PROGRESS IN PEDIATRICS

RECENT ADVANCES IN OUR KNOWLEDGE OF RACHITIS

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ETIOLOGY

Schmorl¹ gives a very extended review of the subject and I shall use his work freely without further reference to it. The following hypotheses have been advanced and are supported by more or less pathologic-anatomic data:

Artificial rachitis in animals: Most of the authors who have undertaken these experiments believe that rachitis is a disturbance of the calcium metabolism, and that it results either from giving too little calcium in the food, or that the normal calcium in the food is not absorbed in sufficient amounts, or finally, that it is absorbed and the bones are not able to assimilate it in a normal manner. The experiments have led to varying results. In most instances feeding a calcium-poor food, or an acid food, or a combination of the two, has resulted in a disease of the bone which was, in gross appearance, very similar to rachitis. Miwa and Stoeltzner² found that there were certain differences between this artificial disease of the bone and true rachitis. There was slight disturbance in the endochondral ossification and a very considerable "osteoporose" and Stoeltzner therefore called this artificial disease pseudo-rachitic osteoporosis.

Götting³ and Schmorl confirmed these results. Clinically the rosary and enlarged epiphyses come in those cases in which there is a deficit of calcium in the bone. Such bone is more easily broken. It is a generally accepted fact that pseudorachitic osteoporosis comes as a result of a calcium-poor food; that it is the physiologic reaction of an organism with healthy bones; and that the bone substance is qualitatively normal but

1. Schmorl: Die pathologische Anatomie der rachitischen Knochenkrankung mit besonderer Berücksichtigung ihrer Histologie und Pathogenese. *Ergebn. d. inn. Med. u. Kinderh.*, 1909, iv, 403.

2. Miwa and Stoeltzner: Ueber die bei jungen Hunden durch kalkarme Fütterung entstehende Knochenkrankung, *Beitr. z. path. Anat. u. allg. Path.*, 1898, xxiv, 578.

3. Götting: Ueber die bei jungen Tieren durch kalkarme Ernährung und Oxalsäurefütterung entstehenden Knochenveränderungen. *Virchow's Arch. f. path. Anat.*, 1909, cxvii, 1.

has quantitatively less calcium than the corresponding normal bone. This phase of the subject will be treated in more detail later.

An acid food causes the same microscopic picture as a food containing a diminished amount of calcium and must come into the same class as pseudorachitic osteoporosis.

Recently an attempt has been made to prove that some of the diseases of metabolism are due to a disturbance of the function of certain glands having an internal secretion. These are, respectively, the thyroid, parathyroid, thymus and adrenal glands. These attempts have not been successful.

Finally, rachitis has been considered an infectious disease. Schmorl has been unable to isolate any organism to which he could attribute rachitis, except in the case of two rats twenty-four hours old with a disease of the bone which was morphologically similar to a moderately severe rachitis. These observations corresponded with those of Morpurgo,⁴ who found a diplococcus in the bones of young rats which were clinically rachitic. J. Koch⁵ believes that negative findings are due to poor staining methods and the difficulty of demonstrating bacteria in bones. He was able to demonstrate bacteria both in culture and section in the epiphyses of ribs of children with rachitis who had died in the course of measles, diphtheria, pertussis, scarlet fever, gastro-enteritis, etc. The kind of bacteria found in his cases were often different, and most prominent among them were streptococci, bacteria coli, and staphylococci. In the majority of these cases the heart blood was sterile and the bacteria which were found in the epiphyses were not part of a general infection. He concludes with Kassowitz that rachitis is principally a vascular change of the epiphyses and adds that this change is due to bacterial infection of the part.

PATHOLOGY

The Calcification of Bone in Rachitis

Lehnerdt⁶ summarizes the literature on this phase of the subject from seventy odd papers, the references for which will not be given in this review but may be found in the original.

