STUDIES IN THE METABOLISM OF RICKETS¹

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I. IS RICKETS DUE TO A DEFICIENT SUPPLY OF CALCIUM TO THE BONES?

THE CALCIUM CONTENT OF THE BLOOD, MUSCLE, AND BRAIN, IN EXPERIMENTAL RICKETS IN DOGS.

AN historical sketch of the more important investigations already recorded upon rickets prepared by one of us (L. F.) was published as an introduction to Miss Ferguson's Report to the Medical Research Committee, 'A Study of Social and Economic Factors in the Causation of Rickets', Special Report Series No. 20, 1918.

It is unnecessary to recapitulate this. It showed clearly that the etiology of the disease is no better understood now than when Glisson described it in the seventeenth century, in spite of all the work that has been accomplished since then.

As Albu and Neuberg (1) say, after a full consideration of the calcium metabolism in rickets and of the various theories which have been advanced as regards the nature of the disease, 'Die Geschichte der Rachitis ist mit einer Fülle neuer Hypothesen aber wenigen Tatsachen bereichert worden'.

That rickets is not simply an impaired calcification of bone or an exaggerated decalcification, as so many consider it to be, is shown by its clinical features and by the nature of the pathological changes in the bones. The general malaise of the child, the profuse sweating, the intense muscular weakness and the tendency to the development of tetany, all indicate some general disturbance of which the bone changes are merely one manifestation, and any explanation of the nature of the disease must explain this group of symptoms.

Further, the pathology of the bone changes and the formation of the characteristic osteoid tissue mark it as a disease *sui generis*, totally different from conditions of a mere failure in calcification.

Since one of the most patent changes is the softening of the bones, great

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² Throughout this and the next part Noël Paton and Leonard Findlay are responsible for the general plan of the work, Noël Paton for the experimental and Leonard Findlay for the clinical part. J. Sharpe is responsible for the chemical analyses.

interest has, for long, centred round the behaviour of lime salts in the etiology of the disease. It is possible that in considering the relationship of calcium to bone development its significance as an essential constituent of all the tissues and its importance in maintaining and controlling their activities may have been forgotten. A due proportion of calcium ions is essential alike for muscular activity and for the control of the nervous system, and the store of calcium in bone is well known to act as a source of supply when this is cut off from without, as in starvation. Changes in the amount of lime salts in bone may thus have a significance altogether outside the skeleton.

Broadly speaking, the diminished amount of calcium in the bones must be due to one, or all, of three causes :

1. A deficient supply of calcium to the bones, due to either
 - (a) A deficient supply of calcium in the food.
 - (b) A deficient absorption of calcium from the food.
2. The inability of the growing bone to fix the calcium brought to it, or,
3. A non-retention of calcium by the rachitic bone, i. e. decalcification.

Normal ossification involves the two processes of the deposition of lime salts (calcification) and the re-absorption and removal of these (decalcification), as the growth extends outwards, and as the spongy cancellous tissue of bone is produced. The salts removed in the process of re-absorption are available to be used again in the calcification as it spreads outwards.

Under normal conditions these two processes are perfectly co-ordinated. If this co-ordination were upset in the direction of failure of the growing part of the bone to use the lime from the normally decalcifying part, the same result on the metabolism of the lime would be produced as would be caused by a simple exaggeration of decalcification.

Deficient supply of calcium was formerly very generally considered as the cause of the bone changes, but the experimental work recorded seems to negative this possibility.

One of the first workers was Roloff (2), who made investigations upon the nature and cause of a condition called 'Knochenbrüchigkeit', which occurred in endemic fashion among cattle, sheep, and swine, and which was occasionally observed also in horses and goats. Clinically it was said to resemble, according to the age of the animal, rickets or osteomalacia. The animal became lame, disinclined for exercise, seemed to suffer pain, and curvature and fracture of the bones resulted. It was more apt to occur during the winter months, both in young and in old animals, and less frequently in animals performing work than in those housed all day long in stables. Pathologically, it was characterized by softening of the bones, with a decrease in the calcium content, great thinning of the bony trabeculae, increase of the marrow, widening of the epiphyseal line, and the formation of what was called by him 'osteoid' tissue. By 'osteoid tissue' he meant a transition from bone to marrow on the inner aspects of the trabeculae, and he stated that it is simply what is found normally, but occurring at the

wrong stage when the lamellae are fully formed and have ceased to increase at the periphery. He looks upon it as a definite decalcification, and he does not seem to associate it with any change of the epiphyseal lines. Roloff (2) concluded that the condition was due to a deficient amount of calcium in the diet. Most of his paper, however, is devoted to a theoretical discussion with numerous chemical analyses of the different food stuffs and his arguments are anything but convincing. Although he mentions the disease as occurring in certain farms where the stock was well fed, and absent in other farms where the animals were poorly fed; and although he gives analyses of the milk of two sets of sheep, one with affected and the other with non-affected lambs, in which the milk consumed by the former was richer in fats, protein, and salts than that consumed by the latter, he adheres to his opinion and explains away these disturbing facts by merely stating that animals do not all take the same amount of any one food, nor equal amounts of different elements in a mixed diet, so that *in all probability* the affected animals had consumed less of the calcium-rich food stuffs! The increased demand for calcium during pregnancy and lactation he considers the reason for the condition occurring more frequently in pregnant and suckling animals.

Weiske (3) shortly afterwards unsuccessfully attempted to induce a similar condition experimentally by feeding an adult goat and growing lambs on a calcium-poor diet. The animals died, but their bones were not deficient in calcium. Examination of Weiske's diets shows that they were insufficient in the essential proximate principles. The animals seem to have died simply from inanition.

E. Voit (4) experimented upon growing dogs. In his first experiment a young dog was fed upon a calcium-poor diet and developed symptoms resembling those of rickets. In his next experiment three pups of a litter were taken, and one was killed to serve as a check. The other two were fed, the one upon a calcium-poor diet of lean horse flesh with bacon (*Speck*), and the other upon the same diet with the addition of bone ash. The first developed the symptoms of rickets, lost its appetite, and finally suffered from diarrhoea with bloody stools. Both were killed on the 29th day of the experiment.

Voit states that the bones were soft, the epiphyseal lines more than twice as wide as normal, definitely irregular, and that the change from cartilage to bone was also irregular, and not sudden as occurs in normally growing bone. The chief change between the bones in the normal and the diseased animals was the irregular arrangement of the cartilage cells preparatory to the deposition of calcium.

Undoubtedly this description suggests the rachitic picture, but from his estimation of width of the epiphyseal line, this would seem to be much less marked than is usually met with in experimental rickets. Further, there is an absence of any mention of a definite delay either of calcification or of ossification.

The amount of calcium was markedly reduced, not only in the bones, but also in the muscles, blood, and other organs. He confesses, however, that he

obtained more calcium from the body than could be accounted for in the food, a finding which makes it somewhat difficult to estimate the value of the results.

As Stoeltzner (5) rightly says, 'the epoch-making work of Pommer (6) on rickets in 1885 gave a new conception of the disease'. It was he who first described the essential characteristics of rachitic bone. The chief features of rickets are, according to him, the formation of osteoid tissue, the increased and irregular formation of cartilage, the delay in calcification, and the delay in ossification, the trabeculae being composed in great part of a non-calcified osteoid tissue. Conclusions based upon work published prior to that of Pommer must be accepted with caution. Weiske chiefly depended on chemical analysis, and Roloff and Voit's histological descriptions are not sufficiently detailed.

Stoeltzner reinvestigated the question in conjunction with Miwa (7) in 1898. These authors fed a growing dog of large race on a diet of flesh and distilled water, and got the clinical and naked eye pathological features of rickets. Histological examination, which was carried out in great detail, revealed, however, no true rachitic changes but simply osteoporosis. The bones were soft, the marrow abundant, the epiphyseal lines slightly thickened, but there was neither irregularity in calcification nor delay in ossification, and any bone that was laid down was fully formed.

Oehme (8) still later experimented on growing dogs with a calcium-poor diet, and found a condition of osteoporosis apparently due to the absorption of the already calcified bone to supply the calcium for the growing part. By the administration of strontium phosphate to these dogs a condition resembling rickets was produced.

Dibbelt (9) (1910) has also studied the influence of a calcium-poor diet in pregnant animals and their suckling young, and states that he has found that the tissues, but chiefly the bones, part with calcium in order to supply the needs of the foetus and young animals. The bones of the foetus remain normal, while those of the mother undergo a marked change which Dibbelt calls osteomalacia. Since the milk of animals fed on a calcium-poor diet contains less calcium, changes in the bones of the young arise. These changes are characterized by a hypoplasia of the osseous tissue, and the production of osteoid tissue, in his opinion not identical with true rickets. In this conclusion he is supported by the work of Carl Rose (10). Dibbelt remarks that these changes were as marked as those found in experiments with confined animals by Findlay (11) but the changes in Dibbelt's cases, according to his published illustrations, are nothing like so marked, either to the naked eye, or histologically, as those in Findlay's animals, which showed great widening and irregularity of the epiphyseal lines, delay in calcification and ossification and the formation of osteoid tissue, features which do not appear in Dibbelt's figures. Schmorl, who examined Findlay's specimens, pronounced the changes identical with those which occur in human rickets.

Stoeltzner (12) from an examination of all the evidence definitely rejects the view that rickets is due to a decreased supply of calcium, and, from a consideration

of the experimental work upon the influence of strontium on bone formation, concludes that the essential change in rickets is an inability of the ossifying tissue to fix calcium. He further emphasizes the fact that calcium, like strontium and phosphorus, stimulates the formation of ossific uncalcified tissue, but that, while strontium is not fixed to any great extent and leads to soft bone, calcium normally is fixed and leads to the production of hard bone.

That a deficiency in the supply of calcium is not the causal factor in rickets is further indicated by the results recorded by Watson and Noël Paton (13) on the development of rickets in young dogs. In all the pups the calcium intake was ample, and it was as great in those on separated milk as in those on whole milk. Further, it was smaller in those in the bread experiments which escaped rickets than in those on oatmeal experiments which developed it.

These observations seem to show that a calcium-poor diet produces an osteoporosis with changes in the bones which somewhat resemble, to the naked eye, those seen in rickets, but which lack the characteristic histological features.

In the next paper metabolic studies are recorded which seem to show that rickets is not due to diminished absorption of calcium from the alimentary canal.

If rickets were due to a failure in the supply of calcium, either from deficiency in the food or from imperfect absorption, a marked decrease in the lime of the blood and tissues, other than bone, should be manifest, especially as the work of Aron (14) has shown that in young dogs on a diet insufficient to allow of proper growth, the skeleton increases to a much greater extent than the other tissues, while the proper proportion of its inorganic constituents is maintained.

The Calcium Content of the Tissue and Blood.

1. *Calcium of the tissues.* Stoeltzner (5) examined the calcium content of the tissues in three rachitic children and found that the tissues other than the bones were richer in calcium than the tissues of healthy children. Brubacher (15) obtained similar results. He based his conclusions on the analyses of three non-rachitic and six rachitic children. One of the former was a premature child of twenty-eight weeks, another a dead-born of thirty-six weeks, and the remaining child was four years old. Of the six rachitic children examined, one was an example of so-called congenital rickets (? congenital syphilis) and was one month premature; one of the children was one year old, one was one year and seven months, one three years and ten months, one twelve years and eight months, and the remaining child was supposed to be under one year. He does not state the stages of the disease when the examinations were made, but since in all of them the bones contained much less ash than normally, it may perhaps be concluded that the cases were examples of active or at least unhealed rickets. The normal and rachitic material of such a series is, nevertheless, hardly comparable, and Brubacher's results cannot therefore be accepted as conclusive.

Aschenheim and Kaumheimer (16) found the calcium of the muscles of rachitic children markedly reduced. In their six cases the calcium varied from

0.0255 to 0.057 per cent. in the fat-free dried substance, against 0.065 to 0.0817 given as the normal.

2. *Calcium of the blood.* As regards the calcium of the blood many observations have been recorded with the most diverse results. This is probably because different methods of analysis have been used by different workers. Katzenellenbogen (17), using Wright's method, found no difference in the calcium content of the blood at different ages except that in the newly born it was relatively low. He found no difference between the amount of calcium in naturally and in artificially fed children. On a calcium-poor diet the percentage in the blood was decreased. In rickets the amount was found to be normal, but in spasmophilia rather decreased.

Aschenheim (18) found in adults and children 8 to 10 mg. calcium per 100 c.c. of blood. In rickets it was generally lower but in some severe cases actually higher. In osteomalacia it was very high.

Howland and Marriott (19) made a series of observations on the calcium content of the blood serum. They state that in almost all instances, irrespective of age, and always in infants, the calcium content was above 10 mg. and seldom more than 11 mg. In two of their seven adult cases, however, estimations of 9.2 and 9.8 are recorded. In uncomplicated rickets they say that no deviation from the normal was observed, yet their average figure for rachitic cases was 9.4 mg., and one estimation of 7.9 mg. is recorded which is distinctly below the lowest for normal infants. They estimated the calcium by a colorimetric method depending upon the decolourization of ferric thiocyanate by oxalate, a method which they admit 'requires a considerable experience in the various manipulations and in the final readings'.

Denis and Talbot (20) have recently published a paper on the calcium in the plasma of the blood of children suffering from a wide variety of diseases. They used a modification of Lyman's (21) nephelometric method and got results varying from 1.00 to 13.5 mg. per 100 c.c. plasma! The average result of all their 119 examinations was 6 to 8 mg. In the active stage of rickets readings varying from 2.0 to 8.0 were obtained, but in all the severe cases the disease was complicated by other conditions. In twenty-one cases convalescent from rickets, but also complicated with other diseases, they found variations from 4.5 to 11.2 mg. They remark that 'While in some of these cases the calcium values are distinctly below normal, the interpretation of the results is seriously complicated by the fact that several of the patients who gave low calcium values were also suffering from other maladies, (pneumonia predominating) which might also affect the calcium level in the blood. No conclusions can, therefore, be drawn from these figures.'

