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TYPHOID FEVER AND PREGNANCY

WITH SPECIAL REFERENCE TO FŒTAL INFECTION

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THE number of published cases in which investigation has been made upon the typhoid reaction in the fœtus is small. The following case is therefore recorded by the kind permission of Dr. W. Hale White, under whose care in Guy's Hospital the patient was.

The patient, aged 24 years, had had three children and two miscarriages. She was seven and a half months pregnant when she became feverish and complained of headache. The fever increased and at the end of a week she was drowsy, with flushed face and furred tongue. The pulse-rate was 110 per minute and two typhoid spots were seen on the abdomen. On the eighth day she was delivered of a live fœtus. There was no difficulty during the labour and there was no excess of hæmorrhage. The infant weighed four pounds and died three quarters of an hour after delivery. The mother seemed much relieved after her labour; her pulse became slower and her fever ran the ordinary course for nearly a fortnight longer. Her temperature ranged between 103° and 104° F. She was frequently sponged. On the twenty-first day of the fever she was worse, her pulse became weak, and she died on the twenty-fourth day of the disease. At the necropsy there were found typical typhoid ulcers throughout the ileum, cæcum, and ascending colon. Involution of the uterus had taken place normally. The placental site looked natural. The necropsy of the child, performed immediately after death, revealed no pathological changes. Culture tubes were inoculated with blood from the heart, liver, spleen, and kidneys, and remained sterile after 48 hours' incubation at 37° C. Unfortunately no bacteriological examination was made of the maternal blood. Widal's test was carried out on the mother and on the child. Blood taken from the mother at the time of labour gave a positive reaction in 5 per cent. solution, a partial in 0·5 per cent. The fœtal serum reaction was negative even at 50 per cent.

Table I. is a summary of the cases of a similar nature that we have found recorded in the literature.

Among the problems which present themselves are the following :—

1. *Are typhoid bacilli transmitted from the mother to the fœtus?*—In ten cases (Nos. 5, 10, 11, 14, 22, 23, 24, 26, 27, and 30 in Table I.) typhoid bacilli were found in the fœtal organs or blood. In Case 26 it is just possible that the fœtus may have been infected after birth. In Bolton's and in Fordyce's cases (Nos. 14 and 5) the fœtuses were born dead. The bacilli must therefore have entered the fœtuses before birth. In 11 cases (Nos. 1, 12, 13, 15, 16, 18, 19, 25, 28, 29, and our own) the typhoid bacilli were looked for in the fœtus and not found. Thus in about half of the published cases of typhoid fever in pregnant women typhoid bacilli have passed into the fœtal blood. In such cases they were probably freely circulating in the mother's blood but we have no proof of this. In future cases particular attention should be paid to the bacteriology of the maternal, as well as of the fœtal, blood.

It is interesting to note that when bacilli have been found in the fœtus delivery has been late in the fever. The times are: Third week, third week, twenty-fourth day, sixth week, fourth week, twenty-ninth day, and twenty-fifth day of a relapse ; whereas in those cases in which no bacilli were found the times were comparatively early—viz., tenth day, tenth day, third week, third week, and eighth day from the onset of the mother's fever. It would seem, therefore, that the *duration* of the typhoid fever is an important factor in determining infection of the fœtus. This raises the question whether, in cases where the fœtus is viable, labour should not be induced as early as possible in order to save the child from infection.

2. *Does the typhoid agglutinin occur in the serum of a fœtus born of a mother suffering from typhoid fever?*—That agglutinins do sometimes so occur in the fœtal serum is well established. Positive reactions have been found in seven cases (Nos. 1, 5, 6, 8, 9, 14, and 20 in Table I.).

3. *Can the typhoid serum reaction occur in the fœtus in which no bacilli have been found?*—The evidence that this can be so is slender. Out of the seven cases in which a positive serum reaction was obtained in the fœtus three only were examined for bacteria. In two (Nos. 5 and 14) typhoid bacilli were found. In one (No. 1) bacteria were looked for but not found. This is the only case of the kind. It is so important that we give Etienne's [14] account of it in his own words :—

..... La malade tombe dans le collapsus et elle succombe à 8 heures. A l'autopsie, on constate que les lésions intestinales sont

TABLE I.—TABLE OF RECORDED CASES OF EXAMINATION FOR TYPHOID BACILLI OR FOR WIDAL'S TEST IN FŒTUSES BORN OF MOTHERS SUFFERING FROM TYPHOID FEVER.

