange juice.

Eddy - bananas added to the diet have the same marked effect on Ca retention.

Binger)
Salvesen)
Hastings)
McIntosh)
Rinjiro)
Randoin)

produced tetany in dogs by intravenous injection of alkaline phosphate obtained maximum growth of rats on rations highest in mineral content, especially with salts of alkalies metals.

Page - the alkaline reserve of blood of rabbits fed on acid forming
diets is less than blood of those fed on base forming diets.

Borak - dogs on acidic diets - (gain more in weight) than those on basic diet.

(has a high water retention) (lower N retention)

Endocrine Glands

The parathyroid glands appear to have a very important role in calcium and phosphorus metabolism. Greenwald (quoted by Lusk (64)) gives the following explanation of parathyroid function:

1. Maintains Ca in solution in the plasma in excess of quantities otherwise possible.
   (according to Van Slyke and Peters (106) if the Ca of the diet is low, parathyroid hormone maintains the blood Ca above the tetany level of 7 mgm./100cc. even though it must do so at the expense of bone.)

2. It is believed to form a component with Ca that somewhat resembles Ca citrate in its general properties.

3. The calcium is in non-ionic but probably diffusible form and is in equilibrium with the ionic calcium in the solution.

4. The beneficial effect of the various forms is believed due to their effectiveness in increasing the amount of calcium in solution in the blood and other tissues.

5. Limits the amount of calcium bones absorb in excess of the normal. An equilibrium is reached when bones are saturated with calcium.

6. Allows serum to dissolve more calcium; it increases the physiological solubility of Calcium and phosphorus in the proportion found in bone.

7. The influence exerted upon calcium seems to be confined to the fraction combined with protein (in blood and lymph).

Starling (95) and Coppip (according to Lusk (64)) agrees with the phenomena of tetany and blood calcium control. Bogert (15) says that parathyroid extract can be used to raise the calcium level of blood.

106. Van Slyke and Peters - Quantitative Clinical Analysis
95. Starling, E. H. - Human Physiology
64. Lusk, G. - The Science of Nutrition
15. Bogert and McKittrick - JBC 54: 363; 1922
15. Bogert and Trail - JBC 54: 587; 1922
and Aub et al (3) find that when parathyroid hormone is administered to an individual with calcium deficiency, it decreases blood phosphorus and increases urinary calcium and phosphorus. Removal of the parathyroids, according to Hess (44) results in a decreased calcium of blood which cannot be controlled by giving calcium. The symptoms, he says, are greater in the young, the pregnant, or the lactating individual.

Differences from these opinions are that the parathyroid hormone may be necessary for the formation of a substance with the above functions rather than executing the same itself; and that instead of exerting a direct influence upon calcium, the change in the calcium level is a secondary effect as a result of the increase of blood and excretory phosphate (106, 25) or that it is a secondary effect of the detoxification (by parathyroid hormone) of some toxic product which probably affects calcium (36).

Cantarow (25) states that both thyroid and parathyroid extracts decalcify bones. Bauer et al (4) in further discussing the effects of the thyroid upon calcium and phosphorus, gave the following results:

In hyperthyroidism —— 25% increase in excretion of Ca
In myxedema ———— Ca excretion decreased
Administration of thyroid extract to normal individuals — increase of calcium and phosphorus excretion.

Hammett (33) states that in thyroidectomy the ossification of bones is markedly reduced so that bone contains less absolute and relative ash, which is so changed in nature that the percentage of P and Mg are higher than normal, accompanied of course by a decreased percentage of calcium.

In conclusion as to the functions of both thyroid and parathyroid glands, Hammett (33) states: "It therefore is clear that although the calcium retaining ability of the organism is reduced by the lack of the

5. Aub et al - A. J. Physiol. 90: 270; 1929
44. Hess - Rickets, Osteomalacia, and Tetany
106. Van Slyke and PETERS - Quantitative Clinical Analysis
25. Cantarow, A. - Calcium Metabolism and Calcium Therapy
33. Hammett, F. S. - JEC 57: 285; 1925
function of both is shown by the greater excretion of this element by it's lower concentration in the blood, and by the decreased ossification of the bones, the process of calcification of the ash is undisturbed. This is evidence that the formation of a bone ash of normal calcium content is not directly related to thyroid or parathyroid function."