According to Pommer, all newly formed bone first deposits osteoid material which later becomes calcified. This calcification goes on so

4. Morpurgo: Ueber eine infectiöse Form der Knochenbrüchigkeit bei weissen Ratten. Verhandl. d. Deutsch. path. Gesellsch., 1900, iii, 40; Beobachtungen an Serienschnitten von osteomalacischen und rachitischen Knochen. Verhandl. d. Deutsch. path. Gesellsch., 1909, xiii, 51.

5. Koch, J.: Untersuchungen über die Lokalisation der Bakterien, das Verhalten des Knochenmarkes und die Veränderungen der Knochen, insbesondere der Epiphysen, bei Infektionskrankheiten mit Bemerkungen zur Theorie der Rachitis. Ztschr. f. Hyg. u. Infectiöskr., 1911, lxix, 436.

6. Lehnerdt: Warum bleibt das rachitische Knochengewebe unverkalkt? Ergeb. d. inn. Med. u. Kinderh., 1910, vi, 120.

quickly in health that the osteoid layer remains thin. In rachitis the characteristic picture is one with a broad osteoid layer which is the result of some interference with the deposit of lime salts.

Other writers believe that the abnormal amount of osteoid tissue in rachitis is due to the fact that calcium has been robbed from the bone which was once calcified, and others that all bone substance formed during the active or florid stage of rachitis was uncalcified.

A calcium deficit in the bones in rachitis may be attributed theoretically to the following causes:

- I. A primary deficit of calcium in the food.
- II. A secondary deficit of calcium, there being sufficient calcium in the food.
 - (a) It is either not absorbed in sufficient quantities for the needs of the growing bone, or
 - (b) It is absorbed in sufficient quantity but is excreted again in abnormal amounts; and
 - (1) Either considerable calcium is lost as a result of an abnormal digestion, or
 - (2) A sufficient quantity is absorbed into the organism, but for some reason cannot be used in the bone and therefore is excreted again.

I. PRIMARY CALCIUM DEFICIT

It has long been known that rachitic bones are poor in calcium and on the basis of this knowledge an attempt was made to produce artificial rachitis in animals by feeding them food low in calcium. These experiments caused clinical changes similar to those seen in rachitis and the question came up as to whether true rachitis was produced or not. Chemical analyses of these bones showed that they had a low ash and calcium content. Stoeltzner and Miwa's experiments showed that these changes were not outside of physiologic limits, and these writers concluded that they had to deal with a pseudorachitis giving it the name pseudorachitic osteoporosis. These bones, as mentioned above, show a low ash and calcium content, but they do not lose relatively as much magnesium as do the bones of true rachitis. In the former the loss of phosphoric acid goes hand in hand with the loss of calcium, while in the latter there is relatively less phosphorus lost than calcium.

The rosary and enlargement of the epiphyses comes in all cases in which there is a diminution in the deposit of calcium. Such bones are easily broken. Finally, in pseudorachitic osteoporosis the abnormally broad zone of growth cannot be demonstrated under the microscope and is always present in true rachitis. The two diseases are, therefore, best differentiated by the pathologist. On the basis of these facts Lehnerdt agrees with Stoeltzner and Miwa that pseudorachitic osteoporosis is a

result of a food containing a low amount of calcium, is the physiologic reaction of an organism with healthy bones to a calcium-poor food and that the bone substance is qualitatively normal and quantitatively diminished in amount. A deficit of calcium in the food, therefore, cannot cause true rachitis.

Aron⁷ concludes that the normal infant takes only as much calcium from human milk as it requires for growth. Some of the cases in which rachitis develops on human milk are due to too small a percentage of calcium in the milk.