Lyman's method has been severely criticized by Kramer and Howland (22) on the ground of the variable results obtained in different normal individuals.

All these investigators used serum, assuming that the calcium of the blood is present in the plasma alone. They had apparently accepted the results of Abderhalden, obtained in the horse, as valid for man, although the older analyses

of Schmidt and the results recorded by Rona and Takahashi (23) seem to point to a certain proportion of the calcium being present in the blood-corpuscles. The more recent work of Cowie and Calhoun (24) gives the following results :

		Mg. Ca per 100 c.c.	
		Ox.	Man.
Whole blood		7.82	8.45
Serum		8.67	12.07
Washed corpuscles from defibrinated blood		2.07	3.47
Unwashed "	" " " "	4.98	4.26

The results of three observations made by us confirm their findings. (For method, see below.)

Age.	Ca in Mg. per 100 c.c.		Corpuscles (calculated).
	Whole Blood.	Serum.	
7 years	9.0	14.0	3.0
17 "	7.8	12.7	1.5
27 "	7.8	12.7	1.5

Taking the plasma as 56 per cent. and the corpuscles as 44 per cent. of the blood, this gives in 100 c.c.'s of whole blood the proportion of calcium in serum and corpuscles in mgs.—

		1	2	3
Serum		7.64	7.1	7.1
Corpuscles		1.36	0.7	0.7
Percentage in corpuscles		15	9	9

It is therefore manifest that calcium determinations should be made upon the whole blood, in spite of the trouble caused by the presence of iron in the corpuscles.

Present Investigations.

A. Method of Analysis.

The same method was employed all through the work for determining the calcium content of food, faeces, brain, and blood.

A known weighed amount, or in the case of blood and milk, a measured volume, of the material was dried and then ignited in a silica basin until all or most of the carbon was driven off, care being taken not to employ too great or prolonged heating. The residue was dissolved in hydrochloric acid and a little water, filtered and well washed. Any free carbon left after the treatment with hydrochloric acid was then further ignited and again treated with hydrochloric acid and water, and added to the first filtrate. To the filtrate excess of ammonium hydrate was added and then an excess of acetic acid. The calcium was thus brought into solution, and any precipitate of phosphate of iron was filtered off and well washed with hot water. Oxalic acid was added to the filtrate, precipitating the calcium as oxalate. The determination was finished in the usual way by dissolving in sulphuric acid and titrating with N/10 potassium permanganate.

B. *Results.*

1. *The Calcium Content of Muscle and Brain.* The following determinations of the calcium content of muscle and brain were made in the two litters of pups used for the observations recorded in the *British Medical Journal* (25).

Table showing Calcium Content of Muscle and Brain in Rachitic and Normal Pups in mg. per 100 gm.

Designation of Animals.	Muscle.				Brain.			
	Controls.		Rachitic.		Controls.		Rachitic.	
	Average for Litter.		Average for Litter.		Average for Litter.		Average for Litter.	
Litter 1	0.013		0.010		0.010		0.013	
	0.010	0.011	0.016	0.014	0.017	0.013	0.012	0.012
			0.016				0.011	
Litter 2	0.015		0.014		0.015		0.016	
	0.017	0.015	0.012		0.013	0.013	0.011	
	0.014		0.015	0.014	0.013		0.015	0.013
			0.013				0.012	
			0.015				0.013	
Average of all animals	0.014		0.0138		0.013		0.0127	

From the above table it is seen that, if all the controls are grouped and all the rachitic pups are put in a separate group, the average calcium content of both brain and muscle is exactly the same as in health. If, however, each litter is taken separately it is seen that in one litter the rachitic muscle is richer in calcium than that of the healthy animal, whereas the brains of the controls are slightly richer in calcium than the brains of the rachitic animals. In the other litter the calcium content of both normal and rachitic brain is alike, but the muscle in the case of the controls is slightly richer in lime. There is, however, very little difference between the healthy and diseased animals, and when the individual figures are examined the range of variation and overlap are seen to be so great that it must be concluded that neither brain nor muscle show any deviation from the normal.

2. *The Calcium Content of the Blood.* (a) *At Different Ages.*

As already indicated, Howland and Marriott, from their observations upon human serum by a colorimetric method, concluded that the calcium content of the blood is uninfluenced by age, thus confirming the conclusions of Proskauer (26). Neurath (27), however, found the calcium content highest at birth, sinking later to a lower level in the adult.

We have made a series of analyses of the whole blood in the human subject and in dogs. These are given below.

Calcium Content of Human Blood at Different Ages in Per Cent.

No.	Sex.	Age.	CaO in Blood.
1.	f.	2	0.016
2.	m.	4	0.016
3.	f.	7	0.013
4.	m.	9	0.013
5.	f.	17	0.011
6.	m.	27	0.011

Calcium Content of Blood of Dogs at Different Ages in per Cent.

No.	Age.	CaO in Blood.
1.	11 weeks	0.019
2.	11 "	0.019
3.	11 "	0.013
4.	13 "	0.015
5.	13 "	0.020
6.	Adult	{ 0.011
7.	Adult	{ 0.010
8.	Adult	0.011
9.	Adult	0.011
		0.012

These results seem to show that the calcium content of the blood is higher in young growing children and dogs than it is in the adult.

(b) In Rachitic and in Normal Pups.

The calcium content of the blood was also determined in the pups used in the experiments recorded in the *British Medical Journal* (25), and in those recorded in the *British Journal of Experimental Pathology* (13).

The following table gives the results :

Calcium Content of the Blood in the Rachitic and Normal Pups in per Cent.

Litter.	Controls.	Average per Litter.	Rachitic.	Average per Litter.	Age.
1	0.015 0.020	0.017	0.014 0.017 0.020 0.016 0.021 0.016	0.017	13 weeks
2	0.019 0.019 0.019	0.017	0.015 0.016 0.013 0.018	0.015	11 weeks
3 (a) (b) (c)			0.012 0.012 0.011*	0.012	20 weeks
4 (a) (b) (c) (d)			0.011 0.010 0.011 0.011*	0.010	17 weeks

* = rickets very slight.

Pups 3c and 4d appeared normal, but showed signs of commencing rickets by X-ray photographs although on post-mortem examination no marked softening of the bones was found. They are therefore included along with the rachitic.

These figures seem to show that in experimental rickets in dogs there is no decrease in the calcium content of the blood.

On account of the difficulty of obtaining a sufficient supply of blood for analysis from infants, we have been able to make only a few observations on the calcium content of the blood in spontaneous rickets, but the investigation is still in progress.

Conclusions.

1. Changes in bones, simulating somewhat those in rickets, can be caused by feeding on a calcium-low diet, but the condition is of the nature of osteoporosis and not true rickets.

2. The tissues other than bone in experimental rickets in dogs are not deficient in calcium.

3. The calcium content of the blood in experimental rickets in dogs shows no divergence from the normal.

4. No support is given to the view that rickets is due to a deficient supply of calcium to the bone.

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II. THE CALCIUM BALANCE IN NORMAL AND RACHITIC CHILDREN.

A. INTRODUCTORY.

In the previous part evidence was adduced which seemed to negative the view that rickets is due to a failure in the supply of calcium.

Since in experimental rickets in dogs the amount of calcium in the tissues (muscle and brain) is not markedly decreased, the diminution in the calcium content of the bone would seem most probably to be due: (1) to a failure of the growing bone to fix the lime-salts, either (*a*) supplied in the food, or (*b*) made available by the process of decalcification by which spongy bone is produced, or (2) to an exaggeration of the process of decalcification. Although the onset of late rickets and the development of cranio-tabes at first sight would seem to indicate that increased decalcification alone may be operative, these conditions may just as well be explained by a failure to use, for fresh bone formation, the lime set free in the normal process of decalcification. The fact that the manifest changes are most marked at the growing ends of the bones is rather against the idea that the process is primarily one of decalcification.

The chief evidence against the decalcification theory is the contrast in the behaviour of the metabolism of calcium in rickets and in osteomalacia, diabetes, and fasting.

In osteomalacia there is an increased output of lime which may be so marked that more is excreted than is ingested, and apparently chiefly by the urine, so that a negative balance may be produced. Goldthwait, Painter, Osgood and McCrudden (1) record the results of a metabolism experiment extending over a period of eight days in a case of osteomalacia of sixteen years of age. The intake of lime was 4.56 gm. and the total output 5.66 gm., 1.80 gm. being present in the faeces and 3.85 gm. in the urine. Neumann (2) has also published a similar investigation extending over a period of six days, in which the total intake of lime was 2.965 gm., and the total output was 2.6 gm., 1.7 gm. being excreted by the urine and 0.9 gm. by the faeces.

In diabetic acidosis, too, there is an increased output of calcium, also mainly by the urine. Von Noorden (3) has observed its occurrence, and he quotes some observations by Gerhardt and Schlesinger to the effect that the daily intake of lime in one case was 0.81 gm., and the output 1.127 gm., 76 per cent. of which was excreted by the urine. These workers noted that the administration of 20 gm. of sodium bicarbonate per diem hardly altered the total excretion, but modified the proportion present in the urine and faeces, so that only 48 per cent. was excreted by the urine. Von Noorden holds that it is only when acidosis ensues in diabetes that decalcification occurs, but Kahn and Kahn (4) have

recorded in diabetes without acidosis a negative calcium balance which must indicate decalcification.

In rickets, there is, in marked contrast to the above, a decreased amount of lime in the urine and an increased amount in the faeces (Schabad (5)), and it has therefore usually been assumed that in this disease an amount of lime larger than normal is excreted by the intestinal tract, but the difficulty of determining how much of the calcium of the faeces has simply passed through the intestine unabsorbed and how much has been excreted into the gut has always left this question undecided. The recent work of Grosser (6) on the calcium metabolism in rickets under the administration of lime-salts shows that excretion by the intestine may take place to a large extent. His experiments consisted in the administration by the mouth and subcutaneously of various lime-salts to normal and rachitic children. Some of his series of observations extend over 40 days, and each was divided into periods of 3 or 4 days, for each of which estimations of the intake and of the output of calcium by urine and faeces are given. The chief excretion was usually in the period after that during which the lime-salt had been given. In one case 120 per cent. of the intake appeared in the faeces and 0.8 per cent. in the urine. In another case 107 to 127 per cent. of the intake appeared in the faeces, and between 0.8 and 1.7 per cent. in the urine. The increased excretion by the bowel indicated from these results is confirmed by another case in which 50 per cent. of the calcium was given subcutaneously, and yet 70 per cent. of the total daily intake appeared in the faeces and only 6.0 per cent. in the urine.

It will be shown later that the amount of calcium excreted by the gut depends largely upon the amount of faeces, but in Grosser's cases the daily weight of dried faeces was practically the same throughout the observations.

These results upon children confirm those previously obtained by Ragnar Berg upon himself (7).

Schabad (5), who supports the view that decalcification occurs in rickets, argues that this is indicated by the occurrence of a negative calcium balance, but, as already indicated, such a conclusion is not warranted. He made five investigations of progressive rickets, three of three days, one of five days, and one of seven days, and it was in his experiments of three days alone that he obtained a negative balance. The danger of drawing conclusions from such short metabolic studies will be dealt with later (p. 364).

Schabad also records (*loc. cit.*) the case of a rachitic child of 6,720 grm. in which he estimated the calcium of the body, and found that it amounted to between 21 and 22 grm., whereas the normal child at birth, weighing 3,000 grm., contains about 37.5 grm.; thus, without making allowance for the addition of calcium after birth, some 15 grm. had been lost from the body. He argues that the result indicates an exaggerated decalcification, but, as already indicated, the loss of calcium might just as well be explained by a failure of the growing bone to use the calcium set free by the normal process of decalcification in ossification.

With an increased decalcification an increased calcium content of the blood might be expected unless the lime is so quickly excreted that no time is given for its accumulation. In the previous paper we have shown that, in experimental rickets in dogs at least there is practically no change in the calcium content of the blood. In osteomalacia, on the other hand, a definite increase in the calcium of the blood has been recorded by Maurice Loeper and Béchamp (8), 100 c.c. of blood containing .01 gm. of calcium, in contrast to .0065 gm. to .007 gm. in the normal individual.

The evidence is thus against rickets being due primarily to increased decalcification.

A failure to fix calcium by the bone-forming tissues may be due:

(1) To the calcium or some other constituent of bone, e.g. the phosphorus, being presented to it in abnormal form, so that the process of formation of the calcium complex characteristic of bone is prevented, or,

(2) To some change in the ossifying tissue by which the power of forming this calcium complex is lost.

Both of these might result from the existence of some generalized metabolic disturbance, which would thus bring the bone condition into accord with the general disturbance of health seen in rickets.

A study of the calcium balance cannot prove or disprove any of these possibilities, but, as a preliminary to an attempt to investigate them, it is necessary to have a knowledge of how far and in what respects the metabolism of calcium in rickets differs from the normal.

A very large number of observations upon this has been recorded. Some of the more important of these have been referred to in the introduction to 'A Study of Social and Economic Factors in the Causation of Rickets' (9).

A study of these records, however, shows that in many cases the conclusions drawn are unwarranted, because certain disturbing factors have not been sufficiently considered in the observations made. Of these we find that the following are the most important: (1) the short period of many of the studies; (2) the influence of age on retention of calcium; (3) the relationship of the retention of calcium to the intake; (4) the effect of the nature of the calcium compound ingested, and (5) the stage of the disease.

1. The Danger of Short Period Studies of Calcium Metabolism. The Relationship of Calcium Output to the Weight of the Faeces.

Consideration of the results of previous investigations and of our own early experiments has shown us that in the study of the metabolism of such a substance as calcium it is dangerous to draw conclusions from experiments extending over short periods such as three days. The difficulty of carrying on metabolic experiments on children for more prolonged periods probably accounts for so many workers being content with such brief studies.