**********

Another gland having an effect upon calcium and phosphorus is the anterior lobe of the pituitary. This gland (95) "is in some way responsible for the growth of the body, ** while it's removal or degeneration gives rise to the arrested development of the bony skeleton."

**********

Wir (111) isolated from the thymus, spleen, and lymph nodes of a calf two substances, one of which is capable of lowering serum calcium, and the other serum phosphorus. He found that in the very young the effect was much greater than in the half-grown animal.

Miscellaneous Factors

It seems generally agreed (47, 25, 15, 106) that an acid condition of the intestines increases absorption of calcium. Van Slyke and Peters give as proof the following figures:

1.5 gms. Ca / day —— (71% excreted in feces
(29% excreted in urine

above + 300 cc HCl —— (68% excreted in feces
(32% excreted in urine

above + 15 gms. NaHCO₃
instead of HCl —— (78% excreted in feces
(22% excreted in urine

95. Starling, E. H., Human Physiology
111. Wir, J. H. — CDA 6(3); 225; 1922
47. Hess and Weinstock — AJDC 54:345; 1927
106. Van Slyke and Peters — Quantitative Clinical Analysis
25. Canterow, A. — Calcium Metabolism and Calcium Therapy
15. Bogert and McKittrick — JBC 54; 263; 1922
The total excretion remains constant.

Van Slyke and Peters say that an extreme acidosis may cause loss of calcium through:

1. systemic acidosis
2. dehydration (causes loss of basic metals).

Bogert (13) and Hess (44) and Canterow (25) are agreed that the concentration of the $\text{Ca}^{++}$ ions in blood varies directly as the pH. Hess gives the following formula as a buffer of blood $\frac{\text{NaHPO}_4}{\text{NaH}_2\text{PO}_4}$ and states that when this ratio is less than 1 Ca can be inactivated. Hess states further that alkalosis is associated with tetany (low Ca) and acidosis with rickets (probably of normal Ca, low P type). Bogert (15) finds that phosphates given to children do not change the blood pH, whether the salt is acid or alkaline.

The sympathetic nervous system seems to have a definite effect upon Ca content of serum. Zondek (quoted by Berg et al (3)) believes the nerves control the distribution of ions within the cells and cell membranes.

Berg et al in their experiment found that stimulation of the sympathetic system gave rise to a decrease in the calcium level of blood, probably due to an increase of calcium at the area of stimulation. Hess and Sherman (45) working on section of the sympathetic system, found that procedure gave rise to a disturbance and increase of blood calcium. Thus these two groups working in different ways found results that confirmed each other. Berg et al found that severing the vagus nerve increased serum calcium. Zondek found that

stimulation of the vagus nerve led to a preponderance of K.
stimulation of the sympathetic nerve led to a preponderance of Ca.

13. Bogert and McKittrick - JEC 54: 365; 1922
44. Hess, A. F. - Rickets, Osteomalacia, and Tetany - 1929
25. Canterow, A. - Calcium Metabolism and Calcium Therapy
Blood phosphorus was but slightly affected by the nerve experiment.

That crude fiber increases the loss of calcium through feces and thus hinders utilization has been demonstrated by Bogert (15) Sjollema (94), and Hunt et al. (52) (the latter reporting that fineness of cell division is the reason why cattle can better assimilate green hay.) Bloom (11) attributes to fiber the power of increasing the total quantity of feces excreted by young animals, but he states that the low retention obtained on a spinach diet was not due to unsuitableness of the ash or to cellulose as such. Proof of his statement was found in his experiment of feeding spinach alone and spinach with filter paper, the latter of which resulted in the higher retention.

Mineral from animal sources is reported (15, 90, 81) to be better utilized than that from vegetables as the origin.

Van Slyke and Peters (106) give diarrhea as a cause of decreased absorption, and further state that absorption is increased by factors which tend to keep calcium in solution in the intestines.

It is not strange to note that Bogert (15) reports fast eating as a hindrance to utilization of minerals.