Bahrtdt and Edelstein⁸ found the average CaO in human milk to be 0.0426 per cent., while Schabad⁹ found that the calcium content of human milk is greater at the beginning of nursing than at the end, and that there is a progressive diminution in the percentage of calcium during the course of lactation, falling off from 0.045 per cent. to 0.031 per cent. The decrease is constant and regular in some women and in others irregular and with great variations. The average percentage of calcium in human milk on which healthy babies were fed is 0.044 per cent. and rachitic babies 0.039 per cent. Rachitis is possible with a large percentage of calcium in the milk, even with 0.055 to 0.088 per cent. The milks on which children develop rachitis contain larger amounts of the organic constituents, for example, fat, than do the milks of healthy babies. The caloric value of the rachitogenic milk is therefore higher. For every 100 milk calories in rachitis there were 63 mg. of calcium and in health 76.5 mg. It is obvious, therefore, that the rachitic baby must either take the required amount of food calories containing too little calcium or to obtain the necessary quota of calcium it must take too much food. It is, according to Schabad, impossible to increase the amount of calcium in human milk. He believes that the clinical manifestations due to a calcium deficit in the food are not true rachitis but are pseudo-rachitic osteoporosis.

II. SECONDARY CALCIUM DEFICIT

Sufficient proof has not been obtained from complete metabolism experiments to warrant the conclusion that a decrease in the retention of calcium is responsible for its decreased absorption. Either the gastrointestinal canal must be in such a condition that there is an increased excretion of calcium or the newly formed bone is in such condition that, during the active stages of rachitis, the calcium which has already been

7. Aron: Kalkbedarf und Kalkaufnahme beim Säugling und die Bedeutung des Kalkes für die Aetiologie der Rachitis. *Biochem. Ztschr.*, 1908, xii, 28.

8. Bahrtdt and Edelstein: Das Kalkangebot in der Frauenmilch. *Jahrb. f. Kinderh.*, 1910, lxxii, Suppl., p. 16.

9. Schabad: Der Kalkgehalt der Frauenmilch. Zur Frage der ungenügenden Kalkzufuhr als Ursache der Rachitis. *Jahrb. f. Kinderh.*, 1911, lxxiv, 511.

absorbed into the body cannot be deposited in the normal manner and is therefore reexcreted into the intestine.

Birk¹⁰ and Rothberg found that there was a negative calcium balance (i. e., more calcium was excreted from the body than was ingested in the food) in those cases in which there were large amounts of fat in the food. In their whole milk experiments the ash balance was always negative, this being more marked in young children, and both these writers concluded that milk-fat had an unfavorable influence on the retention of ash, more especially calcium and magnesium. They believed, furthermore, that there was first an excess of fatty acids in the intestine and that these fatty acids withdrew the salts (among them calcium) from the body to form soaps. The calcium retention increased as the soap formation decreased. Birk concluded that rachitis was due to a primary disturbance of digestion. Lehnerdt considers that this conclusion is not based on sufficient proof, especially because the fatty acids can combine with only relatively small amounts of the alkaline salts. Bahr¹¹ considers that there were more bases excreted by the rachitic children reported by Birk, than could be combined with the soaps present. Freund¹² found that with an increase of fat and the formation of soap stools there was no diminution in the calcium balance.

Birk¹³ performed a series of experiments on two healthy and two rachitic children to see if cod-liver oil had an unfavorable action on the digestion of fat and caused demineralization of the body. The action of the cod-liver oil and phosphorus caused a doubtful negative mineral balance to improve in the two rachitic children and had no effect on the healthy children because they retained only as much mineral salts as they needed in growth. The absolute amount of soaps in the stools of the rachitic children was considerably larger than that in the stools of the healthy children, while the percentage of soap in the stools of the rachitic children was reduced. Freund¹⁴ commented on the fact that the absolute amount of soap in the stools of the healthy children was the same before and after the administration of phosphorus and cod-liver

10. Birk: Ueber den Magnesiumsatz des Säuglings. *Jahrb. f. Kinderh.*, 1907, lxxvi, 300; Rothberg: Ueber den Einfluss der organischen Nahrungskomponenten auf den Kalkumsatz künstlich genährter Säuglinge. *Jahrb. f. Kinderh.*, 1907, lxxvi, 69.

11. Bahr: Untersuchungen über das Symptom der Seifenbildung und die Ausscheidung der Basen im Darm des Säuglings. *Jahrb. f. Kinderh.*, 1910, lxxi, 249.