As already indicated, the excretion of calcium in rickets, in contrast to that

in osteomalacia and diabetes, is mainly by the gut, some 96 per cent. of the whole being passed in the faeces.

One of us (J. S.) soon found that in each case the calcium formed a fairly fixed percentage of the dry faeces (Tables I, II, III, and IV), and, since the weight of faeces varies considerably from day to day, the calcium output also varies. Hence, if a day on which a large motion is passed falls within a short period of observation a fallacious negative balance may result.

The following observations illustrate these points, which are also substantiated by the results of studies recorded later in this paper. See also Charts I and II.

TABLE I (Waite). *Early Rickets.*

Day.	Amounts in Grm.				
	Intake CaO.	Wt. of Dry Faeces.	CaO in Faeces.	% of Dry Faeces.	Quantity Retained.
1	1.70	17.2	1.97	11.48	-0.27
2	1.70	16.4	1.68	10.24	0.02
3	1.70	13.8	1.29	9.38	0.41
4	1.70	11.25	0.84	7.50	0.86
5	1.70	11.25	0.84	7.50	0.86
6	1.70	16.6	1.64	9.88	0.06
7	1.70	3.9	0.36	9.40	1.34

CHART I. Showing relationship of CaO to weight of faeces. Weight of CaO output in gm. on left ordinate. Weight of dried faeces in gm. on right ordinate. Days on abscissa. (CaO output drawn to eight times the scale of the dried faeces weight.) The average of 4 and 5 is expressed as a single point.

TABLE II (H.). *Normal.*

Day.	Amounts in Grm.				
	Intake CaO.	Wt. of Dry Faeces.	CaO in Faeces.	CaO % of Dry Faeces.	Quantity Retained.
1	1.81	5.0	0.765	15.33	1.045
2	1.67	10.0	1.430	14.33	0.240
3	1.74	4.0	0.664	16.66	1.076
4	1.83	14.8	2.131	14.47	0.301
5	1.67	7.5	1.057	14.19	0.613
6	1.84	5.3	0.800	15.12	1.040
7	1.79	17.1	2.479	14.58	-0.689
8	1.67	7.1	1.036	14.61	0.634
9	1.72	12.5	1.875	15.00	-0.155
10	1.90	5.6	0.677	12.18	1.223
11	1.72	8.5	1.190	14.00	0.530
12	1.72	5.0	0.710	14.25	1.010

Had the first three days been taken alone, a positive balance of only 0.05 gm. per day would have appeared, while the last three days would have

indicated a daily positive balance of no less than 0.75 gm. In striking a balance the inclusion of the last day would introduce a manifest error.

But perhaps the most marked example is afforded by the study of H., ♀, 8 $\frac{3}{4}$ months old, where the increased excretion of CaO in the days when a large amount of faeces were passed is strikingly shown.

Had the study in this case been made upon the 7th, 8th, and 9th days, a negative balance of 0.210 gm., or 0.07 per day, would have appeared, while the next three days would have given a positive balance of 2.763 gm. or 0.921 per day.

CHART II. Showing relationship between CaO output and the weight of dried faeces, in case of Child H. (CaO output drawn to four times the scale of weight of dried faeces.) Day periods on abscissa.

TABLE III (Calligan). *Tetany.*

Day.	Intake CaO.	Wt. of Dry Faeces	CaO in Faeces.	CaO % of Dry Faeces.	Quantity Retained.
1	3.38	27.8	2.79	10.05	0.59
2	3.38	22.6	1.77	7.86	1.51
3	3.38	20.5	2.32	11.34	1.06
4	3.38	6.8	0.77	11.39	2.61
5	3.38	20.7	1.95	9.30	1.43
6	4.50	26.4	3.04	11.53	1.46
7	4.50	25.2	2.85	11.34	1.65
8	4.50	23.7	2.92	12.34	1.58

TABLE IV (McArdle). *Rickets.*

Day.	Intake CaO.	Wt. of Dry Faeces.	CaO in Faeces.	CaO % of Dry Faeces.	Quantity Retained.
1	1.77	10.0	1.32	13.21	0.45
2	1.77	9.0	1.00	11.14	0.77
3	1.77	6.2	0.61	9.99	1.16
4	1.77	3.6	0.37	10.38	1.40
5 and 6	3.54	19.2	1.92	10.05	1.62
7	1.77	4.5	1.48	10.72	1.29

These results are fully borne out by an analysis of the cases recorded by Orgler (10).

Conclusion. Since the excretion of the calcium in the faeces varies with the weight of the dry faeces, and since the latter varies considerably from day to day, studies of calcium metabolism over periods of three days are unreliable.

2. *The Influence of Age on the Calcium Balance and on the Excretion by the Faeces and Urine.*

(A) *Age*.—In certain of the investigations recorded the influence of age upon the calcium metabolism has not been sufficiently recognized, and although rickets chiefly affects children under 3 years of age, the occurrence of cases of late rickets at a more advanced age renders it necessary to consider the normal retention of lime at different ages.

Many studies are available, but in comparing them with one another and with our own results, not only have the possible disturbing elements of differences in the diets and in the amount of calcium contained to be taken into account, but the differences in the weights of the individuals must also be considered.

To render a comparison possible the intake, output, and retention must therefore be expressed in relationship to unit of weight. Accordingly, not only in our own cases, but in our study of the results of others, we have, as far as possible, calculated the findings in terms of per kilo body weight.

Throughout this paper we use the terms 'utilization' of calcium and calcium 'available' to mean the difference between the calcium ingested and that excreted in the faeces. While in infants this practically represents the amount retained, since over 96 per cent. is excreted in the faeces, in older individuals this is not the case, since, as age advances, an increasing proportion is excreted in the urine. (See p. 370.)

(a) *Previous Investigations.*

Details with reference to authorship and place of publication, &c., of previous work considered by us are given in Appendix III. In the discussion of findings, and in the charts on pp. 368 and 369 this material has been combined and averages drawn.

The cases during infancy, i. e., until one year of age, have been divided into two groups according to whether the children were naturally or artificially fed, because, although the intake of calcium in the case of breast milk is decidedly less than in the case of cows' milk, the utilization of the calcium, as shown by Langstein and Meyer (11), is better. The difference between the percentage retention of breast-fed and bottle-fed infants is made most striking when the amounts are expressed in terms of unit of body weight (Chart III).

The series of breast-fed infants considered comprised only children under six months of age. In the newborn infant the intake averaged 0.014 and the retention 0.013 gm. per kilo; under one month the intake was 0.08 and the retention 0.05 gm.; for children from one to three months the intake averaged 0.11 and the retention 0.041 gm.; and from three to six months of age the intake was 0.063 and the retention 0.030 gm. per kilo of body weight.

Studies of a much larger series of children (Chart III) fed upon cow's milk are available. The intake was very much greater, above one month being 0.12 to 0.21 gm. per kilo, but the retention, on the other hand, distinctly less, being between 0.021 and 0.032 gm. per kilo. In spite of the variation of intake and the declining intake per kilo from three months onwards, the retention per kilo remained remarkably constant. It would seem from these previous observations that in the healthy infant during the first year of life, although the retention varies to some extent with the intake, it is fairly constant, averaging between 0.02 and 0.03 per kilo of body weight.

CHART III. Showing average CaO intake and CaO retention, per kilo body weight at different ages, in healthy children fed on human and on cow's milk, recorded by previous investigators. Grm. per kilo body weight on ordinate. Age of children and number of cases on abscissa.

CHART IV. Showing relationship of utilization of CaO to intake in authors' healthy cases, compared with those recorded by previous observers (Ahlqvist, Schabad, and Herbst) from 2 to 13 years, expressed in gm. per kilo body weight per diem.

In healthy children over one year of age (Chart IV) the intake of calcium per kilo was found gradually to decline, reaching at 7 years about 0.05 gm., owing to the fact that as the children got older the calcium-rich milk became less and less the predominant constituent of the diet; nevertheless, the amount retained remained fairly constant, though varying somewhat with the intake. As age advanced the percentage utilization of the calcium was found to increase, so that on Chart IV the lines showing intake and output, though gradually declining, tend to converge.

(b) *Present Observations.*

We are fortunate in being able to record a very full series of observations on the calcium metabolism in normal individuals at different ages (Chart V). Those made on infants and children under 4 years of age were carried out specially

to afford a normal standard for the study of the metabolism in rickets, while those on older subjects were made in the course of an investigation on the digestibility of bread from flour of different milling standards (Appendices I and II).

The studies may be divided into four groups: (1) those on infants under one year; (2) those on children under 4 years of age on a diet chiefly of

CHART V. Relationship of CaO intake to utilization in authors' healthy individuals from 6 months to 44 years. Grm. per kilo body weight on ordinate. Age on abscissa.

milk; (3) those on boys from 4 to 12 years, fed on bread and milk; and (4) those on older persons taking a more mixed diet. The results may be briefly summarized in the following table:

Calcium in Grm. per Kilo as CaO.

Age in Years.	Intake.	Output in Faeces.	% Utilized.
0-1	0.23	0.15	35
2-4	0.17	0.13	23
8-12	0.07	0.03	57
12-13	0.037	0.02	52
16-17	0.030	0.006	80
18-48	0.025	0.01	40

The utilization of calcium is thus fairly proportionate to the rate of growth, showing a marked increase beginning about the eighth year and reaching a maximum just before puberty. This, however, does not necessarily mean an increased retention since the excretion by the urine increases as age advances (p. 370).

In Charts IV and V these findings have been graphically represented. When the observations of previous workers are recalculated and drafted in the same way they are found to be in general accord with the authors' results.

Chart V shows a steady decline in intake as age advances, the fall being most rapid during the earlier years of life. The availability, generally, is proportionate to the intake. (See next section.)

(B) *The Relative Amount of Calcium excreted by the Faeces and Urine at Different Ages.*—Previous investigators have observed the fact that the proportion of calcium excreted by the urine increases as age advances.

This simply means that in older individuals any surplus absorbed over that

required for growth and metabolism of bone is got rid of by the kidneys instead of by the bowel as in infants. This is very clearly shown in the following table which gives the results of seven-day observations made upon two normal children, and upon five older males used for experiments on the digestibility of various breads.

CaO Excretion by Urine in Normal Individuals.

Name.	Age.	CaO in grms.		% Excreted by Urine.
		In Diet.	In Urine.	
Dodds	8	1.99	0.18	9.0
Lawson	9½	1.99	0.15	7.6
F. M.	12	1.22	0.09	7.3
Don. B.	13	1.25	0.11	7.4
J. W.	17	1.28	0.34	26.6
D. B.	34	1.22	0.27	21.6
J. R. T.	44	1.22	0.33	27.0

The comparatively large proportion of calcium excreted in the urine after the age at which growth has nearly ceased is clearly demonstrated. This leads to a decreased retention of the calcium absorbed.

Conclusions. 1. The large intake during the first year of life, about 0.2 gm. per kilo, is due to the purely milk diet. The retention or utilization is high and is almost 35 per cent. of the intake. This is considerably higher than the average of cases previously observed.

2. Between the age of 1 and 4 years, through the increased size of the child, the relatively lower caloric demands, and the fact that cereal foods are added to the milk, the intake of calcium is lower, about 0.17 gm., and the utilization is correspondingly reduced, being about 23 per cent. of the intake.

3. Between 8 and 12 years of age, the intake is still smaller, 0.07, but the amount utilized is hardly, if any, less than during the earlier age period, and there is thus a better percentage utilization of calcium—about 57 per cent.

4. Between 1 and 10 years a utilization of between 0.03 and 0.05 gm. CaO per kilo body weight seems to meet the requirements of the child.

5. From 12 to 13 years of age the intake per kilo body weight falls further (0.037), as does the utilization, but not proportionately, the percentage utilization of the calcium being still high—almost 52 per cent.

6. The intake per kilo remains about the same till just before puberty, when the utilization is still higher. It may amount to about 80 per cent. But at this period the excretion by the urine shows a marked increase.

7. In adult life the intake falls and the utilization is reduced.

8. The high intake of calcium in infants and young children on a diet of cow's milk is due to the proportion of calcium being unduly high in relationship to the energy value of the milk. Cows' milk has 0.14 per cent. of CaO, while human milk contains about 0.03 per cent., but the energy value per litre is practically the same.

3. *The Relationship of the Utilization of Calcium to the Intake.*

In comparing the investigations of different workers with one another it is found that the influence of the amount of calcium in the food per unit of body weight upon the calcium balance has not received due consideration.

The results just recorded on the effect of age on the utilization of calcium show that, calculated per kilo of body weight, there is, at least over short periods, not only a relationship between the age and the utilization of calcium, but also between the amount ingested and utilization. This is most strikingly shown in Cases 1 of the normal series, and in 2, 5, and 7 of the rachitic series (Summary Table, p. 378); and is also indicated in Chart VII, where the intake and utilization in both the normal and rachitic cases are arranged in order of intake, irrespective of age; and in Chart IV in which our own results and those based upon the recalculation of the results of previous investigators are compared.

In adults the same relationship between intake and availability or utilization holds, as will be seen by the following table constructed from our bread experiments. The number after the initial indicates the bread which was used. (Appendix I.)

Initials.	Age.	Intake.	Utilized.	% Utilized.
J. W. 1	17	0.037	0.033	83
J. W. 2	17	0.032	0.024	74
D. B. 1	33	0.032	0.026	58
J. B. 1	17	0.029	0.025	86
J. R. T. 1	43	0.028	0.018	50
J. R. T. 2	43	0.026	0.012	46
D. B. 2	33	0.024	0.015	59
J. B. 2	17	0.025	0.017	66
J. W. 3	17	0.025	0.016	65
J. B. 3	17	0.023	0.016	69
D. B. 3	33	0.022	0.009	39
J. R. T. 3	43	0.019	0.008	39

As to whether Stoeltzner's (*loc. cit.*) suggestion that the increased supply of calcium acts as a stimulant to ossification, and thus increases the deposition of calcified bone, is right; we have no evidence. There is, undoubtedly, evidence that there may be brought about a temporary accumulation of lime salts which, however, are later excreted. The results of many investigators suggest this, but perhaps the clearest evidence is afforded by those of Grosser (*loc. cit.*).

