addition of cod-liver oil. He also claims that the muscular flabbiness of rickets can be cured by the same line of treatment. He believes that the cereals have a neutralizing action on the antirachitic factor, so that on high cereal diets the dose of cod-liver oil must be increased. Vining³ also believes in a dietetic error, probably carbohydrate excess, as one of the causes of the "debilitated state," although he considers the toxic factor to be more important.

An investigation was made of the diets of the children attending the out-patient department, and it was found that as a general rule they were all on the same badly balanced diet, which was too liberal in calories for the output of energy in the day. This diet was ridiculously high in carbohydrate, which was mainly cereal, and low in animal proteins and fats. Although all the children of the poor were on this badly balanced diet they did not all show flabbiness, and some had remarkably good tone. This difference was seen to occur even in the same family. Further, many of these flabby children were treated for months on therapeutic doses of cod-liver oil with no improvement, but at the same time it must be noted that the cereals were not restricted, as such a measure was impracticable when dealing with the out-patient class of patients. It is obvious from the above that other factors besides diet must be concerned in the production of muscular hypotonia.

It is interesting in this connexion to note the reports of Holt and Fales⁴ on children in an institution in New York. These children received a most liberal diet, but one which included a large excess of carbohydrate (over 60 per cent.), and yet they were in most excellent physical condition. Practically the same portion of food was allowed to both the younger and older children, but both increased normally in weight and remained in good health.

CONFINEMENT AND LACK OF EXERCISE.

That rickets, and especially lack of muscle tone, is due to confinement has been the opinion of the Glasgow school for many years. Recently Galbraith⁵ stated that although cod-liver oil caused a deposition of calcium in the bones and healed bony manifestations of rickets, nevertheless the muscular flabbiness remained as ever. He reports rapid cures of flabbiness with massage and exercise.

That actual immobility does not necessarily produce lack of muscle tone is suggested by a study of the results of the open-air treatment of children suffering from tuberculous hips or spines, gross rickets, or congenital malformations. These children during their treatment are confined in splints for long periods, but they are lightly clad and exposed to both moving fresh air and sunshine, and under these conditions retain excellent muscle tone. This can be explained by the work of Leonard Hill⁶ as due to the stimulating effects of sunshine and moving fresh air on metabolism. It is a matter of common observation that normal children with good tone who are confined to bed as a result of some acute illness rapidly become flabby, but after being up soon evince a desire to move about and quickly recover their muscle tone. This is in marked contrast with the true flabby child, who shows no desire for exercise. Undue confinement sometimes occurs even in the homes of the well-to-do, and though the children are taken out of doors they may not get sufficient walking exercise, as they are sometimes kept too much in their perambulators. At the same time these children are receiving an over-liberal diet and are excessively warmly clad.

Inquiries into the histories of the hospital cases showed that many of these flabby children had practically no exercise during the day, only being taken out for about one hour in the morning. The majority were confined to small quarters which were badly lit and badly ventilated. When the children reach the age of 4 or 5 years they are allowed out by themselves and also commence school; at this age the number of hypotonic children rapidly decreases. The superior tone of the calf muscles as compared to the arm muscles also becomes very remarkable at this age, although the same contrast to a lesser degree is seen in younger children. This is obviously due to the fact that the calf muscles are those most exercised. Another interesting point noted was the frequent complaint that the children were always tired and slept much during the day.

From the above facts it would appear that lack of exercise and confinement, though very important factors in the production of hypotonia, will not by themselves produce flabbiness but must be correlated with others in order to have this effect.

TOXIC THEORY.

Vining³ has suggested that toxic absorption from either the throat or bowel plays a most important part in the production of the debilitated state. Wills and Warwick⁶ showed that children with septic tonsils as a rule had excellent muscle tone, but that true hypertrophy of the adenoid tissue of the throat was associated with flabbiness of the muscles. There is no evidence that toxic absorption is taking place from the bowel. The constipation which is present in a number of the cases is rather the result of the atonicity of the abdominal and bowel wall muscles than the cause of this condition. Against the toxic theory is the fact that in tuberculosis, syphilis, and rheumatism, all of which are chronic toxæmias, flabbiness may occur but is certainly not characteristic.

