LXXV. CALCIUM CONTENT OF THE BLOOD DURING PREGNANCY. PART II.

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A PREVIOUS investigation gave the results of a study of the calcium content of the blood during normal cases of pregnancy [Widdows, 1923].

That work has been extended to cases other than normal, and the present paper records results obtained where previous pregnancies had shown departures from the normal.

The earlier work had established the following two points. First, that the very heavy demand that undoubtedly is made by the foetus for calcium at certain stages of its development is met by a very perfectly balanced calcium metabolism as at no time is the variation of the calcium content of the serum very marked. Second, that in the later stages of pregnancy there is a distinct tendency for the calcium content of the blood to decrease, and to increase directly after confinement with a recovery to normal, with further increase during the early stages of lactation.

While working on the normal cases a certain number showing previously abnormalities such as miscarriages, stillbirths, etc. were investigated, but no definite relationship was detected between the abnormality and the calcium content of the blood.

Having established the normal variations in the calcium content of the blood, it was thought that a systematic study of these cases of abnormal pregnancies, on the same lines as those followed before, might lead to some more definite results.

A large number of such cases have now been investigated, and as in the earlier work particular attention has been paid to those periods at which an abrupt change in the calcium metabolism of the foetus seems to occur. The samples of blood for analysis were taken between the 3rd and 4th months, the 6th and 7th months, and the 8th and 9th months, and they were taken from the same individual at these different periods. The analyses were made on the serum in all cases, and the procedure was the same as that detailed in the earlier paper.

The cases studied had shown in earlier pregnancies miscarriages, stillbirths, excessive vomiting during the later stages of pregnancy, albuminuria, eclampsia.

The amount of calcium is always given in milligrams per 10 cc. of serum. The average calcium per 10 cc. of serum is 0.99 milligram.

Table I is a reproduction of the table showing the results for the normal cases.

Table I.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found
3-4 months	23	22	1.11
6-7 "	27	24	0.996
8-9 "	25	24	0.94
Post-confinement within 14 days	18	18	0.994

In Table II the figures are the mean for the different periods of all cases, showing the above abnormalities, without classification.

Table II.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	39	36	1.07	1.2	0.91
6-7 "	82	72	1.00	1.2	0.71
8-9 "	86	77	1.00	1.14	0.79
Post-confinement within 14 days	68	67	0.988	1.17	0.72
3-4 months	47	44	1.03	1.13	0.73

The above numbers show a drop in the calcium content after the 4th month of pregnancy. From the 6th till the 9th month however it remains almost constant, whereas in normal cases there was a distinct drop during the 8th-9th month. There is the same tendency to rise after confinement as in the normal cases.

The cases in this table have been analysed and arranged in groups, and as far as possible those cases collected together which are characterised by only one abnormal factor. The results are shown in Tables III, IV, V, etc.

In Table III the results are drawn from cases showing anyone or all of the following characteristics: stillbirths, miscarriages, and premature births.

Table III.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	23	20	1.09	1.2	0.98
6-7 "	43	40	0.998	1.14	0.71
8-9 "	34	33	0.993	1.14	0.79
Post-confinement within 14 days	37	37	1.00	1.17	0.75
3-4 months	19	19	1.04	1.13	0.95

These results are similar to those shown in Table II.

In Table IV cases have been collected showing miscarriages as their only abnormality.

Table IV.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	19	15	1.10	1.2	0.99
6-7 "	19	18	1.02	1.16	0.99
8-9 "	10	10	1.02	1.14	0.94
Post-confinement within 14 days	13	13	1.00	1.17	0.81
3-4 months	8	8	1.03	1.07	0.97

The striking point about the above numbers is the very slight variation of the calcium value from the 6th to the 9th month. Also the calcium content of the blood throughout the pregnancy is high.

In two cases the calcium of the urine has been estimated, and in both cases it has been found to be very high. In one case the total output of calcium in the form of calcium oxide per day was 0.44 g. and in the other 0.847 g. per day. The normal output of calcium in the form of calcium oxide varies from 0.2 to 0.35 g. per day.