Conclusion. The utilization of calcium tends to vary directly with the supply in the food.

4. *The Character of the Food.*

Although most of the children who develop rickets are still upon a diet mainly consisting of milk, the possible effects of variation in the food constituents must be considered in comparing the results of different studies.

As already indicated, the percentage utilization of calcium in human milk is better than in cows' milk (p. 367). The reason for this is not apparent.

From experiments upon dogs fed upon horse-flesh Kochmann and Petzsch (12) concluded that an increase of the proteins, and the addition of starch or fat to the food leads to a smaller retention of calcium, but the results recorded hardly justify this conclusion. They argue that this is not due to decreased absorption but to some influence upon intermediate metabolism, by which more lime is set free from the store in the bones and excreted.

It is difficult to see how the absorption of lime from the gut can be modified by the protein or carbohydrate content of the diet, but the ready formation of insoluble calcium soaps of the higher fatty acids renders it possible that the amount of fat in the diet may modify the absorption of lime.

The fact that under normal conditions the faeces contain an amount of phosphoric acid sufficient to combine with nearly all the calcium as tri-calcium phosphate renders it improbable that calcium soaps are normally formed to an extent to carry off much of the calcium. The amount of calcium in such soaps is usually between 10 and 20 per cent., and thus generally over 80 per cent. is excreted as calcium phosphate.

Kochmann and Petzsch found that the addition of 50 grm. of fat to the diet of the dog, while decreasing the absorption of lime, did not alter the proportion of P_2O_5 to CaO in the faeces.

Telfer (13) finds that increasing the milk-fat from 21.6 grm. per diem to 43.2 grm. does not modify the absorption and retention of calcium.

The fatty acids are probably absorbed as rapidly as they are formed and only, as in the case of obstruction to the passage of bile to the intestine and probably in pancreatic disease when their amount in the gut is enormously increased, do they displace the phosphoric acid by forming calcium soaps. The phosphoric acid is then absorbed and excreted in the urine. This has been shown to be the case in congenital obliteration of the bile ducts by Telfer. (Paper appearing in *The Biochemical Journal*.)

Hutchison's observations (14) have demonstrated that in rickets there is no decrease in the digestion and absorption of fats.

The possibility of the disease being associated with an increased excretion of calcium soaps by the bowel may therefore be dismissed.

The contention of Orgler (15) and Freund (16) that certain fats have a more prejudicial action on the retention of lime than have others has been tested by Telfer (13) in this laboratory. His results show no differences in the calcium retention with similar amounts of butter-fat and of cod-liver oil.

Conclusions. 1. The calcium of human milk is utilized to a greater proportion than that in cows' milk.

2. The increase of milk-fat does not decrease the utilization of calcium in either normal or rachitic children since, apparently, the fatty acids are rapidly absorbed, and only about one-tenth of the total calcium is combined in soaps.

3. When the digestion and absorption of fat is arrested, as in obliteration of the bile ducts, the proportion of lime combined in soaps in the faeces is large, and a diminished utilization probably results.

5. *Stage of Disease.*

Some of the older workers on the metabolism in rickets gave too little consideration to the stage of the disease at which the observations were made.

Schabad (5) drew attention to the varying degree of retention of calcium according to the stage of the disease and produced evidence to show (1) that it is only in the early stages that a negative balance is obtained, but (2) that in fully developed rickets the retention is positive although below the normal, and (3) that in healing rickets the retention of calcium is definitely above the normal. These conclusions have been already referred to and the danger of accepting the results of short-period studies has been indicated.

From the chronic nature of the disease, it is clinically impossible to decide in any case of rickets whether the process is progressing or healing, in fact, it may be progressing at one place and healing at another, and therefore it is only on the grounds of probability that cases can be selected for investigation. It is, of course, more likely that in the younger cases the disease is early and progressive, while, in older children, there is always a greater possibility of the disease being either advanced or tending towards recovery, although it might be some time before the clinical changes are sufficiently marked to be appreciated. This is a criticism that may be raised against the selection of the series of cases recorded in this paper, but we purposely chose those with marked clinical signs and symptoms.

There is at least some indication that the most severe disturbances in metabolism may precede the appearance of symptoms. Birk and Orgler (17) record the case of a breast-fed infant which gave a negative calcium balance at the age of $1\frac{1}{2}$ months, but which presented no clinical manifestations of rickets till the age of $4\frac{1}{2}$ months, although at $2\frac{1}{2}$ months and $4\frac{1}{2}$ months metabolic studies revealed daily calcium retentions of 0.079 and 0.071 gm. We have also had the opportunity of making a somewhat similar observation. One of our cases (Waite), chosen as a normal control because of the absence of any physical signs of rickets, at the age of eight months gave a very low positive balance of 0.05 gm. per kilo per day with an intake of 0.283 gm., but on being seen a few months later presented a most severe degree of rickets.

In the series of investigations which are now in progress we are selecting only the youngest cases with any suspicion of the disease.

B. COMPARISON OF THE CALCIUM BALANCE IN NORMAL AND RACHITIC CHILDREN.

In our series of observations, an attempt was made to guard against the various difficulties and fallacies to which attention has been drawn, as vitiating some of the previously recorded results.

(1) We have carried on the experiments for six or seven days when possible, and in the experiments of shorter duration we have had the patient upon the

diet for at least three days before the study was started. In two of the three-day observations a repetition of another three days was made.

It will at once be evident that many such prolonged studies must end in failure, some disturbance in the health of the child, e.g., vomiting, or some mistake in the feeding, or in the collection of the excreta, necessitating its termination and leading to a loss of its results.

(2) The records, both in normal and in rachitic children, have been arranged according to age so that they are comparable. They have been charted both according to age (Chart VI) and to intake of calcium (Chart VII).

(3) All the cases selected, except two of late rickets, were chosen because they appeared to be in the active stage of the disease with the characteristic symptoms well developed.

(4) The two cases of late rickets were studied on account of their comparative rarity, and on account of the possibility that in them evidence of abnormal decalcification might be discovered.

1. *Methods.*

We have estimated the calcium excreted by the faeces only, because in young children, especially female children, it is difficult to obviate some loss of urine. Since, however, in infancy, over 96 per cent. of the calcium is excreted by the bowel, the amount in the urine is of little significance. Schabad (*loc. cit.*) has shown that in the active stage of the disease the proportion of calcium in the faeces is higher than in the normal child. In the series of cases recorded by Orgler (15) the calcium in the urine in health was 1.9 per cent. of the total, whereas in rickets it was only 1.4 per cent. Such comparatively small amounts may safely be discarded, and indicate that the balance may be estimated from the calcium of the food and the faeces.

The difference between the intake in the food and the output in the faeces represents what may be called the 'available' calcium, or calcium utilized, although not necessarily the calcium retained. In comparing normal and rachitic children, as already indicated, the differences between the 'available' in the two groups may be taken as a measure of the differences between the amounts of calcium retained, except that the slightly lesser output by the urine in the case of rickets may possibly tend to magnify slightly the apparent retention.

(a) *Method of collecting faeces.* In older children no difficulty was experienced in collecting the faeces uncontaminated by urine, so long as the children were confined to bed.

For young male children, however, a special device called a 'metabolism bed' was made by having a couple of short mattresses, about 10 inches thick, placed in the bottom of the bed, and separated from one another by a distance of eight inches. The child is firmly fixed so that the buttocks are suspended over the space between these mattresses. The penis is placed into the end of

a piece of rubber-tubing, and the urine thus drained directly into a separate vessel, e.g., a urinal attached to the side of the bed. In this way urine and faeces may be collected separately.

The child is supported and kept in position by means of a firm calico arrangement, to which the child is fixed, stretched taut between the top and the bottom of the bed. The calico arrangement is composed of a body piece with

FIG. 1. Diagram of Metabolism Bed.

- A.A. Mattresses with space between.
- B. Patient.
- C. Calico arrangement.
- D. Jackinette pouch.

FIG. 2. Diagram of Calico Arrangement.

- A. Body piece with binder.
- B. Leg pieces.
- C. Tapes for stretching between top and bottom of bed.

a binder attached so that the trunk is controlled, and two leg pieces to which the legs and thighs are bandaged with the legs held slightly apart. This piece of apparatus requires to be made to fit the child, special attention being paid to the size of the body piece and width of the leg pieces. The fork is situated at the lower end of the sacrum, just at the upper end of the natal cleft. (Figs. 1 and 2.)

A blanket is lightly placed over the child with a wire cage on top, which keeps the weight of any extra bed-clothes off the child and the apparatus.

It might be expected that a child confined in this way for periods sufficiently long (seven days) to collect material for metabolism experiments would be cross and irritable. Fortunately this is not the case, and the children so confined are usually quieter than the others in the ward. So well behaved are they that one married confrère considered the advisability of providing himself with one for home use. We have had normal children admitted to the wards, treated in this way for control experiments, visited by their parents during the course of the investigation, and in no case was any opposition raised to its continuance.

(b) *Control of diet.* In the earlier experiments, when the diet was composed entirely of milk, the exact quantity to be taken by the child was measured, and samples of the morning and evening milks examined. In the later experiments, one half ounce more than the amount of the feed was measured, thoroughly mixed, and the extra half ounce removed and retained for examination along with similar samples of all feeds for 24 hours. In the case of a mixed diet, two identical meals were prepared, one for the child and one for examination; any food which the child did not consume was also retained for examination.

(c) *Method for the determination of calcium.* The same method was

employed all through the work for determining the calcium content of food, faeces, brain, muscle, and blood.

A known weighed amount or volume of the material was dried, and then ignited in a silica basin until all or most of the carbon was driven off, care being taken not to employ too great or prolonged heating. The remainder was dissolved in hydrochloric acid and a little water, filtered and washed well. Any free carbon left after treatment with HCl was then further ignited and again treated with HCl and water and added to the first filtrate. It was found by this means that no calcium was caught by the carbon. To the filtrate excess of ammonium hydrate was added and then an excess of acetic acid. The calcium was thus brought into solution, and any precipitate of phosphate of iron was filtered off and well washed with hot water. Oxalic acid was added to the filtrate, precipitating the calcium as oxalate. The determination was finished in the usual way by solution in sulphuric acid and titration with N/10 potassium permanganate.

(d) *Test of Accuracy of the Process for estimating Amount of Calcium.*

100 c.c. normal ox blood taken						
Calcium oxide content (determined)	.	.	.	.	.	0.011 grms.
Calcium oxide (pure) added	.	.	.	.	.	0.100 "
Total CaO to be recovered	.	.	.	.	.	0.111 "
Number of grm. of CaO recovered	.	.	.	.	.	0.1105 "

The estimation was then carried out in the manner described above.

2. Results.

The main results of our investigations are given in the Summary Tables, p. 378, in Appendix II, and in Charts VI and VII.

As already indicated (p. 371), in health the most striking features of the calcium metabolism are the definite relationship which the 'utilization' bears to the intake, (p. 366) and the gradual rise in the percentage utilization as age advances (see Charts IV and V).

In rickets the same features are observed. Chart VI, in which the individual rachitic figures are compared with the *averaged* figures for healthy children of the same age periods, shows a fairly close correspondence between the intake and retention per kilo body weight, and also a better percentage utilization of the lime as age advances. The correspondence between intake and retention is, however, not so absolute as in health. The older cases show a closer correspondence than the younger cases, a point which may be explained by the probability of the disease being more active and progressive in some of the latter. Perhaps the most striking feature of the rickets cases is the erratic behaviour of the utilization, e. g. a slightly increased intake may be accompanied sometimes by an increased and sometimes by a decreased utilization.

In no case was a negative balance observed, and the curve of the rachitic cases corresponds fairly closely with that found in health. In a few cases the utilization

departed from the normal standard, and an analysis of the case histories unfortunately does not always furnish an adequate explanation (see p. 378).

In Nos. 1 and 3 the retention is undoubtedly below the normal. No. 1 is the case previously referred to (p. 373), as probably resembling that described by Orgler, which gave a negative calcium balance before the clinical manifestation of rickets appeared. This was a child of eight months which seemed quite healthy and was used as a control, when a very low calcium utilization was found. On being seen four months later, however, very marked signs of rickets were present. At first sight this case would seem to indicate that the earliest sign of rickets may be a deficient calcium utilization, and to support the contention that during this period of the disease a low positive or even a negative calcium balance may occur. But the daily amount of dry faeces was high, and the large excretion of lime may be due to this.

CHART VI. Showing intake and utilization of CaO in authors' cases of rickets arranged according to age and compared with averages of authors' healthy cases. Number of rachitic cases on abscissa.

Consideration of No. 3 must include discussion of 4, as these two experiments refer to the same child—4 following on 3 at an interval of two days. In this case the calcium intake and daily weight of dried faeces were practically identical during both studies, yet in the first period (3) the retention is low, and in the other period (4) within normal limits. This case was also a young child of fourteen months with an extreme degree of rachitic deformity. It illustrates the danger of short-period experiments. The average of the two periods is probably a more correct indication of the metabolism.

Cases 10 and 11 as shown in Chart VII, where the cases are arranged according to intake, seem to have abnormally low retentions, but reference to Chart VI, in which the cases are arranged according to age, demonstrates a normal retention, and this occurred in 11, in spite of a relatively high faecal output.