CONSTITUTIONAL DEFECT.

The theory is put forward by Czerny⁷ that there is a type of child who is born with a particular constitution which he calls the "exudative diathesis." In this type the muscles are flabby, the child is inactive, shows general enlargement of the lymph glands, and is prone to infections of the mucous membranes. Whether such a child exists or not it is difficult to say. Certainly every clinician knows that there are infants who from birth are firm, quick in their movements, inclined to be under weight, and difficult to fatten, while other infants are slow in their movements, flabby, sleep a great deal, gain weight easily, and do this on a low calorie intake. In the former the metabolic fires are burning rapidly, while in the latter these fires are burning slowly.

CONCLUSIONS.

1. A consideration of the first two theories—namely, diet and lack of exercise—suggests that factors which tend to depress metabolism produce flabbiness, while factors which tend to stimulate metabolism cure flabbiness.
2. The factors which tend to depress metabolism and produce flabbiness are confinement, and lack of exercise, fresh air, and sunshine; overclothing with consequent heat retention, overfeeding or over-calorying in relation to the child's output of energy in the day; feeding with a diet too high in cereals, too low in animal fat and protein, and defective in vitamins.
3. The factors which tend to stimulate metabolism, and therefore cure flabbiness, are the reduction of the diet and especially of the cereals, retaining in the diet a sufficient amount of animal fat and protein; the administration of cod-liver oil; and stimulation by sunshine, fresh air, exercise, massage, and open-air treatment, with scanty clothing to increase heat loss from the skin.

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BLOOD CALCIUM AND INORGANIC PHOSPHATES IN CHILDREN WITH MARKED LACK OF MUSCLE TONE.

BY

LUCY WILLS, M.B., B.S.LOND.

(From the Biochemical Department, Hospital for Sick Children, Great Ormond Street, and the Pathological Department, Royal Free Hospital.)

It is well recognized that extreme lack of muscle tone is a characteristic accompaniment of bony rickets, and many consider this symptom as definitely part of the rachitic syndrome. This flabbiness is, however, characteristic of a type of child frequently seen in any out-patient department

and generally classified as debilitated, though when the child is under 3 the diagnosis of rickets is sometimes made on this flabbiness alone, even if there are no signs of either past or present bony rickets. This association of poor muscle tone and rickets suggests the possibility that the so-called debilitated flabby child may be suffering from mild rickets. It was with a view to testing this hypothesis that the present investigation was undertaken, which is only part of a general study of the "flabby child." Further, in a previous study,¹ when working in the Ear, Nose and Throat Department of the Royal Free Hospital, it was shown that children with true hyperplasia of the lymphoid tissue of the nasopharynx, as distinct from those with enlarged lymphoid tissue resulting from previous infection, had poor muscle tone. In fact, it was this study of the adenoid child that led to the present wider investigation.

NATURE OF INVESTIGATION.

Investigations of the blood in cases of rickets have shown characteristic changes: the serum-calcium value is more variable than in normal cases, and the average figure slightly lower, and the inorganic phosphates are in nearly all cases markedly lowered. A study of these two components was therefore undertaken in two control groups—one of normal children and one of sick children—and in a group of flabby children, to ascertain if there was any constant characteristic departure from the normal in the latter group.