Sherman and McLeod (91) found that animals receiving adequate calcium but were deficient in other growth-promoting factors retained more calcium than animals of the same weight but less than animals of the same age.

Bacterial invasion of weakened tissue has been suggested as a cause of rickets (15, 82). Proof given by Robertson is the susceptibility of rachitic children to infections.

15. Bogert and McKittrick - JBC 54:363; 1922
34. Sjollema, B - JBC 57: 271; 1925
52. Hunt et al - JBC 55: 789; 1925
90. Sherman, H. G. - Chemistry of Food and Nutrition
81. Roberts, L. J. - Nutrition Work with Children - 1927
106. Van Slyke and Peters - Quantitative Clinical Analysis
91. Sherman and McLeod - JBC 64: 429; 1925
82. Robertson - The Chemical Basis of Growth and Senescence - 1925
<table>
<thead>
<tr>
<th>Experimenter</th>
<th>Age Group</th>
<th>Calcium</th>
<th>Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Range gms.</td>
<td>Average CaO  Ca</td>
</tr>
<tr>
<td>Orgler (Hess 44)</td>
<td>artificially fed infants</td>
<td>17-18</td>
<td>175</td>
</tr>
<tr>
<td>Blaumberg (Hess 44)</td>
<td>breast fed infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Killer (Hess 44)</td>
<td>breast fed infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tober &amp; Noll (Hess 44)</td>
<td>breast fed infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bruck (Hess 44)</td>
<td>artificially fed infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendel (67)</td>
<td>children</td>
<td>0.01/kg</td>
<td></td>
</tr>
<tr>
<td>Orr et al (Lusk 64)</td>
<td>irradiates children</td>
<td>2.81</td>
<td>1.79</td>
</tr>
<tr>
<td>Lusk (64)</td>
<td>7 1/4 yrs.</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td>Sherman (89,90)</td>
<td>3-15 yrs.</td>
<td>15-62</td>
<td>increase with age</td>
</tr>
<tr>
<td>Sherman (89,90)</td>
<td>3-15 yrs.</td>
<td>0.01/kg</td>
<td></td>
</tr>
<tr>
<td>Wang, Kern, Kaucher (108)</td>
<td>children</td>
<td>0.004 - 0.025 CaO</td>
<td>0.14</td>
</tr>
<tr>
<td>McLester (65)</td>
<td>children</td>
<td>1.00</td>
<td>above maintenance</td>
</tr>
</tbody>
</table>

44. Hess, F. A. - Rickets, Osteomalacia and Tetany - 1929
67. Mendel - Nutrition: The Chemistry of Life
64. Lusk, G. - The Science of Nutrition
89. Sherman, H. C. - Chemistry of Food and Nutrition
65. McLester - Nutrition and Diet in Health and Disease
## Table V

Calcium and Phosphorus Requirements

<table>
<thead>
<tr>
<th>Experimenters</th>
<th>Age Group</th>
<th>Calcium</th>
<th>Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range gms. 1 da</td>
<td>Average or advised amt.</td>
<td>Range</td>
</tr>
<tr>
<td>Orgler (Hess 44)</td>
<td>breast fed infants</td>
<td>15-17</td>
<td>.15 CaO</td>
</tr>
<tr>
<td>Schabad (Hess 44)</td>
<td>breast fed infants</td>
<td></td>
<td>.17 CaO</td>
</tr>
<tr>
<td>Roberts (31)</td>
<td>2 - 6 yrs.</td>
<td>1.5 - 1.0</td>
<td>1.0 Ca</td>
</tr>
<tr>
<td>Mendel (69)</td>
<td>man children</td>
<td>.87-.89</td>
<td>.88 Ca</td>
</tr>
<tr>
<td>Henderson &amp; Weakley (42)</td>
<td>growing animals</td>
<td></td>
<td>.35% Ca</td>
</tr>
<tr>
<td>Sherman and Hawley (59)</td>
<td>for storage</td>
<td></td>
<td>1.00 Ca</td>
</tr>
<tr>
<td>Sherman, Rose &amp; Rose (Lusk 64)</td>
<td>man</td>
<td>1.00 Ca</td>
<td></td>
</tr>
<tr>
<td>Hergheiler (Lusk 64)</td>
<td>man maintenance</td>
<td>.86 Ca</td>
<td></td>
</tr>
<tr>
<td>German (Lusk 64)</td>
<td>man maintenance</td>
<td>1.5 Ca</td>
<td></td>
</tr>
<tr>
<td>Horneman (Lusk 64)</td>
<td>man maintenance</td>
<td>1.7 Ca</td>
<td></td>
</tr>
<tr>
<td>Bertram (Lusk 64)</td>
<td>man maintenance</td>
<td>.4 Ca</td>
<td></td>
</tr>
</tbody>
</table>