Studies 5, 12, and 13 all show utilizations somewhat above the normal. Nos. 5 and 6 must be considered together as they refer to two examinations in the same child at an interval of seven days. Here, with the higher intake, there

SUMMARY							
<i>Children Normal</i>							
No.	Name.	Age in Years.	Weight in kilos.	CaO Intake in Grm.		CaO Output in Grm.	
				Daily.	Per Kilo per Day.	Daily.	Per Kilo per Day.
1.	Harby	$\frac{6\frac{1}{2}}{12}$	7.4	2.34	0.316	1.02	0.137
2.	H.	$\frac{8\frac{3}{4}}{12}$	7.7	1.75	0.228	1.23	0.159
3.	Brown	$\frac{2\frac{1}{2}}{4}$	12.8	2.02	0.158	1.64	0.128
4.	Bryson	$\frac{4}{8}$	15.9	2.86	0.180	2.01	0.126
5.	Dodds	$\frac{4}{8}$	24.0	1.99	0.083	0.87	0.037
6.	Lawson	$\frac{9\frac{1}{2}}{12}$	28.0	1.99	0.071	0.95	0.034
7.	Alexander	$\frac{9\frac{1}{2}}{12}$	26.0	1.72	0.066	0.72	0.027
8.	Jack	10	27.0	1.92	0.071	0.65	0.024
<i>Children and Adults</i>							
9.	J. W.	16	51.0	1.90	0.037	0.22	0.004
10.	J. B.	16	53.0	1.57	0.029	0.19	0.003
11.	D. B.	33	57.0	1.77	0.031	0.74	0.013
12.	J. R. T.	43	62.0	1.77	0.028	0.88	0.014
9a.	J. W.	16	51.0	1.64	0.032	0.43	0.008
10a.	J. B.	16	53.0	1.31	0.025	0.44	0.008
11a.	D. B.	33	57.0	1.51	0.026	0.82	0.014
12a.	J. R. T.	43	62.0	1.51	0.024	0.61	0.009
13.	F. M.	12	35.1	1.22	0.034	0.57	0.016
14.	Don. B.	13	30.1	1.25	0.041	0.63	0.020
9b.	J. W.	17	51.0	1.28	0.025	0.45	0.009
10b.	J. B.	17	53.0	1.25	0.023	0.38	0.007
11b.	D. B.	34	57.0	1.25	0.021	0.76	0.013
12b.	J. R. T.	44	62.0	1.22	0.019	0.74	0.012
<i>Children with Rickets</i>							
1.	Waite	$\frac{8}{12\frac{3}{4}}$	6.0	1.70	0.283	1.37	0.228
2.	McArdle	$\frac{1\frac{1}{2}}{12\frac{3}{4}}$	6.1	1.77	0.290	0.82	0.134
3.	Wilson (1)	$\frac{1\frac{1}{4}}{11\frac{1}{4}}$	6.15	1.63	0.265	1.46	0.237
4.	Wilson (2)	$\frac{1\frac{1}{4}}{11\frac{1}{4}}$	6.15	1.69	0.275	1.19	0.193
5.	Young (1)	2	7.2	1.20	0.166	0.40	0.055
6.	Young (2)	2	7.2	1.34	0.186	0.86	0.119
7.	Crombie	2	9.4	2.98	0.317	1.35	0.144
8.	Duncan	$\frac{2\frac{3}{4}}{11\frac{1}{2}}$	8.2	1.5	0.183	1.0	0.122
9.	McNeil	$\frac{2\frac{3}{4}}{11\frac{1}{2}}$	6.3	1.83	0.290	0.97	0.154
10.	Scully	3	9.0	1.43	0.159	1.14	0.127
11.	Judge	4	11.0	1.64	0.149	1.32	0.120
<i>Late</i>							
12.	Brown	7	14.2	1.60	0.113	0.43	0.030
13.	Campbell	13	37.2	3.30	0.088	0.78	0.021

TABLES.

mainly on Milk Diet.

CaO Available in Grm.			Faeces in Grm.			Diet (Milk in c.c. Bread in grm. Butter in grm.) per Day.	Duration of Experiment in Days.
Daily.	Per Kilo per Day.	%	Daily Weight	Per Kilo per Day.	% of CaO.		
1.32	0.178	56.4	13.10	1.77	7.80	Milk, 1376 with a little virol	5
0.52	0.069	29.7	8.50	1.10	14.56	Milk, 1000	12
0.38	0.030	18.8	8.15	0.64	20.21	Milk, 1190, S. Laura	4
0.85	0.054	29.7	12.80	0.80	15.67	Milk, 1701, S. Laura	4
1.10	0.046	55.3	7.80	0.32	11.39	Milk, 1000; Bread, 225; Butter, 25	7
1.04	0.037	52.2	8.60	0.31	11.00	Milk, 1000; Bread, 225; Butter, 25	7
1.00	0.039	58.1	9.80	0.38	7.40	Milk, 1000; Bread, 23; Butter, 2	7
1.27	0.047	66.1	8.50	0.31	7.70	Milk, 1,129	3

on Bread Diets.

1.68	0.033	88.4	23.20	0.45	0.96	Bread I	7
1.38	0.026	87.3	17.00	0.32	1.14	" "	7
1.03	0.018	58.2	30.90	0.52	2.43	" "	7
0.89	0.014	50.2	34.20	0.55	2.60	" "	7
1.21	0.024	73.8	39.00	0.76	1.12	Bread II	7
0.87	0.017	66.4	38.00	0.71	1.17	" "	7
0.69	0.012	45.7	47.90	0.82	1.73	" "	7
0.90	0.015	59.6	36.10	0.70	1.70	" "	7
0.65	0.018	53.3	22.10	0.63	2.66	Bread III	7
0.62	0.021	49.5	28.50	0.94	2.24	" "	7
0.83	0.016	64.8	25.10	0.50	1.82	" "	7
0.87	0.016	69.5	26.00	0.50	1.45	" "	7
0.49	0.008	39.2	30.24	0.53	2.52	" "	7
0.48	0.007	39.3	26.50	0.43	2.80	" "	7

chiefly on Milk Diet.

0.33	0.055	19.4	2.4	0.4	9.58	Milk, 1000	6
0.95	0.156	53.1	1.2	0.2	10.58	Milk, 1041	7
0.17	0.028	10.4	1.9	0.31	12.6	Milk, 931	3
0.50	0.082	29.5	1.9	0.31	10.0	Milk, 931; Bread, 62; Butter, 6	3
0.80	0.111	66.6	0.9	0.12	6.16	Milk, 883; Bread, 675; Butter, 8	3
0.48	0.067	35.8	1.7	0.24	7	Milk, 769; Bread, 81; Butter, 9	3
1.63	0.173	54.6	2.2	0.23	6.43	Milk, 1753	9
0.50	0.061	33.3	1.2	0.15	10.50	Milk, 961	4
0.86	0.136	47.0	1.7	0.27	8.40	Milk, 1000; porridge, 72.4	6
0.29	0.032	20.2	1.4	0.15	9.18	Milk, 664; Bread, 84; Butter, 9	3
0.32	0.029	19.5	1.5	0.14	8.45	Milk, 940; Bread, 114; Butter, 12	4

Rickets.

1.17	0.083	73.1	0.8	0.06	3.50	Milk, 997; Bread, 107; Butter, 10	about 3
2.52	0.067	76.3	0.4	0.01	5.04	Milk, 1247; Bread, 108; Butter, 10	„ 3

is a lower retention, in spite of the fact that for three days previous to the second period (6) and during the period the child was receiving phosphorated oil and cod-liver oil. The difference between the faecal output during the two periods explains this—the weight of the dried faeces during the second period being practically double that during the first. In estimating the influence of cod-liver oil and phosphorus on the utilization of calcium, the large somewhat loose motions which frequently accompany their administration—the persistence of which sometimes necessitates the discontinuance of the treatment—must be kept in mind.

CHART VII. Showing relationship of CaO retention to intake, expressed in gm. per kilo body weight, in authors' cases of rachitic and healthy children, arranged in order of intake. CaO in gm. per kilo body weight on ordinate. No. of cases on abscissa.

Nos. 12 and 13 were examples of late rickets in children of seven and thirteen years respectively that came under observation during the summer at a season when the disease tends towards spontaneous recovery. In No. 12 the symptoms were of nine months' duration, and in No. 13 of four months' duration, but both children greatly improved during the short period they were under observation. The high retention may in part be explained by the retrogressive nature of the lesions, but the better utilization of the lime at this age must also be borne in mind.

The results of previous workers have given rise to the general assumption that a negative balance is not infrequently obtained, and undoubtedly many experiments have been published which record it. But, as already stated, in many of the series the period of the investigation was too short, e. g. in Schabad's series it was in three-day experiments that negative balances were obtained. In other cases the negative balance could be explained by the large excretion of faeces. Chart VIII shows the maximal and minimal calcium utilization calculated from these cases, both healthy and rickety, expressed per kilo of body weight, arranged according to age. It will be seen that negative balances are recorded both in health and in rickets, and we have obtained similar results in short-period studies. In the face of such findings it cannot be maintained that a negative balance is characteristic of any stage of rickets.

In Appendix III will be found details with reference to authorship, place of

publication, diet, faecal output, &c., with the intake and output of calcium expressed per kilo body weight.

Since our work was completed we have read a paper by Holt, Courtney, and Fales (18) upon the 'Calcium Metabolism of Infants and Young Children'. From the results recorded they draw certain definite and far-reaching conclusions, but the only record of the duration of the periods of study is a statement in a previous paper upon Fat Metabolism ('Fat in the Stools of Breast-Fed Infants', p. 8) (19), where it is said: 'In eleven instances, not only was a record of the exact daily

CHART VIII. Showing maximal positive and negative retentions of CaO in health and rickets recorded by various authors. Age on abscissa. Grm. CaO per kilo body weight on ordinate.

fat intake obtained but the stools were collected for definite periods, twenty-four or forty-eight hours.'

In reply to a letter sent to Dr. Holt asking him to let us know the duration of the studies, he was good enough to write as follows: 'In most cases the values reported are averages, for two or three days; frequently for longer periods. The values for infants are mostly for three- and four-day periods; those for older children nearly all two or three days. Values for children with rickets or chronic intestinal indigestion were usually four-day periods.' The periods of study seem to us too brief. It is to be hoped that in a future publication the details of these experiments will be published so that one may be enabled to estimate the value of the conclusions.

A consideration of our results and of the work of previous investigators which we have analysed does not seem to indicate the profound disturbance in the calcium metabolism which many have assumed to be characteristic of rickets. As already indicated, we have not in any case found a negative balance over periods adequately long to allow of a reliable conclusion being drawn. In the early stages of the disease the positive balance may be low, indicating a lowered fixation of lime-salts in the bones, but as the process advances the approach of calcium balance to that in health seems to indicate that the process may still be advancing in one region while recovery may be taking place in another. While in severe cases the implication of the bone may be general, in most cases, as clinical experience indicates, it is more marked in some bones than in others.

Of the calcium taken in the food as cows' milk, only some 0.02 grm. per kilo seems capable of being utilized even in the normal infant. How much is actually absorbed from the bowel and how much is excreted into it we do not know.

In rickets the disturbance in the utilization is less marked than might be expected. In the four normal cases under four years of age, the utilization averaged 33.6 per cent. of the intake, corresponding very closely with Ahlqvist's results (20). In the eleven rachitic cases it was 35.4 per cent. In the four normal cases between eight and ten years, the utilization averaged 58 per cent. In the two cases of late rickets, aged seven and thirteen years, it averaged 74.7 per cent.

If the cases, normal and rachitic, recorded by Rothberg, Orgler, Schabad, Cronheim and Müller, Birk and Klotz, are arranged so that the ages of the two groups roughly correspond, 33 studies of 14 normal children and 25 studies of 14 rachitic children, all between $2\frac{1}{2}$ months and $10\frac{1}{2}$ months, are available for comparison.

Author.	Non-rachitic.			Rachitic.		
	Age.	Average Daily Intake.	Average Daily Retention.	Age.	Average Daily Intake.	Average Daily Retention.
	months.			months.		
Rothberg	$5\frac{1}{2}$	0.26	0.039	4	0.22	0.027
				$4\frac{1}{2}$	0.11	-0.013
				9	0.12	0.014
Orgler	$2\frac{1}{2}$	0.18	0.032	$4\frac{1}{2}$	0.06	0.020
	$2\frac{1}{2}$	0.25	0.027	$4\frac{1}{2}$	0.20	0.022
	$5\frac{1}{2}$	0.18	0.019	$6\frac{1}{2}$	0.17	0.044
	$5\frac{1}{2}$	0.20	-0.035	$6\frac{1}{2}$	0.20	0.061
	$6\frac{1}{2}$	0.18	0.019	$7\frac{1}{2}$	0.12	-0.096
	$6\frac{1}{2}$	0.25	-0.094	$7\frac{1}{2}$	0.18	0.009
Schabad	$3\frac{3}{4}$	0.047	0.023	5	0.05	0.026
				5	0.22	0.02
				6	0.05	0.013
Cronheim and Müller	4	0.22	0.044	6	0.22	0.082
	4	0.22	0.042	6	0.22	0.032
	4	0.22	0.020	6	0.21	0.064
	4	0.22	0.058	6	0.19	0.073
	4	0.22	0.029	6	0.21	0.046
	4	0.18	0.002			
	4	0.18	0.028			
	4	0.18	0.020			
	4	0.18	0.018			
	4	0.16	0.005			
	4	0.18	0.059			
	4	0.19	0.060			
	6	0.19	0.011			
	6	0.19	0.030			
Birk	9	0.12	0.056	8	0.11	0.002
	9	0.16	0.071	8	0.10	0.010
	$10\frac{1}{2}$	0.14	0.030	8	0.10	-0.008
	$10\frac{1}{2}$	0.13	0.032	8	0.09	0.006
Klotz	7	0.11	0.008	$9\frac{1}{2}$	0.14	-0.012
	7	0.13	0.008	$9\frac{1}{2}$	0.16	0.03
	9	0.10	0.005	$9\frac{1}{2}$	0.17	0.02
	9	0.09	0.004	$9\frac{1}{2}$	0.14	-0.003
	9	0.08	0.007			

Averages.	Non-rachitic.		Rachitic.	
	Intake.	Retention.	Intake.	Retention.
Rothberg	* (1) 0.26	0.039	(3) 0.15	0.009
Orgler	(3) 0.21	-0.005	(3) 0.15	0.010
Schabad	(1) 0.047	0.023	(3) 0.20	0.012
Cronheim and Müller	(4) 0.19	0.030	(2) 0.21	0.059
Birk	(2) 0.14	0.047	(2) 0.10	0.002
Klotz	(3) 0.10	0.006	(3) 0.15	0.009
Average =	(14) 0.16	0.02	(16) 0.14	0.017

* Number of Cases averaged.