The first control group (Group 1) consisted of twelve normal healthy children of the hospital class, aged 2 to 11 years. The second control group (Group 2) consisted of thirty-one children, aged 2 to 12 years, with enlarged and inflamed tonsils and adenoids, each of whom had, however, excellent muscle tone. This group was included not only to compare two groups of sick children, but also in the hope of obtaining further evidence in support of the classification of cases of adenoids into those with septic enlargement and those with true hyperplasia. The third group was made up of children, aged 1 to 12 years, with poor muscle tone. These cases were selected by Dr. Donald Paterson at Great Ormond Street Hospital, and had the following characteristics: soft flabby muscles, resulting in such abnormalities as large pendulous bellies, hollow backs, hyperextensible joints, and flat-feet; most had large tonsils. The children were brought to hospital for vague disorders, lassitude, or weakness. Children with any definite organic lesion were excluded from the series. No case with any suggestion of bony rickets was included.

METHODS.

Kramer and Tisdall's² method was used for the estimation of calcium in serum, and Briggs's³ modification of the Bell-Doisy method for the inorganic phosphates in plasma. The plasma used for the phosphate solutions was always separated from the corpuscles within half an hour of drawing the blood; specimens showing any haemolysis were discarded. Owing to the difficulty of obtaining sufficient blood from small children both determinations could not always be done on the same patient.

RESULTS OF CALCIUM DETERMINATIONS.

Blood-calcium values for children have been determined by many authorities, and the majority are agreed that in normal children the serum-calcium value lies between 9.5 and 11.5 mg. calcium per 100 c.cm. of serum, with higher values in young infants. Jones and Nye⁴ and Denis and Talbot,⁵ using Lyman's method, report a much larger range, which has not been confirmed by other workers. Anderson,⁶ working with whole blood, reports a wide range of normal values, but, as the question of corpuscular calcium is still in dispute, it is difficult to assess the value of her findings. In children suffering from rickets there is no very marked decrease in the serum-calcium values, such as is found in tetany and some cases of nephritis, but the range is much greater. Expressed in milligrams of calcium per 100 c.cm. of serum or plasma, the following ranges and averages are reported: Kramer, Tisdall, and Howland,⁷ 8 to 11.1, average 8.6; von Meysenbug and co-workers,⁸ 7.9 to 9.8, average 8.6; György,⁹ 7.2 to 10.7, average 8.5. Mayer,¹⁰ however, reports high serum-calcium values in early cases of florid rickets.

In the present investigation the blood-calcium values for the group of children with hypotonic muscles and for the control groups are set out in Table I. The values for the

TABLE I.—Blood-calcium Values.

	Type of Case.	Age.	No. of Cases.	Milligrams Calcium per 100 c.cm. serum.		
				Lowest.	Highest.	Average.
Group 1	Normal	2-11	10	10.1	11.0	10.4
Group 2	Inflamed tonsils and adenoids but good muscle tone	3-12	20	8.7	10.6	9.8
Group 3	Poor muscle tone	2-9	30	6.6	10.6	9.0

Note.—If Groups 2 and 3 are combined as a control group the range becomes 8.7 to 11.0, with an average of 10.1.

normal children (Group 1) are, without exception, above 10 mg. per 100 c.cm. of serum, and range from 10.1 to 11.0 mg. The values for the other control cases (Group 2) have a lower average—9.8 mg. of calcium per 100 c.cm. of serum, with a range of from 8.7 to 10.6 mg.; only one value, however, was below 9 mg. The general health of the individuals of Group 2 varied; some were in good health at the time, although their tonsils and adenoids were enlarged as the result of previous infection; others, on the other hand, were in very poor condition, with acutely inflamed tonsils, aural and nasal discharges, etc., but all had excellent muscle tone. The cases with poor muscle tone (Group 3) gave serum-calcium values averaging 9.0, with a range of from 6.6 to 10.6 mg. per 100 c.cm.; of the 30 cases only 5 showed a value of 10 mg. or more.

It has been suggested that there may be a seasonal tide for calcium as well as for the inorganic phosphates of the blood (Hess¹¹). The present study was made during the months of April, May, and June; no seasonal change was indicated during that period in any group, but the figures and time are both too limited for any deductions to be drawn.

RESULTS OF INORGANIC PHOSPHATE DETERMINATIONS.