44. Hess, A. F. - Rickets, Osteomalacia, and Tetany
46. Lusk, G. - The Science of Nutrition
89. Sherman and Hawley - Calcium and Phosphorus Metabolism in Children
69. Mendel, L. B. - Nutrition: The Chemistry of Life - 1923
81. Roberts, L. J. - Nutrition Work with Children - 1927
Chapter V
Summary of Requirements

Tables 4 and 5 are presented to show the calcium and phosphorus retention and requirements respectfully as given by the many experiments studied. As will be seen from the two tables the mean calcium requirement falls at about 1 gm. per day, with the range reaching from .4 gms. to 1.7 gms. Figures for phosphorus taken from the retention chart range from .022 for infants to 1.79 for children. Sherman and Hawley (89) state that 750 cc (3 cups) of milk is not enough per day for optimum storage from 3 to 13 years. They advise 1000 cc, or 1 quart. This appears to be in accordance with general opinion. Roberts (61) gives 1 quart of milk as optimum for storage and 1 pint as the barest minimum. This is in accordance with the work of Stearns (96) who found that the normal Ca:P retention ratio ranged from 1.95:1 to 2.1:1 for infants to 1:1 to 1.5:1 for children. Mendel (70) and Wanger et al (108) advises liberal amounts of both to take care of poor assimilation of faulty eating habits. Stiles (99) states that these quantities must be supplied in sufficient quantity and variety during growth. The danger to do this is only occasional. The actual trouble is with the assimilation rather than with the diet. Moore (70) states that a perverted taste for dirt or chalk indicates a lack of minerals.

The requirements for vitamin D seems to be unanimously agreed to be as stated by Sherman (90): "Inversely proportional to the adequacy of the inorganic food supply." Roberts (61) states that all children need sunlight as well throughout the entire year. Hess (44) states that all infants need protective therapy administered either to mother or child.

Sherman, states that growing animals can adjust against a lack of Ca, Na, K, or Mg, but not against Ca or P. He further shows that Modern American diets are more apt to be deficient in calcium than any other
nutrient in the diet. He further says that with an adequate calcium
diet there is sure to be enough phosphorus for maintenance, though this
is not true of growth, pregnancy, or lactation. Roberts (81) states that
the greatest danger of deficiency comes at about the age of 2 to 5, be-
cause at that period parents are apt to let down on rules.

Roberts gives a report of incidence of calcium, phosphorus disorders
in Gary, Indiana, which, though not typical of the American diet because
of the large proportion of foreign population, does show a serious need
for education. Of 6,015 children from 2 to 6: 41.6% showed bone or
muscle defects. 64.7% showed decayed teeth. Only 13.9% of the children
were getting 1 pint of milk daily. 57.2% of the children were getting no
milk at all.

Roberts states that the diet may be:

1. Insufficient in amount
2. Insufficient in kind
3. Faulty as to eating habits.

89. Sherman and Hawley—JBC 55:375: 1927
70. Moore, C. U.—Nutrition of Mother and Child—1924
99. Stiles, R.C.—Nutritional Physiology—1928
86. Stearns, C.—JBC 42(2): 749:—1931
50. Sherman, H.C.—Chemistry of Food and Nutrition
The writer concludes from this study of many experiments, that the calcium and phosphorus content of the diet, together with such complementary factors as the vitamins, is one of the most if not the most important essential for growth. The many functions of these elements, as well as their integral role in bone growth, serve as an index of their foremost position in nutrition. A survey of American dietaries shows that they are apt to be lacking minerals and this too merits much consideration. This is the reason why Sherman and others stress the importance of a quart of milk per day for each child. We should then let no stone be unturned in supplying these needs amply, as indicated in the summary of diets given by Boyd (21) and Hanke (42) on page 56, and the means of incorporating milk in the diet, as suggested by Sherman (90) on the same page.