12. Freund: Zur Wirkung der Fettdarreichung auf dem Säuglingstoffwechsel. *Jahrb. f. Kinderh.*, 1905, lxi, 36.

13. Birk: Untersuchungen über den Einfluss des Phosphorlebertrans auf den Mineralstoffwechsel gesunder und rachitischer Säuglinge. *Monatschr. f. Kinderh.*, 1908, vii, 450.

14. Freund: Physiologie und Pathologie des Fettstoffwechsels im Kindesalter. *Ergebn. d. inn. Med. u. Kinderh.*, 1909, iii, 139.

oil and that in the rachitic children there was a lower percentage of soap and a larger amount of neutral fat and fatty acids when using phosphorus and cod-liver oil. If the soaps were responsible for the loss of calcium in rachitis the condition would be similar to that produced in animals and there would result not rachitis but pseudorachitic osteoporosis.

Lehnerdt apparently considers the following hypothesis of Stoeltzner most plausible — that the newly formed bone remains uncalcified because it is not in condition to impregnate itself with the calcium which is brought to it in the body fluids. When the calcium is rejected by the bone it must be excreted and returned to the intestine, where it combines with the fatty acids to form soaps. If this is true, calcium is the cause of the excessive formation of soaps instead of being a result of an abnormal fat digestion.

The acid theory of the pathogenesis of rachitis is without foundation because animals fed on acids do not develop rachitis and there is no diminution in the alkalinity of the blood.

Stoeltzner's¹⁵ theory that the bone in rachitis is unable to deposit calcium in the normal manner is developed as follows: There are three stages in the development of bone: (1) the osteoid, in which the bone does not possess the power of depositing salts; (2) the potential, in which it obtains the power, and (3) the actual, in which calcium is deposited. If there is too little calcium in the food the stages progress in a normal manner except that the advance from the potential to the actual stage of deposited calcium should not take place because of the lack of calcium, and one should find abnormal amounts of osteoid tissue. This, however, is not the case. The old bone, which has already calcified, gives up its calcium to the new bone and the new bone continues to develop in the normal manner, passing from the potential to the actual stage. Thus the newly formed bone is constructed at the expense of the old bone because there is not enough calcium at hand to supply all the demands of the growing skeleton. The abnormally broad zone of osteoid tissue of true rachitis is not seen in experimental rachitis (pseudorachitic osteoporosis) because there is merely a deficit of calcium in the food, and not a condition which makes it impossible to deposit calcium.

Lehnerdt¹⁶ experimented with animals and found by substituting strontium for calcium in the food, that bone changes only came when there was a deficit of calcium. The severity of strontium pseudorachitis

15. Stöltzner: Die zweifache Bedeutung des Calciums für das Knochenwachstum. *Arch. f. d. ges. Physiol. (Pflüger)*, 1908, cxxii, 599.

16. Lehnerdt: Zur Frage der Substitution des Calciums im Knochensystem durch Strontium. I. Der Einfluss des Strontiums auf die intrauterine Entwicklung des Knochensystems. *Beitr. z. path. Anat. u. z. allg. Path.*, 1909, xlv, 468; II. Strontiumfütterung an säugende Tiere. *Beitr. z. path. Anat. u. z. allg. Path.*, 1909, xlvii, 215; Phosphorsklerose und Strontiumsklerose, *Jahrb. f. Kinderh.*, 1910, lxxii, 395, 610.

depends on the amount of the deficit. This condition is rapidly cured when calcium is again given in the food. Lehnerdt concludes, as a result of his own observations, that true rachitis is in all probability a disturbance of the intermediary metabolism and he considers that "domestication" plays an important rôle in the subject. Rachitis is not a disease of the free, wild animal, but is often found in animals confined in zoological gardens. Similarly the children of a pastoral race are apt to develop it when confined to a city.