The inorganic phosphate values in normal children, as established by various authorities, average for whole blood 4.0 mg., and for serum and plasma 4.1 mg. per 100 c.cm. With the exception of Jones and Nye⁴ and of McKellips, De Young, and Bloor,¹² the latter working on infants, who give a range of from 1.9 to 5.4 and 1.2 to 4.6 mg. per 100 c.cm. respectively, authorities seem agreed that the normal range is from 3.2 to 6.5 mg. per 100 c.cm., but that the values are nearly always over 4.0 mg.

In contrast with the normal is the characteristic low value found in most cases of active rickets, uncomplicated by tetany. Howland and Kramer,¹³ for example, give a range of from 0.6 to 3.2 and an average of 2.0 mg. per 100 c.cm. of serum; Anderson⁶ gives from 2.5 to 5.3, with an average of 3.3 mg. per 100 c.cm.; György⁹ gives from 1.6 to 2.9, with an average of 2.4 mg. per 100 c.cm.

In Table II are given the values for the inorganic

TABLE II.—Values for Inorganic Phosphate.

	Type of Case.	Age.	No. of Cases.	Milligrams per 100 c.cm. Plasma.		
				Lowest.	Highest.	Average.
Group 1	Normal	5-10	5	4.1	6.1	4.8
Group 2	Inflamed tonsils and adenoids but good muscle tone	3-12	20	2.9	5.1	4.1
Group 3	Poor muscle tone	1-11	25	2.5	6.1	4.5

phosphate in the three groups under consideration in the present investigation. There is no difference between the values in Groups 2 and 3; the figures in both groups cover the same range, and with five exceptions fall within the normal limit. The five normal cases comprising Group 1 give a slightly higher average, but a larger number might have shown a wider range. The findings are not such as would be expected if the condition in Group 3 (flabby children) is regarded as akin to florid rickets.

Kramer, Tisdall, and Howland⁷ state that in normal blood the product of the calcium and inorganic phosphate values should be 40 or over, while in rickets it is reduced below this value. György⁹ uses the quotient of the organic phosphate into the calcium values, and states that in normal cases this figure should be 1.95, in rickets 3.5, and in tetany 1.4. Five cases in Group 3 of the present investigation show a lowered product, but a lowered quotient also, due to the lowering of the calcium value, while the phosphate value remained normal. The quotient (with one exception, where it is 1.32), though lowered, is never as low as in cases of tetany, and the significance of this change is not evident.

CONCLUSIONS.

The serum-calcium values found in the group of normal children agree with those of other workers. The values obtained in Groups 2 and 3 show a wider range than the normal, the difference being more striking in Group 3 (hypotonic children) than in Group 2. In Group 3, moreover, the average calcium value is 9 mg., a slightly lower figure than the average of 10.4 found in the normal cases. Five cases in Group 3 have values of 10 mg. or more, and many other of the cases have but a slightly lowered value; and further, inversely, a few cases in Group 2 have lowered values though good tone. It is therefore clear from these two facts that muscle hypotonus is not immediately dependent on the serum-calcium level, as it can occur with either high or low values. A wide range of calcium values is probably constantly associated with this poor tone, even as a similar range has been shown to be associated with rickets, but it does not operate as a causative agent. The fact that Group 2 had a greater range than the normal suggests that such variation occurs in other conditions of ill health.

The inorganic phosphate figures for the three groups, with a few exceptions which occur both in Groups 2 and 3, fall within the limits of the normal and do not differ from each other. In contrast with these findings are those recorded in cases of bony rickets where low inorganic phosphate values are constantly found and are considered by most authorities as typical of the disease. Anderson,⁶ however, as a result of her work on rickets, suggests the need for further investigation of blood phosphates in disease "causing and probably preceded by considerable muscular inactivity and atonicity," before deciding whether a low blood phosphorus is an exciting cause or merely a result of rickets. The normal values found in Group 3 (flabby children) are of interest in this connexion, as they do not suggest any association between lack of muscle tone *per se* and a low inorganic phosphate level in the blood, such as is frequently found in rickets.