This shows a percentage retention of 12.5 per cent. in case of the normal and of 12.1 per cent. in the rachitic.

The whole trend of the evidence suggests that the disturbance in the metabolism of calcium is probably not the primary factor in the disease, but that it is secondary to some other error of metabolism which is both the cause of the disturbance in the process of ossification and of the general symptoms of the disease.

3. Conclusions.

1. The 'utilization' of calcium, i. e. the difference between the intake in the food and the excretion in the faeces, in health and in rickets is fairly proportionate to the intake, but in rickets the parallelism is not so strict as in health.

2. The utilization of calcium in health and in rickets is influenced by age, the percentage utilization increasing with age up to thirteen years, but, since the excretion by the urine likewise increases, this does not necessarily mean increased retention (see p. 370).

3. The percentage of calcium in the dry faeces is a more or less fixed proportion, especially for each individual, and hence the amount excreted varies with the weight of dry faeces. Short studies of calcium metabolism are therefore of little value.

4. In rickets the utilization and retention of calcium in some cases falls below the normal, and these would seem to indicate a more progressive stage of the disease.

5. In other cases of rickets, especially in those of some duration, the retention of calcium may be above the normal for that age, probably indicating the stage of recovery.

Our thanks are due to Miss Agnew for the preparation of Appendix III.

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APPENDIX I.

Bread Experiments.

The results here recorded were obtained during a study of the digestibility of breads made from flours of different milling standards, and of mixtures of flours from wheat and maize (Report by the Food (War) Committee of the Royal Society on the Digestibility of Breads) (3206).

The breads used were :

- Bread I. 80 per cent. milled wheat-flour.
 Bread II. 90 per cent. milled wheat-flour.
 Bread III. 80 per cent. wheaten-flour and 20 per cent. maize-flour.

Diets with the amount of calcium determined in the different constituents—

Bread I.

	Daily.	CaO.
Bread	800 grm.	0.78 grm.
Mince	150 "	0.13 "
Margarine	50 "	0.00 "
Jelly	50 "	0.05 "
Café au Lait	90 "	0.48 "
Chocolate	75 "	0.13 "
Cheese	75 "	0.33 "
		1.90 "

Bread II.

Bread	800 grm.	0.46 grm.
Mince	130 "	0.11 "
Margarine	50 "	0.00 "
Jelly	40 "	0.04 "
Café au Lait	90 "	0.48 "
Chocolate	30 "	0.13 "
		1.22 "

Bread III.

Bread	800 grm.	0.46 grm.
Mince	130 "	0.11 "
Margarine	50 "	0.00 "
Jelly	40 "	0.04 "
Café au Lait	90 "	0.48 "
Chocolate	30 "	0.13 "
		1.22

APPENDIX II.

*Details of Individual Studies.**Normal.*

Name.	Age.	Days.	CaO grm.			Dried Faeces grm.			
			In Diet.	In Faeces.	Available.	Weight.	% CaO.		
James Harby	6½ months	1	2.34	0.75	1.59	10.7	7.00		
		2	2.34	1.10	1.24	12.0	9.24		
		3	2.34	1.29	1.05	15.0	8.62		
		4	2.34	1.03	1.31	14.7	7.00		
		5	2.34	0.94	1.40	13.2	7.14		
H.	8¾ months	1	1.81	0.765	1.045	5.0	15.33		
		2	1.67	1.430	0.240	10.0	14.33		
		3	1.74	0.664	1.076	4.0	16.66		
		4	1.83	2.131	-0.301	14.8	14.47		
		5	1.67	1.057	0.613	7.5	14.19		
		6	1.84	0.800	1.040	5.3	15.12		
		7	1.79	2.479	-0.689	17.1	14.58		
		8	1.67	1.036	0.634	7.1	14.61		
		9	1.72	1.875	-0.155	12.5	15.00		
		10	1.90	0.677	1.223	5.6	12.18		
		11	1.72	1.190	0.530	8.5	14.00		
		12	1.72	0.710	1.010	5.0	14.25		
Andrew Brown	2½	1	2.02	2.32	-0.30	11.2	20.72		
		2	2.02	1.95	0.07	9.4	20.87		
		3	2.02	0.30	1.72	1.5	20.21		
		4	2.02	1.99	0.03	10.5	19.04		
Charles Bryson	4	1	2.86	3.01	-0.15	19.2	15.76		
		2	2.86	0.25	2.61	1.7	15.14		
		3	2.86	2.83	0.03	17.2	16.57		
		4	2.86	1.97	0.89	13.0	15.20		
Dodds	Male	8	7	1.99	0.89	1.10	7.8	11.39	
Lawson	"	9½	7	1.99	0.95	1.04	8.6	11.00	
Alexander	"	9½	7	1.72	0.72	1.00	9.8	7.40	
Jack	"	10	3	1.92	0.65	1.27	8.5	7.70	
F. M.	(III)	"	12	7	1.22	0.58	0.64	22.1	2.66
Don B.	(III)	"	13	7	1.25	0.63	0.62	28.5	2.24
J. W.	(II)	"	16	7	1.64	0.43	1.21	39.0	1.12
J. B.	(II)	"	16	7	1.31	0.44	0.87	38.0	1.17
D. B.	(II)	"	33	7	1.51	0.82	0.69	47.9	1.73
J. R. T.	(II)	"	43	7	1.51	0.61	0.90	36.1	1.70
J. W.	(I)	"	16	7	1.90	0.22	1.68	23.2	0.96
J. B.	(I)	"	16	7	1.57	0.19	1.38	17.0	1.14
D. B.	(I)	"	33	7	1.77	0.74	1.03	30.9	2.43
J. R. T.	(I)	"	43	7	1.77	0.88	0.89	34.2	2.60
J. W.	(III)	"	17	7	1.28	0.45	0.83	25.1	1.82
J. B.	(III)	"	17	7	1.25	0.38	0.87	26.0	1.45
D. B.	(III)	"	34	7	1.25	0.76	0.49	30.24	2.52
J. R. T.	(III)	"	44	7	1.22	0.74	0.48	26.5	2.80

Normal (continued).

Name.	Age.	Weight Kilos.	Intake.		Output.		Available.		Dried Faeces.		Diet.	Dura- tion in Days.
			Daily.	Per Kilo per Day.	Daily.	Per Kilo per Day.	Daily.	Per Kilo per Day.	Daily Weight.	Per Kilo per Day.		
J. W.	16	51.0	1.90	0.037	0.22	0.004	1.68	0.033	23.20	0.45	Bread I	7
J. B.	16	53.0	1.57	0.029	0.19	0.003	1.38	0.026	17.00	0.32	"	7
D. B.	33	57.0	1.77	0.031	0.74	0.013	1.03	0.018	30.90	0.52	"	7
J. R. T.	43	62.0	1.77	0.028	0.88	0.014	0.89	0.014	34.20	0.55	"	7
J. W.	16	51.0	1.64	0.032	0.43	0.008	1.21	0.024	39.00	0.76	Bread II	7
J. B.	16	53.0	1.31	0.025	0.44	0.008	0.87	0.017	38.00	0.71	"	7
D. B.	33	57.0	1.51	0.026	0.82	0.014	0.69	0.012	47.90	0.82	"	7
J. R. T.	43	62.0	1.51	0.024	0.61	0.009	0.90	0.015	36.10	0.70	"	7
F.M.	12	35.1	1.22	0.034	0.57	0.016	0.65	0.018	22.10	0.63	Bread III	7
Don. B.	13	30.1	1.25	0.041	0.63	0.020	0.62	0.021	28.50	0.94	"	7
J. W.	17	51.0	1.28	0.025	0.45	0.009	0.83	0.016	25.10	0.50	"	7
J. B.	17	53.0	1.25	0.023	0.38	0.007	0.87	0.016	26.00	0.50	"	7
D. B.	34	57.0	1.25	0.021	0.76	0.013	0.49	0.008	30.24	0.53	"	7
J. R. T.	44	62.0	1.22	0.019	0.74	0.012	0.48	0.007	26.50	0.43	"	7

Rickets.

Name.	Age.	No. of Days.	CaO gm.		Available.	Nature.	Diet.		Dried Faeces grm.	
			In Diet.	In Faeces.			Amount per day grm. c.c.	Daily Weight.	% CaO.	
Wait	$1\frac{1}{2}$	1	1.70	1.97	0.27	Milk	1000	17.2	11.48	
		2	1.70	1.68	0.02		1000	16.4	10.24	
		3	1.70	1.29	0.41		1000	13.8	9.38	
		4 and 5	3.40	1.68	1.72		1000	11.25	7.50	
		6	1.70	1.64	0.06		1000	16.6	9.88	
		7*	1.70	0.36	1.34		1000	3.9	9.40	
McArdle	$1\frac{1}{2}$	1	1.77	1.32	0.45	Milk	1041	10.0	13.21	
		2	1.77	1.00	0.77		1041	9.0	11.14	
		3	1.77	0.61	1.16		1041	6.2	9.99	
		4	1.77	0.37	1.40		1041	3.6	10.38	
		5 and 6	3.54	1.92	1.62		1041	9.6	10.05	
		7	1.77	0.43	1.29		1041	4.5	10.72	
Wilson (I)	$1\frac{1}{2}$	3	1.63	1.46	0.17	Milk	1. 1083 2. 826 3. 997	1. 9.0 2. 11.5 3. 16.0	12.06	
							av. 968	av. 12.2		

* This day is not included in the summary average.

Wilson (II) 2 days after (I)	1½	3	1.69	1.19	0.50	Milk, Bread, and Butter	1. 912+85 2. 912+59 3. 969+60.5 av. 931+68.1	1. 16.5 2. 11.0 3. 8.2 av. 11.9	10.0
Young (I)	2	3	1.2	0.4	0.8	Milk, Bread, and Butter	1. 741+110 2. 655+64 3. 655+77 av. 683+83	1. 10.5 2. 3.5 3. 6.0 av. 6.7	6.16
Young (II) 2 days after (I)	"	3	1.34	0.86	0.48	Milk, Bread, and Butter + 3 drms. per day of Olei phos.	1. 855+78 2. 570+89 3. 883+103 av. 769+90	1. 15.0 2. 7.0 3. 15.0 av. 12.3	7.0
Crombie	2	9	2.98	1.35	1.63	Milk	1753	21.0	6.43
Duncan	2½	4	1.5	1.0	0.5	Milk	1. = 855 2. = 912 3. = 1111 4. = 969 av. 961	1. = 8.5 2. = 9.5 3. = 12.3 4. = 8.2 av. 9.6	10.50
McNeil	2½	6	1.83	0.97	0.86	Milk and Por- ridge	av. 1000 " 72.4	11.6	8.40
Scully	3	3	1.43	1.14	0.29	Milk, Bread, and Butter	1. 712+105 2. 627+109 3. 655+66 av. 664+93	1. 20 2. 7.9 3. 9.4 av. 12.4	9.18
Judge	4	3	1.64	1.32	0.32	Milk, Bread, and Butter	1. 997+125 2. 855+139 3. 969+114 av. 940+126	1. 12 2. 25 3. 10 av. 15.7	8.45
<i>Late Rickets.</i>									
Brown	7	3	1.60	0.43	1.17	Milk, Bread, and Butter	av. 997 av. 117	12.3	3.50
Campbell	13	3	3.3	0.78	2.52	Milk, Bread, and Butter	1. 1339+112 2. 1243+130 3. 1153+112 av. 1246+118	1. 14.2 2. 13.5 3. 18.7 av. 15.5	5.04

APPENDIX III.

Records of Previous Investigations of Calcium Metabolism from which Charts IV and VI were constructed.