v. Hausemann¹⁷ considered that it resulted from too little air and activity. For example, those children born in the fall who are necessarily housed all winter in bad quarters and with poor ventilation had rachitis more frequently than children born in the spring and living under the same circumstances. Schmorl¹ found that in a great majority the disease commenced between the months of November and March. They tend to cure spontaneously during the summer months and to relapse in the fall. Ebbell's¹⁸ attention was attracted to the question of why rachitis is a relatively rare disease in the tropics. A study of its geographical distribution shows that it increases in frequency the greater the distance from the equator, irrespective of race. He concludes that rachitis is the result of lack of light. This assumption was apparently confirmed by some experiments on animals and plants which were deprived of light and in which deformities developed. He thinks that the ultraviolet ray is particularly important and points out that this ray is partially arrested by window glass. Therefore children kept in the house are deprived of the ultraviolet ray in particular. Sittler¹⁹ believes that it is a true disturbance of digestion which is caused in part by unhygienic surroundings, more especially during the winter months. Czerny²⁰ defines rachitis as a congenital constitutional anomaly whose most prominent symptom is the change in the bones and cartilages. There is evidently a general disturbance of nutrition affecting the bones and inducing symptoms on the part of the nervous system. Hutinel²¹ regards a quantitative modification of the bone-marrow as the essential feature of rachitis. He thinks that the qualitative changes are similar to those encountered in ordinary infections; but the remarkable proliferation of the bone-marrow seems to be specific for rachitis. Marfan²² says that one must admit that all

17. v. Hausemann: Ueber Rachitis als Volkskrankheit. Berl. klin. Wehnschr., 1906, xliii, 249.

18. Ebbell: Norsk Mag. f. Laegevidensk., 1909, lxi, ix; abstr. in Jour. A. M. A., 1908, 1, 1390.

19. Sittler: Neuere Ansichten über die Aetiologie der Rachitis. Fortschr. d. Med., 1909, xxvii, 817.

20. Czerny: Die erste Vorlesung in Strassburg, 9 Mai, 1910; Monatschr. f. Kinderh., 1910, ix, 131.

21. Hutinel: Le Rachitisme. Arch. de méd. des enf., 1910, xiii, 81.

22. Marfan: Le Rachitisme et sa pathogenie bailliere et fils, Paris, 1911.

rachitis carry a focus of infection or chronic intoxication. Rachitis does not act like a special single disease but a syndrome in which bony deformity is the most prominent symptom.

The work of Schabad and his pupils on rachitis has been prominent in medical literature and has added much to our knowledge of normal and diseased bone. He²³ found that the dried bones of the newly born infant contained 60 to 65 per cent. of ash and 40 to 45 per cent. of organic material. The amount of ash in the bone varies from birth onward; at first the ash increases and at the second year decreases to 59 to 55 per cent. and during this time there is a corresponding increase in the organic material. The ash begins to increase at the end of the second year up to the adult 68 per cent. of the dried bone substance. The percentage of water in rachitic bone is higher and the percentage of dry substance is lower than in healthy bone. The relation of ash to organic matter is 20:80 in rachitic bone and 60:40 in healthy bone. Krasnogorski²⁴ also found a high water content in rachitic bones with a mineral content of one-half the normal. The calcium and magnesium were especially reduced. These facts left no doubt in the author's mind that the large amount of water in rachitic bones stands in causal relation to the poverty of calcium ions. The disturbance of the intracellular calcium metabolism must change the water content of the organism and have a powerful influence over the entrance of water into the organism. Under this influence the hyaline substance of the bone absorbs water and there results the clinical enlargement of the epiphyses of rachitis. Gassmann²⁵ concludes as a result of his analyses of healthy and rachitic bones that the complex salt $(\text{Ca}_2(\text{PO}_4)_2)3\text{CaCO}_3$ is the same in both instances. Potassium, sodium and chlorin are the same in both but magnesium is increased from 0.50 per cent. in normal bone to 0.53 to 0.74 per cent. in rachitic bones. He concludes, therefore, that magnesium plays an important part in the pathology of the disease.