The balance between the calcium and the inorganic phosphates, expressed either as the product or the quotient of the phosphate and calcium figures, does not appear to be appreciably altered from the normal in Groups 2 and 3, though there is a slightly greater range in the figures in Group 3, owing to the greater variability of the calcium figures. In fact the chemical findings reported above do not appear to support the hypothesis that muscle hypotonus in children is necessarily an indication of some degree of rickets, though the hypothesis can only be adequately tested by a study of the conditions in which these flabby children live and by the result of carefully controlled treatment.

SUMMARY.

1. The average serum-calcium value in 10 normal children (Group 1) was found to be 10.4 mg. and the range 10.1 to 11.0 mg. per 100 c.cm.; and in 20 cases with inflamed tonsils and adenoids but good muscle tone (Group 2) it was 9.8 mg., and the range 8.7 to 10.6 mg.

2. The average value found in 30 cases with marked lack of muscle tone (Group 3) was 9.0 mg., and the range 6.6 to 10.6 mg. per 100 c.cm.

3. The average value of the inorganic phosphates of the plasma was found to be approximately normal in all three groups (50 cases), and there was no difference in the range of values in Groups 2 and 3.

4. Though the calcium values were more variable in Group 3, no relationship between the calcium level in the blood and muscle hypotonus was established.

5. The blood picture of flabby children is not similar to that of rachitic children, though the calcium variation is the same in both conditions.

In conclusion I would express my thanks to Dr. Donald Paterson for selecting the cases of flabby children, to Mr. Gay French for permission to investigate his cases, and to Dr. Harrison for permission to work in the Biochemical Department, Great Ormond Street, and for his valuable help with this work.

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MIKULICZ'S DISEASE ASSOCIATED WITH ARRESTED MILIARY TUBERCULOSIS.

BY

T. W. PRESTON, AND B. L. JEAFFRESON,
M.R.C.S., M.D., B.S.LOND.,

RESIDENT MEDICAL OFFICER,

HOUSE-PHYSICIAN,

CITY OF LONDON HOSPITAL FOR DISEASES OF THE HEART AND LUNGS,
VICTORIA PARK.

The following case seems to be of sufficient interest to merit publication.

E. D., a girl aged 15 years, was admitted to the City of London Hospital, having been diagnosed at her local tuberculosis dispensary as a case of early phthisis. Her history was that three months before coming under our observation she had gradually begun to feel weak and easily tired, developed a slight dry cough, and once brought up a few streaks of blood. At the same time she noticed a marked "puffiness" of the eyelids for which she was treated for subacute nephritis, a trace of albumin having been found in her urine at this time. In regard to her past history, she had been a healthy child except for measles, chicken-pox, and whooping-cough at 3 and 4; at 2, however, she had had a severe illness, the details of which are vague; apparently her chief symptoms were fever and acute pains all over, for which she was kept in bed for about three or four weeks. There was no family history of tuberculosis, and she had two brothers and a sister alive and well. The patient was rather pale, but otherwise did not look particularly ill. She had very little cough, she had no night-sweats, and her temperature was normal.

Repeated careful physical examinations showed a chest apparently little removed from the normal. A radiogram, however, showed the remarkable appearance seen in the accompanying figure, and was suggestive of an acute miliary tuberculosis. A diffuse miliary mottling is observed throughout both lung fields. The possibility that this appearance might have been due to an anthracosis was excluded by the fact that the patient had never been engaged in any dusty occupation. So inconsistent, apparently, was the radiogram with the physical signs and the condition of the patient, that a second film was taken; this showed precisely the same state of affairs. A sputum examination showed tubercle bacilli present; subsequently, however, there have been seven successive negative examinations.

The second point of interest about this case was that there were found to be symmetrical enlargements of the