To assist in assuring us that mineral needs are being taken care of in the child's body, experimenters have given the following diagnostic factors which may be detected by physicians:

1. Number of corpal bones of the wrist that are calcified. (In general the calcified wrist bones should be one more in number than the years of the child's life.)
2. Blood calcium level. (This should be, in children, from 10 to 11.5 mgn. per 100 cc blood.)
3. Blood phosphorus. (This should be in approximately the relation to calcium as found in most important bone constituent, \( \text{Ca}_3(\text{PO}_4)_2 \))
4. Symptoms of rickets
   - Beaded ribs
   - Square-shaped head
   - Bowel legs
   - Pigeon chest
   - Lack of muscle tone

The state of nutrition indicated by height and weight relationships has been much discussed, some writers giving it importance and others not giving it much value. The consensus of opinion seems to be that it is the best single index of nutrition. Rate of growth is of greater importance, the expected gain per year being about 5 lbs. in weight and 2\( \frac{1}{2} \) inches in height. Naturally a child who is extremely small at stature and of weight may be expected to gain more annually in both ways.

Parents in judging themselves, may well be guided by the usual signs of health
Chapter VI

Sources of Calcium and Phosphorus

For the relative and actual amounts of calcium and phosphorus in foodstuffs, the writer wishes to refer to tables 6 and 7, the charts of which comes from the National Live Stock and Meat Board, and figures from Bradley (21), Rose (85) and Sheiman (90). Roberts (81) states that "Milk is the only dependable source of calcium. Chick and Roscoe quoted by Lusk (64) say that milk for children should come from cows getting green food and sunlight. Bell (7) states that acidity affects favorably the solubility of calcium and phosphorus of milk, while temperature affects it unfavorably, a small loss in solubility resulting from boiling temperature.

Osborne and Mendel (64) state that the growing body can use both Ca and P from inorganic sources. Wha, as in Lush (64) found that the calcium of milk is combined with colloids, but acid ionizes all of it.

Blatherwick, Long, and Rose (64) find that the calcium and phosphorus of the following vegetables is well utilized: Carrots, lettuce, asparagus, celery, spinach, summer squash, cabbage. Bloom (11) says that vegetable sources are as good as milk for maintenance but not for growth. Sherman and Hawley (89) found that vegetable minerals were not as well utilized by growing children, 3 to 13 years of age, as those of milk. The writers have no doubt as to the advisability of the liberal use of vegetables in diets for children, but vegetables should be in addition to a liberal amount of milk. Moore (70) suggests giving of milk at other times than dinner, so that it will not detract from the appetite for vegetables.

85. Rose, M. S.-Foundations of Nutrition—1927
90. Sherman, H. G. - Chemistry of Foods and Nutrition
81. Roberts, L. J.-Nutrition Work with Children—1927
70. Moore, C. U. - Nutrition of Mother and Child
Hanke (42) and Boyd et al (21) suggest a daily dietary for children in order to provide the minerals necessary for good dentition as follows:

3 - 4 cups milk
1 egg (2 for pregnant women)
1 teaspoon cod liver oil (Boyd)
1 ounce butter (Boyd)
2 or more different vegetables or fruits
1/4 to 1/2 head lettuce (Hanke)

juice of 1 lemon and 1/2 pint orange juice once or twice a day (Hanke)
Meat once or twice a day (adults, Hanke)
Candy permissible only after meals (Boyd)

Sherman (30) quoting Rose, gives assistance to those having trouble in giving milk to children. A day's diet for a five-year-old may contain the advised quart of milk as follows:

2/3 cup cooked in cereal
1/3 cup creamed eggs
2/3 cup cocoa
1/4 cup (evaporated) in tomato soup
1 ounce top milk in mashed potato
1/4 cup in creamed asparagus
1/2 cup in pudding
1/4 cup in the pudding sauce
1/3 cup in pea souffle
1/4 cup white sauce
1/2 cup colored junket

30. Sherman, H. C. - Chemistry in Foods and Nutrition
42. Hanke, M. T. - Dental Survey - Je. Jl. 1951
### TABLE 6

#### Amount of Calcium in A Serving Of Some Common Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Average Helping</th>
<th>Amount of Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk, Skimmed</td>
<td>8 1/2 oz. (1 cup)</td>
<td></td>
</tr>
<tr>
<td>Milk, Whole</td>
<td>8 1/2 oz. (1 cup)</td>
<td></td>
</tr>
<tr>
<td>Buttermilk</td>
<td>8 1/2 oz. (1 cup)</td>
<td></td>
</tr>
<tr>
<td>Cheese, American</td>
<td>5 1/2 oz. (1 in. cube)</td>
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</tr>
<tr>
<td>Cheese, Cottage</td>
<td>3 1/2 oz. (5 T.)</td>
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<tr>
<td>Cauliflower</td>
<td>4 oz.</td>
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<tr>
<td>Oranges</td>
<td>6 oz. (1 med.)</td>
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</tr>
<tr>
<td>Spinach</td>
<td>4 oz. (1/2 cup)</td>
<td></td>
</tr>
<tr>
<td>Oysters</td>
<td>3 1/2 oz. (1/2 doz.)</td>
<td></td>
</tr>
<tr>
<td>Beans, Navy, Dried</td>
<td>1 oz. (1/2 cup, cooked)</td>
<td></td>
</tr>
<tr>
<td>Celery</td>
<td>2 oz. (2-5 stalks)</td>
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</tr>
<tr>
<td>Egg</td>
<td>2 oz. (1 egg)</td>
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</tr>
<tr>
<td>Bread, White, Milk</td>
<td>2 oz. (2 slices)</td>
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<tr>
<td>Carrots</td>
<td>2 oz.</td>
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<tr>
<td>Beans, String</td>
<td>2 oz. (1/2 cup)</td>
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</tr>
<tr>
<td>Cabbage, Raw</td>
<td>2 oz. (1/2 cup)</td>
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</tr>
<tr>
<td>Peas, Canned</td>
<td>5 1/2 oz. (1/2 cup)</td>
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</tr>
<tr>
<td>Potatoes</td>
<td>5 oz. (1 med.)</td>
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</tr>
<tr>
<td>Peas, Dried</td>
<td>1 oz. (1/2 cup, cooked)</td>
<td></td>
</tr>
<tr>
<td>Oats, Rolled, Cooked</td>
<td>4 4/5 oz. (1/2 cup)</td>
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<tr>
<td>Peas, Green</td>
<td>2 oz. (1/2 cup)</td>
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<tr>
<td>Beef Round, Lean</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Veal Breast</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Lamb Breast</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Veal Leg</td>
<td>4 oz.</td>
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</tr>
<tr>
<td>Liver, Beef</td>
<td>4 oz.</td>
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<tr>
<td>Ham</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Peanuts</td>
<td>1/2 oz. (20 nuts)</td>
<td></td>
</tr>
<tr>
<td>Walnuts</td>
<td>1/2 oz. (8-10 nuts)</td>
<td></td>
</tr>
<tr>
<td>Tomatoes</td>
<td>4 oz. (1 med.)</td>
<td></td>
</tr>
<tr>
<td>Lamb Chops, Broiled</td>
<td>5 1/5 oz. (2 chops)</td>
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<tr>
<td>Pork Chops</td>
<td>5 1/5 oz. (1 chop)</td>
<td></td>
</tr>
<tr>
<td>Rice, White, Steamed</td>
<td>4 oz. (5/4 cup)</td>
<td></td>
</tr>
</tbody>
</table>