Schabad²⁶ reports further that the weight of the skeleton during the first year of life is 16 per cent. of the body weight. The calcium content of the skeleton is 1.25 per cent. of the body weight and 7.7 per cent. of the skeletal weight. The greatest deposit of calcium takes place during the period of greatest growth, i. e., in a breast-fed baby between the second

23. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis. Der Mineralgehalt gesunder und rachitischer Knochen. Arch. f. Kinderh., 1909, lii, 47.

24. Krasnogorski: Ueber die Wirkung der Ca-Ionen auf das Wasserabsorptionsvermögen der Knorpelgewebes und ihre Bedeutung in der Pathogenese des rachitischen Prozesses. Jahrb. f. Kinderh., 1909, lxx, 643.

25. Gassmann: Chemische Untersuchungen von gesunden und rachitischen Knochen. Hoppe-Seyler's Ztschr. f. physiol. Chem., 1910, lxx, 161.

26. Schabad: Zur Bedeutung der Kalkes in der Pathologie der Rachitis. II. Der physiologische Kalkbedarf und Rachitis infolge von unbefriedigtem Kalkbedarf. Arch. f. Kinderh., 1910, lii, 68.

and fourth months, and in a bottle-fed baby between the second and sixth months. The calcium retention of a baby taking human milk may be as high as 70 per cent. of the intake and one taking cows' milk 30 per cent. Although the calcium content of cows' milk is four times greater than that of human milk, the calcium needs during the period of greatest growth can only be furnished by two-thirds milk or richer, because the assimilation of cows' milk is two and one-half times poorer than human milk. A baby may take human milk containing deficient calcium for three months' time without any symptoms of rachitis, and therefore the connection between a low percentage of calcium in the food and rachitis is not established. Rachitis, on the other hand, may develop in a baby taking human milk containing the normal or a diminished amount of calcium. He agrees with Stoeltzner that experimental rachitis caused by feeding animals a calcium-poor food is clinically, anatomically and chemically indistinguishable from spontaneous rachitis, but that histologically it is characterized as a pseudorachitic osteoporosis. Furthermore, it is probable that in man there is a condition other than rachitis in which a deficient amount of calcium in the food causes a pseudorachitis which cannot be differentiated clinically from rachitis, but which has the characteristics of pseudorachitis.

In acute rachitis²⁷ and during the early or florid stage of the disease the calcium balance is either diminished or negative, and as the disease progresses and becomes well developed the calcium balance is either below normal or within normal limits. When convalescence commences there is increased retention of calcium which shows itself earlier than does clinical improvement. During this latter period two to three times more calcium is retained than is normal and when the cure is complete the calcium retention again becomes normal.

The increased excretion of calcium in progressive or florid rachitis goes on exclusively through the intestines and at the same time there is less calcium than usual excreted through the urine. Dibbelt²⁸ obtained the same results and believes that this is evidence against the theories of increased resorption of calcium from the bones or of inability of the rachitic osteoid tissue to take up calcium, because, according to him, they are not compatible with the decreased absorption of calcium in the urine. In either of these condition the urinary calcium should be increased. Schabad interprets these findings as evidence against the acid theory of rachitis.

27. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis: III. Der Kalkstoffwechsel bei Experimenteller. Arch. f. Kinderh., 1910, liii, 380.