In Table V the results are taken from cases where stillbirths have occurred.

Table V.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	2	2	1.01	0.996	0.98
6-7 "	10	10	0.995	1.14	0.95
8-9 "	11	11	0.96	1.1	0.75
Post-confinement within 14 days	8	8	0.994	1.05	0.75
3-4 months	3	3	1.07	1.11	1.07

The above table is, on the whole, in accordance with the results obtained in the wholly normal cases, *i.e.* a distinct fall in the calcium during the last months of pregnancy and an immediate rise after confinement.

Tables VI, VII, VIII, deal with cases showing excessive vomiting during the last months of pregnancy, albuminuria, and eclampsia. The number of cases showing albuminuria and eclampsia are not large and cases are still being studied, but it was thought in connection with the other results it might be interesting to record the observations already made.

In Table VI are recorded the results from cases showing excessive vomiting during the later stages of pregnancy.

Table VI.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	4	4	1.07	1.14	1.01
6-7 "	13	13	1.06	1.2	0.89
8-9 "	16	16	1.02	1.07	0.96
Post-confinement within 14 days	13	13	0.94	1.05	0.73
3-4 months	8	8	1.05	1.11	0.97

In all the above cases the calcium of the blood throughout pregnancy is definitely above the average, as in the case of miscarriage only as the abnormality. During the last month the calcium value tends to decrease but still remains high and immediately after confinement it decreases still further to rise again during the early months of lactation.

The results from cases showing albuminuria are found in Table VII.

Table VII.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	0	0	—	—	—
6-7 "	2	2	0.97	1.04	0.89
8-9 "	11	9	0.95	1.08	0.79
Post-confinement within 14 days	6	6	0.93	1.00	0.84
3-4 months	9	9	1.03	1.08	0.999

In these cases of albuminuria the calcium content of the blood is below normal value during pregnancy, decreases during this time and just after confinement, rising again during the early months after confinement.

Table VIII gives the results obtained from cases showing eclampsia or pre-eclamptic symptoms.

Table VIII.

Stage	Number of specimens analysed	Number of cases investigated	Average calcium found	Range of calcium found	
				Highest	Lowest
3-4 months	3	3	1.05	—	—
6-7 "	4	4	1.03	1.08	0.94
8-9 "	4	4	1.05	1.14	0.96
Post-confinement within 14 days	5	5	0.89	1.04	0.73
3-4 months	1	1	1.05	—	—

Here again the calcium value is high throughout the pregnancy and shows no decrease during the last months. Immediately after the confinement however there is a considerable decrease, the value rising again during the early months after confinement.

These results certainly strengthen one of the conclusions drawn from a study of normal cases; viz. that although at certain stages of its development the foetus makes a very heavy demand for calcium, yet this demand is met by a very perfectly balanced calcium metabolism, because at no time during the pregnancy, even in these abnormal cases, is the variation of the calcium very marked. The most marked change is shown in the few cases of eclampsia which have been studied, where the calcium value drops from 1.05 to 0.89 immediately after confinement.

The values for the blood calcium obtained at the different periods in certain of these abnormal cases are in accordance with those of the normal; many however show a distinct variation.

The results from the cases of stillbirths show the normal variation.

The cases of excessive vomiting and albuminuria show the normal variation up to the 9th month, but a fall directly after confinement, rising again after 3-4 months.

The calcium, throughout the pregnancy, is above the average in the cases of excessive vomiting, but below in those of albuminuria. The cases of miscarriage and eclampsia show also, throughout the pregnancy, a calcium content above the average, but very constant during the last months. There is no decrease between the 8th and 9th months, but a distinct drop immediately after confinement, rising again after 3-4 months.

It has been suggested that the high calcium content of the blood of women in labour is due to a tendency of the hydrogen ion concentration of the blood at a fixed carbon dioxide tension to be increased, the severe muscular effort causing lactic acid to be passed into the blood stream.

