LXXXVIII. A SPECTROGRAPHIC ANALYSIS OF THE METALLIC CONTENT OF MECONIUM.

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IN the course of an investigation into the metallic content of the liver in foetal and infant life, four specimens of meconium were examined. The results were of interest in that they appeared to show that while copper and manganese are excreted in considerable quantities into the bowel during foetal life, iron appears to be almost entirely retained in the body of the foetus. These results were consistent with those obtained by examining the foetal gall-bladder, which contains in particular a notable amount of manganese, this being the only metal which reaches a greater concentration in the foetal gall-bladder than in the foetal liver, and the fact that the spectrogram of meconium is chiefly remarkable for the strength of the manganese lines suggested that there is a continual excretion of this metal by way of the bile during foetal life. These findings were of sufficient interest to merit a more extended survey, the results of which are given in this paper. Twenty-four specimens of meconium were examined, derived from twenty-four healthy full-term infants born at the Maternity Department of the Royal Hospital, Wolverhampton. The first specimen of meconium passed by each infant was that used for analysis. Owing to the extent to which the meconium adheres to the linen, and to the difficulty of separating the faeces formed during intra-uterine life from those formed immediately after feeding had begun, it was not possible to obtain any quantitative results as to the total amount of each metal that had been excreted during the period of intra-uterine life. The investigation has this interest, that it not only helps to elucidate the nature of the metallic interchange between mother and foetus, but it may also give some indication whether, under the conditions of modern life, there is any marked deficiency in the maternal supply of those many metals, which as we now know are necessary to life.

The meconium was separated from the napkin, dried to constant weight at 100° and burnt before the slit of a quartz spectrograph by the method of Ramage [1929]. Quantitative estimations were made by comparing the intensities of the lines so obtained with those derived from burning papers with varying amounts of the standard solution. A specimen of the type of linen napkin was also burnt. This gave weak lines due to Na and K and a strong Ca line, but was otherwise negative. The following table shows the results so obtained for Cu, Mn, Fe, Ca, Mg. (In all cases the percentage of dry weight is indicated.)

Table I.

No.	Percentage of dry weight					
	Copper	Manganese	Iron	Calcium	Magnesium	Silver
1	0.008	0.004	-0.02	0.30	0.24	—
2	0.01	0.002	-0.02	1.05	+ 0.48	—
3	0.01	0.0065	-0.02	0.27	0.12	—
4	0.01	0.003	-0.02	0.27	0.18	—
5	0.02	0.007	-0.02	+ 1.44	0.12	—
6	0.02	0.003	0.025	0.30	0.30	Slight trace
7	0.007	0.007	-0.02	0.18	0.24	—
8	0.012	0.008	0.03	1.05	+ 0.48	Slight trace
9	0.02	0.006	-0.02	0.30	0.15	—
10	+ 0.02	0.006	0.13	0.18	0.09	—
11	0.02	0.0023	-0.02	0.15	0.12	—
12	0.018	+ 0.008	0.04	0.24	0.24	—
13	0.02	0.002	-0.02	0.21	0.21	—
14	0.01	0.008	0.02	0.21	0.21	—
15	0.02	0.005	-0.02	0.36	0.36	—
16	0.008	0.005	0.02	0.21	0.21	—
17	0.006	0.005	-0.02	0.18	0.18	—
18	0.017	0.006	0.02	0.14	0.12	Trace
19	0.02	0.007	0.02	0.30	0.18	—
20	0.019	0.002	-0.02	0.24	0.12	Slight trace
21	0.019	0.008	-0.02	0.36	0.24	—
22	0.019	0.006	-0.02	0.27	0.09	—
23	0.018	0.003	0.03	0.15	0.18	—
24	0.019	0.003	0.02	0.24	0.24	—

Copper. This metal was present in every specimen, usually in quite considerable amounts. The amount varied between 0.006 % and slightly in excess of 0.02 % (measured by the 3274.0 and 3247.5 lines). The bulk of the figures, however, were at the higher end of the scale, fifteen of the twenty-four specimens having a percentage of copper in excess of 0.017. There is therefore a definite excretion of copper by way of the bowel during intra-uterine life. From our previous investigations on the foetal gall-bladder, it is probable that this occurs by way of the bile. Since all the infants were healthy it appears justifiable to assume that the amount of copper supplied by the mothers was more than sufficient to provide for the storage of this metal in the liver which occurs during foetal life. This suggests that with an ordinary working class diet the mother succeeds in providing a sufficient supply of copper for this purpose, though it is possible that the provision of this supply may, in the absence of a sufficient diet, be detrimental to the mother. (It is assumed that any mechanism concerned in the fixing of copper in the foetal tissues was working normally.)