28. Dibbelt: Weitere Beiträge zur Pathogenese der Rachitis. Verhandl. der deutsch. path. Gesellsch., 1910, xiv, 294.

The relation between calcium and phosphorus was then studied by Schabad²⁹ and he found that there was an increased excretion of phosphorus as well as calcium in the acute stage of rachitis. There was relatively so much phosphorus excreted that it could not all have come from the bone and presumably was lost from the phosphorus-rich nervous system. The relation between the phosphorus in the urine and feces in nurslings is 80:20 in health and 65:35 in rachitis; and in the bottle-fed baby 60:40 in health and 40-44:60-56 in rachitis. During convalescence from rachitis the total excretion of phosphorus is lower than normal and the relation between the phosphorus in the urine and the feces returns to the normal figures. The following connection has been established between the calcium and phosphorus excretion: An increased excretion of calcium causes a greater retention of phosphorus, and vice versa. The great loss of phosphorus is important in the disease and may explain the nervous symptoms. Birk and Orgler³⁰ found that a disturbance of the calcium metabolism may be present quite a while before the clinical appearance of rachitis. Orgler³¹ criticizes Schabad's deductions and does not consider them free from error. In one instance he was able to increase the calcium retention by changing the quality of the food, and in another instance an increase in the amount of calcium in the food did not influence the calcium retention at all. Orgler believes that there are two important conditions which regulate the assimilation of calcium: (1) the power of the body to assimilate it, which depends on the intermediary metabolism concerning which we know nothing; and (2) the composition of the food. Aschenheim and Kaumheimer³² examined the muscles of eight children with rachitis and three without rachitis and found that in all cases of rachitis there was a diminution in the amount of calcium which apparently corresponded with the severity of the disease. Bing³³ found excessive thinning of the muscle fibers with loss of striation accompanied by an increase of the muscle-cell nuclei without interstitial infiltration. He found these changes less marked in milder forms of rachitis and never found the same condition in the control muscles examined.

29. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis: IV. Der Phosphorstoffwechsel bei Rachitis. *Arch. f. Kinderh.*, 1910, liv, 83.

30. Birk and Orgler: Der Kalkstoffwechsel bei Rachitis. *Monatschr. f. Kinderh.*, 1910, ix, 544.

31. Orgler: Ueber den Kalkstoffwechsel bei Rachitis. *Monatschr. f. Kinderh.*, 1911, x, 373.

32. Aschenheim and Kaumheimer: Ueber den Aschegehalt der Muskulatur bei Rachitischen. *Monatschr. f. Kinderh.*, 1911, x, 435.

33. Bing: Histopathologische und Elektrodiagnostische Untersuchungen bei rachitischen Kindern mit pseudoparetischen und atonischen Muskelstörungen. *Med. Gesellsch., Basel*, Dec. 6, 1906; Reported in *Cor.-Bl. f. Schweiz. Aerzte*, 1907, xxxvii, 119.

Findlay³⁴ examined the blood in rachitis and summarized his findings as follows: In active and uncomplicated rickets anemia is not the rule but is to be regarded as exceptional, and when it occurs is due to adventitious causes. On the contrary, the amount of hemoglobin and the number of red cells in rachitic children in the series examined are notably in excess of the normal average. The red blood corpuscles, as a rule, vary more in size than in normal individuals of similar ages, but otherwise there is no abnormality. The nucleated red cells, polychromatophils and myelocytes are of the rarest occurrence. In rickety subjects there is little characteristic change as far as the leukocytes are concerned. They may be normal, slightly increased, or even diminished in number. The mononuclears more frequently than the polynuclears show an absolute increase in the number per cubic millimeter.

TREATMENT

Kassowitz³⁵ first recommended phosphorus in the treatment of rachitis. His original prescription, known as phosphorlebertan (phosphori 0.01, ol. jecor aselli, ad 250), still holds first place in Germany in the treatment of rachitis. Kissel³⁶ found in his experiments on animals that phosphorus had absolutely no effect on the skeletal system, and concluded that there was no ground for its use. Despite this report phosphorus continues to be used and many experiments have been performed to prove its efficiency.