In those cases of eclampsia, excessive vomiting and miscarriages the high calcium value might be attributed to the same cause, an increased acidity of the blood. Cook [1924] does find in certain cases of eclampsia a definite fall in the plasma bicarbonate, but attributes this to the effect of the convulsions and the labour itself, and states that it is generally agreed that the acidosis factor plays a negligible part in the "toxaemias" of pregnancy. This is supported by the work of Marrack and Bone [1923].

What connection there is, if any, between these calcium values and the abnormalities studied it is difficult to say. The calcium variation of the blood can be only one of the many influencing factors. Yet the above numbers do show in certain cases a calcium value definitely above the average for blood and in other cases definitely below.

If it is possible to correct this variation from the normal easily, one of the factors that may be a disturbing influence in these particular cases will be eliminated and the study simplified.

J. B. S. Haldane has made experiments showing how the calcium content of the blood can be largely increased or decreased, but the methods employed are too drastic for ordinary patient treatment.

If by a variation of the diet the calcium content of the blood could be appreciably affected this would be the most pleasant method of correction. Since there is always a large reserve of calcium in the bones, and large amounts of calcium are excreted in the urine and faeces, the small variations that occur in the blood calcium are probably regulated by the mechanism in the body for the elaboration of calcium rather than by the quantity of calcium available in the system.

Vines [1921] in his work on the relationship between the ionic and combined calcium of the blood has worked at the subject from this point of view, and his suggested parathyroid treatment may regulate not only the above relationship, which he considers all important, but also the actual total normal amount of calcium.

With regard to the possibility of altering the calcium value by diet, the evidence seems to be very contradictory.

Halverson and Bergeim [1917], Neurath [1911], Katzenellenbogen [1913], Denis and Minot [1920] and Clark [1920] from their experiments conclude that the blood calcium is little affected by the addition of calcium to the diet, and that in any case it is not increased above the normal. Meigs, Blatherwick, and Cary [1919] from their work on cattle come to the same conclusion.

On the other hand, Voorhoeve [1911] found that he could increase the calcium value provided a sufficiently large amount of calcium was added to the food per day. He gave 2.7 g. of calcium oxide per day for several days. Clark however thinks his methods of analysis are open to criticism. Boggs [1908] has also shown that when the calcium content of the blood is low it can be increased by the administration of calcium lactate or acetate. In the case of a haemophylliac [Widdows, 1923] it was found that by the administration of calcium chloride the calcium value of the blood increased from 10.5 to 11.2 mg. per 100 cc. of blood.

These results suggest that when the calcium value is low, by the addition of calcium salts to the diet, the value may be raised to normal. On the other hand, since Halverson and Mohler suggest that under ordinary conditions the plasma calcium is kept nearly constant by means of the enormous calcium reserve in the bones, in the case of a pregnant woman, when the blood calcium is high, a starvation calcium diet might have serious results.

As suggested above it is probable in these abnormal cases the high or low calcium values are only symptomatic of some more deeply seated disturbance involving the calcium metabolism, and that, although in normal cases of pregnancy a diet rich in calcium is of importance to help to counteract the great demand of the foetus for this element in the later stages of its growth, in these abnormal cases there can be no effective treatment until the real cause of the disturbance is discovered.

Table IX has been included in this paper, as it was thought the figures recorded might be of interest in view of Blair Bell's work [1908]. The latter's work suggested that just before the birth of the child the calcium of the blood of the mother should rise, and fall immediately after confinement. During last year it was possible to examine the blood of a few cases under these conditions, and the figures certainly are in agreement with Blair Bell's theory.

Table IX.

Case	Calcium about 8 months	Days before pregnancy	Calcium found	Days after pregnancy	Calcium found
A	0.94	2	0.99	20	0.94
B	0.97	1	1.00	10	0.85
C	—	2	1.1	5	1.06
D	—	3	1.1	2	0.92
E	0.93	2	1.05	10	0.89
F	0.95	3	0.93	9	0.84
G	0.97	3	1.0	2	0.75

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