Manganese. The actual percentage of manganese in meconium is much less than is the case with the other elements, but it must be remembered that in the normal body this metal only occurs in minute traces (about 0.0008 % of the dry substance). The spectrogram of meconium is, however, quite characteristic, and differs from that of all the other tissues we have examined in the intensity of the manganese triplet (4030.8; 4033.1; and 4034.5). It will be seen that this metal is found in amounts ranging from 0.002 % to slightly in excess of 0.008 %. The cases are equally distributed throughout this range. There are four cases which reach the maximum figure of 0.008 %. The significance of these figures may be realised from the fact that in an examination of some 200 adult tissues [Sheldon and Ramage, 1931] the highest figure found, and then only exceptionally, was 0.002 %. It is obvious therefore that the mother supplies the foetus with a great excess of manganese. The reasons for this are obscure. It must be

remembered that no foetal store of this metal is built up in the liver as is the case with copper and iron. The organism appears to maintain the concentration within fairly close limits at all ages, and it would appear that any excess is excreted. It is, however, possible that while manganese is not stored in the foetus, a constant supply is necessary for foetal growth, which is again steadily excreted. From the high content in the gall-bladder of the foetus of this metal, it would appear that the path of excretion is, as with copper, *via* the bile. The figures certainly do not suggest that, in the cases examined, the mother had any difficulty in supplying the foetus with all the manganese it required.

Iron. Iron differs from all the other metals present in meconia in that while with them there was no difficulty in matching the various lines with varying strengths of the standard solution, the iron lines barely reached the intensity of those in the weakest standard used. These standards were originally prepared so as to cover the amounts of the different metals that would, in the quantities burnt, be found in the tissues of the body. In a general examination of the body it was very rare for the iron lines to be too weak for comparison with the least amount of standard employed [for details see Sheldon and Ramage, 1931]. In the case of meconium, however, no less than fourteen specimens (58 %) showed iron lines that were too weak for estimation by this method. In many cases, indeed, the iron lines were only just visible, indicating that only the merest traces of this element were present in the meconium. Iron therefore provides a sharp contrast with the other metals that have just been considered. This may be brought out in another way. The average amount of copper in the human liver at full-term is 0.03 % (dry), and many of the meconium specimens approach this figure. The corresponding figure for iron is 0.25 % (dry). None of the meconium figures approaches this, the highest being 0.13 %, and most of the cases with identifiable amounts are about 0.02 %, or a tenth of the liver figure at birth. Indeed the weakness of the iron lines is as striking a feature of the spectrograms of meconia as is the strength of the manganese, and this investigation entirely bears out the provisional results which led to it. This poorness in iron may be due to several causes. (1) It may be that the avidity of the foetal tissues for iron, and especially of the liver, is such that all the iron received from the mother, however much, is retained. Foetal gall-bladder and foetal bile contain iron in considerable amount, which suggests that during foetal life the metal is excreted by this route, and its absence from the meconium in similar amounts must be ascribed to a reabsorption from the bowel, which is in favour of a marked avidity of the foetal tissues for the metal. The human liver in infancy and at birth shows great variations, however, in its iron content, and it would have been thought that this variation would be reflected in the meconium. (2) An equally possible suggestion is that while the diet of the pregnant mothers in this midland district furnishes adequate quantities of copper and manganese, it is deficient in iron, so that the foetus is compelled to retain all that it receives in order to build up the necessary reserve store. It is probable that both factors are operative, but the problem merits further enquiry.

Magnesium. The bands of this element centred near wave lengths 3820 and 3684 are clearly visible in all the spectra. The metal occurred in amounts ranging from 0.09 % to a figure in excess of 0.48 %. Cases 2 and 8 were exceptional in the amount of magnesium they contained, which was too strong for measurement by this method. Of the twenty-four cases, twenty had figures between 0.09 and 0.24 %. The excretion of magnesium during foetal life appears to be remarkably uniform.

Calcium. All the meconia contained appreciable amounts of calcium, though there was a considerable degree of individual variation. The figures ranged between 0.15 % and the enormous figure of approximately 1.44 %. Whether cases 2 and 5 are due to an increased excretion of calcium by the foetus as a result of some derangement of their calcium metabolism is obscure, but it would appear more probable that in both cases the large amounts found represent an increased supply from the mother. (The results with Ca are, however, in some doubt, since, although every effort was made to obtain specimens free from linen fibres, the spectrogram of the napkins showed that they contained considerable amounts of calcium.)

Sodium and potassium were found in all the specimens. The strength of the sodium lines was remarkably uniform, but the potassium showed a greater degree of individual variation. Traces of rubidium were found in nearly all the specimens. Traces of silver were identified in cases 6, 8, 18, 20.

SUMMARY.

The examination of the first meconium from twenty-four apparently healthy babies gave the following results.

1. Lines due to Na, K, Ca, Mg, Cu, Mn, Fe are recognisable in all. (It is difficult to determine the presence of Zn by this method, and no opinion is offered with regard to this metal.)

2. The most remarkable features of the spectrograms are the strength of the lines due to manganese (and to a less extent, those due to copper) and the weakness of the lines due to iron. The reason for this constant over-supply of manganese to the foetus is obscure.

3. The results suggest that, at any rate under the social conditions of town working class life, the mother is able to supply the foetus with an excess of all metals except iron. Either, however, she is not able to do so in the case of iron, or the avidity of the foetal tissues for this metal is so great that almost all the iron received from the mother is retained, and any excreted into the gut is reabsorbed.

4. The quantities of the metals found indicate considerable variations in the mothers' power to supply them. One case, however, No. 8, shows a high percentage and another, No. 17, a low percentage common to all metals: such general cases are rare.

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REFERENCES.

- Ramage (1929). *Nature*, **123**, 601.
Sheldon and Ramage (1931). *Biochem. J.* **25**, 1608.