Author.	Reference.	Name.	Age.	Con- dition.	Diet.	Aver- age Wt. in Grm.	Dura- tion of Experi- ment in Days.	Aver- age Daily Wt. of Dried Faeces in Grm.	Aver- age Daily Intake per Kilo Body Wt. in Grm.	Average Daily CaO Re- tent ion per Kilo Body Wt. in Grm.
Birk	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1910, ix. 595	I	Newborn	Healthy	Colostrum	3870	5	2.44	0.019	0.014
"	"	III	"	"	Human milk	3470	4	3.22	0.018	0.012
"	"	I (a)	"	"	$\frac{1}{2}$ milk + $\frac{1}{4}$ water + 5 % milk sugar	3620	3	3.4	0.04	0.025
"	"	II (a)	"	"	"	3120	2 $\frac{1}{2}$	4.5	0.28	0.017
"	"	II (b)	4 d.	"	"	3030	2	5.5	0.63	—
Michel	<i>L'Obstétrique</i> , 1896 (quoted by Schabad)	I	5 d.	"	Human milk	3770	3	—	0.07	0.055
"	"	III	5 d.	"	"	2730	4	—	0.09	0.047
Birk	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1911, x. 1	I (b)	6 d.	"	$\frac{1}{2}$ milk + $\frac{1}{4}$ water + 5 % milk sugar	3560	3	2.73	0.07	0.031
Michel	<i>L'Obstétrique</i> , 1896 (quoted by Schabad)	IV	7 d.	"	Human milk	3590	6	—	0.08	0.054
"	"	II	11 d.	"	"	4440	3	—	0.07	0.045
Schlossmann	<i>Arch. f. Kinderh.</i> , Stuttg., 1904, xl. 1	Kubitz	1 m.	"	"	2480	5	—	0.14	0.06
"	"	Kriesch	1 $\frac{1}{2}$ m.	"	"	4200	5	—	0.1	0.04
"	"	Winter	1 $\frac{1}{2}$ m.	"	"	4540	5	—	0.09	0.05
Tobler u. Noll	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1910 ix. 210	Kurt K.	2 $\frac{1}{2}$ m.	"	"	4000	6	4.0	0.06	0.013
Orgler	"	Herbert G. (1)	2 $\frac{1}{2}$ m.	"	$\frac{1}{2}$ milk + $\frac{1}{4}$ Schleim + 5 % sugar	3885	3	5.5	0.18	0.032
"	"	Herbert G. (2)	2 $\frac{1}{2}$ m.	"	Same diet + 1 gr. calc. acet. p. d.	4015	3	6.1	0.25	0.027
Michel et Perret	<i>Bull. de la Soc. d'Obstét. de Paris</i> , 1899 (quoted by Schabad)	—	3 m.	"	Human milk	4760	3	—	0.08	0.037
Meyer	<i>Biochem. Zeitsch.</i> , Berlin, 1908, xii. 422	Kind A. (1)	3 m.	"	Milk, <i>Haferschleim</i> , sugar	5690	3	2.64	—	0.01
Bruck	"	Kind A. (2)	3 m.	"	Milk, <i>Haferschleim</i> , sugar	5680	3	2.89	—	0.01

Bruck	Monats. f. Kinderh., Leipz. u. Wien, 1908, vi. 570	—	3 m.	"	Milk, Mehlsuppe, sugar	3400	4	—	0.087	0.043
Schabad	Arch. f. Kinderh., Stuttg., 1910, lii. 46.	—	3½ m.	"	Human milk	7685	3	—	0.047	0.023
Cronheim	Biochem. Zeitsch., Berlin, 1908, ix. 76.	Lo. (1)	4 m.	"	Milk + water	3890	4	6.1	0.22	0.044
und Müller					+ sugar					
"	"	"	4 m.	"	"	3983	4	7.06	0.22	0.042
"	"	"	4 m.	"	"	4092	4	7.48	0.22	0.020
"	"	"	4 m.	"	"	4129	4	6.90	0.22	0.058
"	"	"	4 m.	"	"	4186	4	6.47	0.22	0.029
"	"	"	4 m.	"	"	7897	4	11.36	0.18	0.002
"	"	"	4 m.	"	"	7997	4	10.75	0.18	0.028
"	"	"	4 m.	"	"	8157	4	11.77	0.18	0.020
"	"	"	4 m.	"	"	8300	4	11.62	0.18	0.018
"	"	"	4 m.	"	"	8453	4	12.17	0.16	0.005
"	"	"	4 m.	"	"	6918	4	—	0.18	0.059
"	Jahrb. f. Kinderh., Leipz., 1909, lvii. 45	II (a)	4 m.	"	¾ milk + milk					
"					sugar					
"	"	"	4 m.	"	"	6923	4	—	0.19	0.06
Blauberg	Zeits. f. Biol., Münch. u. Leipz., 1900, xl. 36	II (b)	5 m.	"	milk + water	6770	6	—	0.04	0.025
Rothberg	Jahrb. f. Kinderh., Leipz., 1907, lxvi. 69	Halm	5½ m.	"	Skim milk + milk	5195	3	—	0.26	0.039
"					sugar					
Orgler	Monats. f. Kinderh., Leipz. u. Wien, 1911, x. 373	Max G. (1)	5½ m.	"	¾ milk + ½ Mehlsuppe + 5 % sugar	6740	3	6.52	0.18	0.019
"	"	"	5½ m.	"	Same diet + 1 gr. calc. acet. p. d.	6825	3	9.2	0.20	—0.035
"	"	Max G. (2)	6 m.	"	¾ milk + milk	6598	4	12.66	0.19	0.011
Cronheim	Jahrb. f. Kinderh., Leipz., 1903, lvii. 45	I (b)	6 m.	"	sugar					
und Müller					"					
Klotz	"	"	6 m.	"	½ milk + ½ Mehlsuppe + malt	6597	4	12.66	0.19	0.03
"	"	"	6 m.	"	"	4200	3	7.52	0.18	0.014
Orgler	Monats. f. Kinderh., Leipz. u. Wien, 1911, x. 373	G. K. (2)	6 m.	"	Soured milk	4200	3	6.42	0.16	0.05
"	"	Kurt S. (1)	6½ m.	"	½ milk + ½ Schleim + 5 % sugar	3990	3	5.1	0.18	0.019
"	"	"	6½ m.	"	Same diet + 1 gr. calc. acet. p. d.	4075	3	8.45	0.25	—0.094
Klotz	Jahrb. f. Kinderh., Leipz., 1909, lxx. 1	H. W. (1)	7 m.	"	½ skim milk + ½ Mehlsuppe + malt	6580	3	9.4	0.11	0.008
"	"	"	7 m.	"	"					
Bruck	Monats. f. Kinderh., Leipz. u. Wien, 1908, vi. 570	H. W. (2)	8½ m.	"	Soured milk	6500	3	6.0	0.13	0.008
"	"	"	8½ m.	"	"	5600	—	—	0.13	0.05
Birk	"	"	9 m.	"	½ milk + ½ Mehlsuppe + 40 gr. malt sugar	5640	3	6.9	0.12	0.056

APPENDIX III (continued)

Author.	Reference.	Name.	Age.	Con- dition.	Diet.	Aver- age Daily Wt. of Dried Faeces.	Aver- age Daily CaO Intake per Kilo Body Wt.	Average Daily CaO Re- tentio per Kilo Body Wt.
Birk	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1908, vii. 450	Sch. (2)	9 m.	Healthy	Same diet + cod oil + phosph. oil	8.2	0.16	0.071
Klotz	<i>Jahrb. f. Kinderh.</i> , Leipz., 1909, lxx. 1	— (1)	9 m.	"	$\frac{1}{2}$ milk + <i>Mehlsuppe</i> + 60 gr. malt	7.7	0.1	0.005
"	"	— (2)	9 m.	"	"	6.0	0.09	0.004
"	"	— (3)	9 m.	"	"	4.13	0.08	0.007
Meyer	<i>Biochem. Zeits.</i> , Berlin, 1908, xii. 422	B. (1)	10 m.	"	$\frac{3}{8}$ milk + $\frac{1}{3}$ <i>Schleim</i> + sugar	2.70	0.15	0.012
Birk	"	B. (2)	10 m.	"	$\frac{1}{2}$ milk + $\frac{1}{2}$ <i>Mehl-</i> <i>suppe</i> + 40 gr.	4.46	—	— 0.0002
"	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1908, vii. 450	K. (1)	10 $\frac{1}{2}$ m.	"	"	7.3	0.14	0.03
"	"	K. (2)	10 $\frac{1}{2}$ m.	"	Same diet + cod malt sugar	11.8	0.13	0.032
Ahlqvist	<i>Studien über den Stoffwechsel</i> , Skand. <i>Arch. f. Physiol.</i> , Leipz., 1916, xxxiv. 1	Erik I	3 y. 6 m.	"	oil + phosph. oil Mixed diet	17.232	0.1074	0.0301
"	"	Erik II	3 y. 6 m.	"	"	12.400		
"	"	Erno	6 y. 1 m.	"	"	12.400	0.1172	0.0338
"	"	Wilhelm I	9 y. 8 m.	"	"	19.400	0.1183	0.0361
"	"	Wilhelm II	9 y. 8 m.	"	"	25.200	0.1324	0.0588
"	"	Gunner I	9 y. 8 m.	"	"	25.500	0.1173	0.0442
"	"	Gunner II	3 y. 9 m.	Lupus	"	14.500	0.1345	0.0467
"	"	2. Radolph	3 y. 9 m.	"	"	14.500	0.1580	0.0575
"	"	5. Arnas	4 y. 3 m.	Scrofula	"	14.700	0.1201	0.0539
"	"	"	4 y. 7 m.	Tuber- culosis	"	14.700	0.1664	0.0735
"	"	Sven I	5 y.	Scrofula	"	15.500	0.0941	0.0192
"	"	Sven II	5 y.	"	"	15.600	0.1032	0.0347
"	"	Rudolf I	5 y. 1 m.	"	"	15.800	0.1017	0.0313
"	"	Rudolf II	5 y. 1 m.	"	"	15.500	0.0997	0.0343
"	"	1. Lauri	6 y. 6 m.	"	"	18.480	0.1003	0.0485
"	"	4. Kalle	6 y. 6 m.	"	"	12.455	0.0874	0.0313
"	"	Lauri I	7 y. 2 m.	"	"	14.422	0.1238	0.0319
"	"	Lauri II	7 y. 2 m.	"	"	18.100	0.1492	0.0367

"	"	"	"	6. Gustaf	8 y. 5 m.	Tuber- culosis	"	"	19-294	0.1464	0.0645
"	"	"	"	3. Arthur Bertel I	8 y. 11 m. 9 y. 1 m.	Scrofula Tuber- culosis	"	"	15-240 18-276	0.0715 0.1081	0.0294 0.0271
"	"	"	"	Bertel II I	9 y. 1 m. 1½ m.	"	"	"	16-605	0.1101	0.0169
Birk und Orgler	"	"	"	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1910, ix. 544	2½ m.	Cranio- tabes	"	Milk + water + 5 % <i>Sorhlet nahrung</i>	5-39	0.2	-0.08
"	"	"	"	"	4½ m.	"	"	"	4-29	0.2	0.027
"	"	"	"	"	4 m.	"	"	"	3-76	0.06	0.021
Rotenberg	"	"	"	<i>Jahrb. f. Kinderh.</i> , Leipz., 1907, lxvi. 6	4½ m.	Rickets	"	Human milk	—	0.22	0.027
"	"	"	"	"	"	"	"	Skim milk	—	0.11	-0.013
"	"	"	"	"	"	"	"	½ milk + ½ <i>Mehl-</i> <i>suppe</i> + malt	—	0.06	0.020
Orgler	"	"	"	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1911, x. 373	4½ m.	"	"	Human milk	3-76	0.06	0.020
"	"	"	"	"	4½ m.	"	"	Human milk + 2 gr. calc. acet. p. a.	—	0.2	0.022
Schabad	"	"	"	<i>Arch. f. Kinderh.</i> , Stuttgart, 1910, liii. 380	5 m.	"	"	Human milk	*11-8	0.05	0.026
Cronheim und Müller	"	"	"	<i>Biochem. Zeitsch.</i> , Berlin, 1908, ix. 76	5 m. 6 m.	"	"	Milk + rice-water	*17-7	0.22	0.02
"	"	"	"	"	6 m.	"	"	Milk + water	5-6	0.22	0.082
"	"	"	"	"	6 m.	"	"	+ milk sugar	—	0.22	0.032
"	"	"	"	"	6 m.	"	"	"	4-56	0.21	0.064
"	"	"	"	"	6 m.	"	"	"	5-1	0.19	0.073
"	"	"	"	"	6 m.	"	"	"	5-0	0.21	0.046
Arndt	"	"	"	Quoted by Schabad in <i>Arch. f. Kinderh.</i> , Stuttgart, 1910, liii. 380	6 m.	"	"	<i>Malzsuppe</i>	—	0.13	-0.002
"	"	"	"	"	6 m.	"	"	"	—	0.13	-0.029
Schabad Orgler	"	"	"	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1911, x. 373	6 m. 6½ m.	"	"	Milk, malt, <i>Mehl</i> Human milk	*8-0	0.05	0.013
"	"	"	"	"	6½ m.	"	"	½ milk + ½ <i>Mehl-</i> <i>suppe</i> + 5 % sugar	5-32	0.17	0.044
"	"	"	"	"	6½ m.	"	"	Same diet + 1 gr. calc. acet. p. d.	7-5	0.2	0.061
Dibbelt Orgler	"	"	"	<i>Die Pathogenese der Rachitis</i> <i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1911, x. 373	7 m. 7½ m.	"	"	Buttermilk	—	0.23	-0.07
"	"	"	"	"	7½ m.	"	"	½ milk + ½ <i>Mehl-</i> <i>suppe</i> + 4 % malt extract	14-15	0.12	-0.096
"	"	"	"	"	7½ m.	"	"	Same diet + 1 gr. calc. acet.	9-9	0.18	0.009

* Faeces weighed before drying.