Birk³⁷ and Schabad³⁸ both concluded that phosphorus in therapeutic doses does not affect the calcium metabolism in healthy children. Such children take only as much phosphorus as they need for growth regardless of the amount in the food. In rachitis cod-liver oil increases the retention of phosphorus and calcium and this action is intensified by the addition of phosphorus to the oil.³⁹ The increased retention of calcium starts three to five days after giving phosphorus and gradually diminishes until at the end of two months it is again normal. This depends on the increased absorption and decreased excretion through the urine and feces. The question now comes up as to whether oils as such in combination with

34. Findlay: The Blood in Rickets. *Lancet*, London, 1909, i, 1164.

35. Kassowitz: Die Phosphorbehandlung der Rachitis. *Ztschr. f. klin. Med.*, 1883-4, vii, 36.

36. Kissel: Ueber die pathologisch-anatomischen Veränderungen in den Knochen wachsender Tiere unter dem Einfluss minimaler Phosphordosen. *Virchow's Arch. f. path. Anat.*, 1896, cxliv, 94.

37. Birk: Untersuchungen über den Einfluss des Phosphorlebertrans, etc. *Monatschr. f. Kinderh.*, 1908-09, vii, 450.

38. Schabad: Der Phosphor in der Therapie der Rachitis. Der Einfluss des Phosphors auf den Kalkstoffwechsel bei rachitischen und gesunden Kindern. *Ztschr. f. klin. Med.*, 1909, lxvii, 454.

39. Schabad: Die Behandlung der Rachitis mit Lebertran, Phosphor und Kalk. *Ztschr. f. klin. Med.*, 1909, lxviii, 94.

phosphorus have a therapeutic action on rachitis. Schabad⁴⁰ investigated the action of phosphorus, cod-liver oil and "sesamol" on the metabolism of calcium, phosphorus, fat and nitrogen and found that "sesamol" and phosphorus did not help rachitis, while cod-liver oil plus phosphorus increased the retention of phosphorus and calcium and the absorption of fat and nitrogen. Schabad and Sorochowitsch⁴¹ used lipanin, i. e., olive a substitute for cod-liver oil, which was supposed to be easily absorbed because it contained free fatty acids. They concluded from their metabolism experiments that lipanin and olive oil increase the absorption of nitrogen and fat but that lipanin has no advantage over olive oil. Lipanin does not increase the retention of calcium in rachitis and is therefore not as good as cod-liver oil in the treatment of rachitis. They say in their most recent article⁴³ that sometimes phosphorus and cod-liver oil does not have a favorable action on the retention of calcium in rachitis, especially if the disease is not approaching a convalescence. At other times they have a favorable action on the calcium retention. They experimented with various other salts combined with cod-liver oil and found that a calcium acetate cod-liver oil had the most favorable action on rachitis because it contained much more calcium.

Most recently Caroline Towles⁴⁴ did a series of metabolism experiments in von Pirquet's clinic in Breslau and was unable to demonstrate that phosphorus cod-liver oil had any action at all on acute rachitis. The most recent work of Towles and Schabad and Sorochowitsch indicates, therefore, that phosphorus cod-liver oil may not have any therapeutic action in the treatment of acute rachitis.

40. Schabad: Phosphor, Lebertran und Sesamöl in der Therapie der Rachitis. Ihr Einfluss auf den Kalk-, Phosphor-, Stickstoff-, und Fettstoffwechsel. *Ztschr. f. klin. Med.*, 1909-10, lxi, 435.

41. Schabad and Sorochowitsch: Lipanin als Ersatzmittel des Lebertrans bei Rachitis. Sein Einfluss auf den Stoffwechsel. *Monatschr. f. Kinderh.*, 1911, ix, 659.

oil with the addition of 6 per cent. oleic acid according to v. Mering,⁴² as

42. v. Mering: Ein Ersatzmittel für Lebertran. *Therap. Monatsch.*, 1888, ii, 49.

43. Schabad and Sorochowitsch: Die Behandlung der Rachitis mit Lebertran-emulsionen und ihre Einwirkung auf den Stoffwechsel. *Monatschr. f. Kinderh.*, 1911, x, 12.

44. Towles, C.: Untersuchungen über den Einfluss des Phosphorlebertrans auf den Stoffwechsel eines rachitischen Säuglings. *Ztschr. f. Kinderh.*, 1910-11, i, 346.