Compiled by National Live Stock and Meat Board

Accepted by American Medical Association

Data obtained from Rose (85) pages 465-475 and Sherman (90) 554-559.
<table>
<thead>
<tr>
<th>Food</th>
<th>Average Helping</th>
<th>Amount Of Phosphorus</th>
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<tbody>
<tr>
<td>Veal Leg</td>
<td>4 oz.</td>
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<tr>
<td>Beef Round, Lean</td>
<td>4 oz.</td>
<td></td>
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<tr>
<td>Veal Breast</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Liver, Beef</td>
<td>4 oz.</td>
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<tr>
<td>Lamb Breast</td>
<td>4 oz.</td>
<td></td>
</tr>
<tr>
<td>Buttermilk</td>
<td>8 1/2 oz. (1 cup)</td>
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<tr>
<td>Ham</td>
<td>4 oz.</td>
<td></td>
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<tr>
<td>Pork Chops</td>
<td>3 1/5 oz. (1 chop)</td>
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<tr>
<td>Milk, Skimmed</td>
<td>3 1/2 oz. (1 cup)</td>
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<tr>
<td>Lamb Chops, Loin</td>
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<tr>
<td>Milk, Whole</td>
<td>8 1/2 oz. (1 cup)</td>
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<tr>
<td>Cheese, American</td>
<td>4 1/5 oz. (1 in. cube)</td>
<td></td>
</tr>
<tr>
<td>Oysters</td>
<td>3 1/2 oz. (1/2 dos.)</td>
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<tr>
<td>Beans, Navy, Dried</td>
<td>1 oz. (1/2 cup, cooked)</td>
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</tr>
<tr>
<td>Oats, Rolled, Cooked</td>
<td>3 1/2 oz. (1 cup)</td>
<td></td>
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<tr>
<td>Peas, Canned</td>
<td>3 1/2 oz. (1/2 cup)</td>
<td></td>
</tr>
<tr>
<td>Egg</td>
<td>2 oz. (1 egg)</td>
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</tr>
<tr>
<td>Potatoes</td>
<td>5 oz. (1 med.)</td>
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<tr>
<td>Spinach</td>
<td>4 oz. (1/2 cup)</td>
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<tr>
<td>Peas, Green</td>
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<tr>
<td>Almonds</td>
<td>1/2 oz. (12-15 nuts)</td>
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<td>Peanuts</td>
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<tr>
<td>Bread, White, Milk</td>
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</tr>
<tr>
<td>Oranges</td>
<td>6 oz. (1 med.)</td>
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</tr>
<tr>
<td>Bananas</td>
<td>4 oz. (1 small)</td>
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</tr>
<tr>
<td>Beans, String</td>
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<td></td>
</tr>
<tr>
<td>Prunes</td>
<td>1 oz. (5 med.)</td>
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<tr>
<td>Carrots</td>
<td>2 oz.</td>
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<tr>
<td>Turnips</td>
<td>2 oz. (1/2 cup)</td>
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<tr>
<td>Beets</td>
<td>2 oz.</td>
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<tr>
<td>Walnuts</td>
<td>1/2 oz. (8-10 nuts)</td>
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<tr>
<td>Apples</td>
<td>4 oz. (1 small)</td>
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</tr>
<tr>
<td>Rice, White, Steamed</td>
<td>4 oz. (3/4 cup)</td>
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</tbody>
</table>

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Data Obtained from Rose (85) pages 465-475 and Sherman (90) 554-559.
Bibliography

Abbreviations used (in order of their appearance in the bibliography):
C, D, A.—Child Development Abstracts.
J, B, C.—Journal of Biological Chemistry
A. J. D. C.—American Journal of the Diseases of Children
Am. J. Hyg.—American Journal of Hygiene
Jr. Exp. Med.—Journal of Experimental Medicine
Jr. Agric. Sci.—Journal of Agricultural Science
Jr. Agric. Exp. Sta., Tech. Blt.—Agricultural Experiment Station Technical Bulletin
Biochem. Jr.—Biochemical Journal
Physiol. Rev.—Physiological Review
Brit. Dent. Jr.—British Dental Journal
Jr. Chd. Dev.—Child Development Magazine
Dept. Lab. Ch., Bur.—Department of Labor, Children's Bureau

Note: The full names of foreign magazines are not given because all work taken from them was obtained through abstracts, which are listed.
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