APPENDIX III (continued)

Author.	Reference.	Name.	Age.	Con- dition.	Diet	Aver- age Wt.	Dura- tion of Experi- ment.	Aver- age Daily Wt. of Dried Faeces.	Aver- age Daily CaO Intake per Kilo Body Wt.	Average Daily CaO Re- tentio per Kilo Body Wt.
Birk	<i>Monats. f. Kinderh.</i> , 1908, vii. 450	T. (1)	8 m.	Rickets	$\frac{1}{2}$ milk + $\frac{1}{2}$ <i>Häfer- schleim</i> + milk sugar	4050	3	5.7	0.11	0.002
"	"	T. (2)	8 m.	"	Samediet + cod-oil and phosph. oil	4050	3	4.7	0.1	0.01
"	"	F. (1)	8 m.	"	$\frac{1}{2}$ milk + $\frac{1}{2}$ <i>Häfer- schleim</i> + milk sugar	5740	3	5.6	0.1	-0.008
"	"	F. (2)	8 m.	"	Samediet + cod-oil and phosph. oil	5840	3	5.4	0.09	0.006
Schabad	<i>Arch. f. Kinderh.</i> , Stuttg., 1910, liii. 380	A. Ivanow	8 $\frac{1}{2}$ m.	"	Milk and rice <i>Schleim</i>	7250	3	*40.8	0.1	0.013
Rothberg	<i>Jahrb. f. Kinderh.</i> , Leipz., 1907, lxi. 6	Buchwäld	9 m.	"	$\frac{2}{3}$ milk + $\frac{1}{3}$ water + milk sugar	6000	3	1.12	1.12	0.004
Klotz	"	1909, lxx. 1	9 $\frac{1}{2}$ m.	"	$\frac{1}{2}$ milk + <i>Mehlsuppe</i> + malt extract	4385	3	9.92	0.14	-0.012
"	"	"	9 $\frac{1}{2}$ m.	"	$\frac{1}{2}$ milk + <i>Mehlsuppe</i> + 1.5 gr. lactic acid	4345	3	5.5	0.16	0.03
"	"	"	9 $\frac{1}{2}$ m.	"	$\frac{1}{2}$ milk + <i>Mehlsuppe</i> + 4.0 gr. lactic acid	4370	3	4.65	0.17	0.02
"	"	"	9 $\frac{1}{2}$ m.	"	$\frac{1}{2}$ milk + <i>Mehlsuppe</i> + 8.0 gr. lactic acid	4350	3	5.97	0.14	-0.003
Schabad	<i>Arch. f. Kinderh.</i> , Stuttg., 1910, liii. 380	Sampron	11 m.	"	Human milk	7550	3	*8.83	0.02	-0.013
Cronheim	<i>Biochem. Zeitsch.</i> , Berlin, 1908, ix. 76	Ja. (3)	11 m.	"	Milk + water + milk sugar	6211	4	13.55	0.22	0.007
und Müller	"	Ja. (4)	11 m.	"	"	6363	4	9.92	0.22	0.020
"	"	Ja. (5)	11 m.	"	"	6478	4	9.45	0.21	0.047
Schabad und	<i>Monats. f. Kinderh.</i> , Leipz. u. Wien, 1911, x. 12	S. S.	1 y.	"	Milk and bread	5640	5	—	0.16	0.038
Sorochowitsch	"	Kurt St. (1)	1 y. 1 m.	"	Full milk	6640	4	11.84	0.19	-0.040
Orgler	"	Kurt St. (2)	1 y. 1 m.	"	$\frac{1}{2}$ milk + $\frac{1}{2}$ <i>Mehl- suppe</i> + $\frac{3}{4}$ sugar	6580	4	5.6	0.11	0.006

			Kurt St. (3)		1 y. 1 m.		Same diet + 2 gr. calc. phos. p. d.	6450	4	5-69	0-17	0-007
Schabad	"	"	"	"	"	"	"	6450	4	5-69	0-17	0-007
"	"	"	"	"	"	"	"	7690	3	*16-47	0-03	-0-008
"	"	"	"	"	"	"	"	7000	3	*28-0	0-12	0-034
Klotz	"	"	"	"	"	"	"	6900	7	*16-14	0-23	0-059
"	"	"	"	"	"	"	"	4425	3	9-4	0-22	-0-11
"	"	"	"	"	"	"	"	4460	3	5-9	0-18	-0-11
Schabad	"	"	"	"	"	"	"	8860	14	*25-86	0-13	0-019
"	"	"	"	"	"	"	"	9750	7	*29-93	0-11	0-016
"	"	"	"	"	"	"	"	7300	7	*19-43	0-19	0-016
Schabad und Soroehowitsch	"	"	"	"	"	"	"	7330	6	*17-16	0-17	0-1
Schabad	"	"	"	"	"	"	"	8000	3	*57-5	0-22	0-06
"	"	"	"	"	"	"	"	8100	7	*26-34	0-16	0-025
"	"	"	"	"	"	"	"	11800	3	*15-6	0-2	0-06
"	"	"	"	"	"	"	"					
"	"	"	"	"	"	"	"	11700	14	—	0-04	-0-002
"	"	"	"	"	"	"	"	11750	14	—	0-04	0-02
"	"	"	"	"	"	"	"	10820	14	—	0-1	0-01
"	"	"	"	"	"	"	"	19450	7	*21-87	0-08	0-042

* Faeces weighed before drying.

APPENDIX IV.

*Clinical Notes.*I. *Normal Cases.*

Case No. 1. B. H., aged $8\frac{3}{4}$ months. Absolutely normal infant.

Case No. 2. J. A. B., aged 6 months. An absolutely normal infant who had a birth weight of $6\frac{1}{2}$ lb., and on admission a weight of 16 lb. 3 oz. He had been fed on milk and water equal parts $\bar{z}$ vi, and $\bar{z}$ ss. Virol every three hours.

Case No. 3. A. B., aged $2\frac{1}{2}$ years, admitted to hospital with primary broncho-pneumonia, otherwise a normal child. Crisis occurred four days after admission, and metabolism experiment was carried out sixteen days later over a period of three days.

Case No. 4. C. B., aged 4 years. Admitted to hospital with chorea and V.D.H. Metabolism experiment carried out after ten weeks' residence when all active manifestations had disappeared.

Case No. 5. R. D., aged 8 years. One week convalescent from lobar pneumonia.

Case No. 6. J. L., aged $9\frac{1}{2}$ years. Absolutely normal child. Admitted to hospital with history of thirst, but observation over a period of three weeks failed to reveal anything abnormal.

Case No. 7. J. A., aged $9\frac{1}{2}$ years. Admitted to hospital as case of epilepsy of three months' duration. Was resident in hospital one month and had only one slight fit one week after admission. Metabolism experiment carried out just before dismissal. Seemed quite a healthy child otherwise.

Case No. 8. D. J., aged 10 years. Admitted to hospital with rheumatic arthritis and endocarditis. Metabolism experiment carried out four weeks later when all active manifestations had disappeared.

II. *Cases of Rickets.*

Case No. 1. Boy, aged 8 months, admitted to hospital on account of irritability of five months' duration. He seemed absolutely healthy except for a questionable laryngismus stridulus heard on two occasions. He had two teeth, and physical examination was negative. This case was used as a control, the diet consisting of undiluted cows' milk $\bar{z}$ vii + $\bar{z}$ i sugar, 5x = 1 litre per day. He was sent home after the completion of the metabolism experiment, but was returned to the hospital four months later when he presented a most marked degree of rickets as evidenced by head sweating, epiphyseal enlargement, rosary and fiddle-shaped deformity of the chest.

Case No. 2. Girl, aged 14 months, admitted to hospital with rickets and broncho-pneumonia. The child had been breast-fed for three months, thereafter on undiluted milk and porridge, and from the age of 11 months on the general diet of the household. For three months she had been getting Virol (1 jar weekly). She had never cut any teeth, and had never been able to sit unsupported. At the time of coming under observation she presented a severe degree of rickets, square head with sutures patent and the anterior fontanelle widely open, a rosary, epiphyseal enlargement and curvature of the long bones of both upper and lower limbs.

There was generalized bronchitis with a patch of broncho-pneumonia. Fever continued for fourteen days after admission and five days later Olei Phos. $\frac{1}{2}$ mm. Olei Morrhuæ 3i was administered thrice daily. Ten days still later a metabolism experiment was carried out over a period of one week on a purely milk diet. The child improved somewhat, especially after the institution of treatment by massage and electricity, but fifteen weeks after admission, i. e. eight weeks after the cessation of the metabolism experiment, she developed broncho-pneumonia and died.

Cases No. 3 and 4 refer to the same child, a girl, aged 14 months, admitted to hospital with broncho-pneumonia. She was a healthy child at birth; was breast-fed for six months; had whooping-cough at 8 months and measles at 10 months, but was said to be enjoying good health until nine days before admission, when cough, fever, and dyspnoea developed. On admission there was a definite broncho-pneumonia involving the right upper and middle, and left lower lobes. There was a severe degree of rickets, she had no teeth, the anterior fontanelle was unduly patent, the epiphyses were enlarged, and a rosary with fiddle-shaped chest was present. Fever subsided two days after admission, and the metabolism experiments were conducted three weeks later for two periods of three days each at an interval of two days. The diet during the first period consisted of undiluted milk, and during the second period of milk with bread and butter.

Cases No. 5 and 6 also refer to the same child, a boy aged 2 years, admitted on account of rickets. He had been breast-fed for six weeks, and thereafter on cows' milk in apparently sufficient quantity. He sat up at 1 year, cut his first tooth at 17 months, but had never walked. He was a markedly rachitic child with large head and overhanging forehead, anterior fontanelle one inch square, rosary and epiphyseal enlargement. The spleen was palpable. Blood examination gave the following: haemoglobin 74 per cent., red cells 3,940,000 and leuc. 10,400. The first experiment, on a pure milk diet was conducted from 29th May till 1st June, seven days after admission. Blood examination (4th June) for calcium gave 0.11 grm. per cent. Olei Morrhuæ and Olei Phos. were commenced on 6th June, and the second metabolism experiment, on a diet of milk, bread and butter, was conducted from 9th till 12th June.

Case No. 7. Girl, aged 2 years, admitted to hospital on account of rickets. She was a healthy child at birth, was breast-fed for two months, and then on undiluted milk till nine months, and later on the 'run of the house'. She cut her first tooth at 6 months, sat up at 9 months, and walked at 1 year and 8 months, but from age of 1 year and 10 months had shown a progressive disinclination to walk, and at date of admission usually refused even to stand. On admission there was marked rickets, as evidenced by large head, open anterior fontanelle, rosary and epiphyseal enlargement. The metabolism experiment on a diet of three pints of milk daily was conducted for nine days. During this period there was a tendency to constipation, and liquid paraffin was administered to counteract it.

Case No. 8. Girl, aged 2 years and 7 months, admitted on account of rickets. She was healthy at birth, was breast-fed for one year, and then on milk, porridge, bread and soup. She cut her first tooth at 10 months and walked at 15 months, but during the last six months had 'gone off her feet'. The father was idle and the mother was working as a lamplighter, and in consequence the child was not taken much out of doors. The child was definitely rachitic, as evidenced by patent anterior fontanelle, rosary, fiddle-shaped chest, epiphyseal enlargement and curvature of bone tibiae.

Case No. 9. Girl, aged 15 months, admitted to hospital with marked rickets, as evidenced by open fontanelle, rosary, fiddle-shaped chest, epiphyseal enlargement, curvature of both femora, and profuse sweating. She was healthy at birth

and was breast-fed for eighteen months, cut her first tooth at 14 months, but had never walked. She had measles at 1 year, and whooping-cough at 14 months, but apparently made good recoveries. Two weeks after admission she received Olei Phos. and Olei Morrhuæ, which were continued for six weeks, when a metabolism experiment of six days' duration on a diet of porridge and milk was carried out. At this date the rachitic condition had not apparently improved.

Case No. 10. Girl, aged 3 years, came under observation on account of her inability to walk. She was a healthy child at birth, was breast-fed for ten months, then on milk and porridge till 18 months, and thereafter on the general diet of the household. She cut her first tooth at 6 months, but never walked. She had scarlet fever at 19 months. At the time of examination she was unable to stand without support, and presented a severe degree of rickets in an open anterior fontanelle, rosary, fiddle-shaped chest, curvature of both clavicles and left fore-arm. There was a slight facial phenomenon, but there had never been noted carpo-pedal spasm or laryngismus stridulus. A metabolism experiment extending over three days was carried out on a diet of milk and bread and butter; the addition of bread and butter to the diet and the small quantity of milk accounts for the relatively small intake of calcium. Blood examination for calcium three days after cessation of metabolism experiment: 0.015 grm. per 100 c.c. whole blood.

Case No. 11. Boy, aged 4 years, came under observation on account of inability to walk. He was a healthy child at birth and had never been breast-fed. He was fed on cows' milk till 14 months, and thereafter on the general diet of the household. He had been resident in the hospital at the age of 2 years and 4 months, on account of rickets. He was unable to walk, but with massage and electricity improved, and was dismissed able to walk. He contracted pneumonia eight months ago, had been practically confined to house since then and had 'gone off his feet entirely'.

On admission he presented marked signs of rickets. The anterior fontanelle was not quite closed, the epiphyses were enlarged, there was a rosary with fiddle-shaped deformity of the chest, and he was quite unable to support himself in the erect posture.

Examination of blood, day after admission, gave following results:

Hb. 72 per cent.

Red cells, 5,120,000.

White cells, 11,200.

CaO per 100 c.c. whole blood 0.011 grm.

One week after admission a metabolism experiment was carried out on a diet of milk, bread and butter, which he had been having since admission, and extended over a period of three days. Seven days after cessation of experiment he developed measles and was removed to an isolation hospital.

Case No. 12. Girl, aged 7 years. Had always enjoyed good health till nine months prior to coming under observation, when she commenced to suffer from pains in the limbs and to be disinclined to play. These symptoms had gradually progressed. On admission to hospital there was definite rickets, as evidenced by rosary, epiphyseal enlargement, and X-ray changes at the ends of the long bones. She was never breast-fed, but had been given various dilutions of milk and water. She walked at 14 months, and until the present illness had presented no symptoms suggestive of rickets. She was one of a family of 15, of whom five had been rachitic.

A metabolism experiment extending over a period of three days and on a diet of milk, bread and butter, was carried out after she had been on this diet for three days. Examination of the blood one week later revealed 0.010 grm. of CaO per 100 c.c. whole blood. She was thereafter treated with Olei Morrhuæ and

Olei Phos. and massage and electricity and left hospital much improved after two weeks' residence.

Case No. 13. Girl, aged 13 years, admitted to hospital on account of pains in the arms and legs of four months' duration.

She was a congenital syphilitic as evidenced by saddle nose, Hutchinson's teeth, interstitial keratitis and scarring round the mouth.

She was said to have been a healthy infant, and to have learned to walk at 2 years. She developed deafness after measles at the age of 6 years. Three years ago she suffered from 'sore eyes' and was practically blind for some time.

Four months ago she commenced to suffer from pains in her limbs, specially severe during the day. Examination revealed, in addition to the above manifestations of old syphilis, epiphyseal enlargement, and X-ray examination of the wrists showed the changes typical of late rickets, viz.: widening of the epiphyseal lines and deficiency of calcium at the lower ends of the diaphyses.

Immediately after admission a metabolism experiment, extending over four days, on a diet of milk, bread and butter, was carried out.

Examination of the blood immediately before the metabolism experiment gave CaO 10 mg. per 100 c.c. of whole blood.

The patient was dismissed I.S.Q. a few days later.