Number of case.	Name of observer.	Month of pregnancy.	Fate of mother.	Fate of fœtus.	Widal's reaction in the mother.	In the fœtus.	
						Bacilli in tissues.	Widal's reaction.
1	Etienne, G.[14]	5	Died.	Taken out at necropsy on fifteenth day of fever.	Positive 1 in 150.	Looked for and not found.	Positive 1 in 200.
2	Dogliotti.[8]	—	—	—	Positive.	Not examined.	Negative
3	Planchu and Gallavardin.[26]	8½	Lived.	Born on ninth day of fever; lived.	,,	,,	,,
4	,, [26]	6	,,	Born alive on thirteenth day of fever; died.	,,	,,	,,
5	Fordyce [15]	5	Died.	Born dead in sixth week.	,,	Present.	Positive.
6	Chambrelent.[6]	8	Lived.	Lived. No record of day of fever when born.	,,	Not examined.	,,
7	,, [7]	8	,,	Born on fourth day of fever; lived.	,,	,,	Negative.
8	Griffiths.[20]	9	,,	Born after three weeks' fever; lived.	,,	,,	Positive.
9	Mosso and Danic.[24]	—	,,	—	,,	,,	(?) ,,
10	Freund and Levi.[15]	5	,,	Born alive in fourth week of fever; died.	Not examined.	Present.	Not examined.
11	Etienne, G.[13]	5	—	Born dead on twenty-ninth day of fever.	—	,,	,,
12	Bolton.[5]	3	Died.	Born dead during third week of fever.	Positive.	Looked for and not found.	Negative
13	,, [5]	8	Lived.	Born alive during third week; died in 12 hours.	,,	,,	,,
14	,, [5]	5	,,	Born dead on twenty-fifth day of relapse.	,,	Present.	Positive.
15	Rous and Lacroix.[29]	8	,,	Twins, born alive on tenth day of fever; died in four days.	,,	Looked for and not found.	Negative.
16	,, [29]	8	,,	Born alive on tenth day of fever; died in three days.	,,	,,	,,
17	Batty Shaw.[4]	9	,,	The mother had typhoid fever at fourth to fifth month of pregnancy; the pregnancy continued and the child was born alive at term, and was fed upon the breast.	Positive at time of fever; positive at time child was born.	Not examined.	Negative, even after five weeks' feeding on mother's milk.
18	Kirton.[23]	6	—	Dead; no details.	Positive.	Looked for and not found.	Negative
19	,, [23]	9	—	Dead; no details.	,,	,,	,,
20	,, [24]	9	—	—	—	Not examined.	Positive.
21	Stengel.[30]	—	—	—	—	,,	Negative.
	Earlier cases in which the details are incomplete; investigated before the days of Widal's serum test.						
22	Eberth.[11]	—	—	Born dead, third week of fever.	Not examined.	Present.	Not examined
23	Hildebrandt.[21]	6½	—	Born dead on twenty-second day of fever.	,,	,,	,,
24	Giglio.[19]	—	—	—	,,	,,	,,
25	Frascani.[17]	—	—	—	,,	Looked for and not found.	,,
26	Janiszeski.[22]	—	—	Infant, premature; lived 15 days.	,,	Present after death.	,,
27	Durk.[9]	—	—	—	,,	Present.	,,
28	Resinelli.[2]	—	—	—	,,	Looked for and not found.	,,
29	Fraenkel and Kiderlein.[16]	5	Died.	Dead; born seventeenth day.	,,	,,	,,
30	Ernst.[12]	9	Lived.	Date of delivery uncertain. The child developed a spotty rash suggestive of typhoid fever; died on the fourth day after birth. No intestinal lesions.	,,	Present.	,,

The figures after the observers' names indicate the numbers of the references at the end of the paper.

discrètes ..... L'autopsie du fœtus est pratiquée immédiatement. Nous constatons l'intégrité absolue de tous les organes, notamment des intestins, de la rate et du foie.

Recherches bactériologiques.—Nous ensemençons sur gélose du sang des cavités cardiaques, du sac hépatique et splénique. Tous ces organes fœtaux sont stériles. Nous dosons minutieusement le pouvoir agglutinatif selon la méthode de Courmont, en nous servant d'une culture sur bouillon de bacille d'Eberth ayant pour point de départ un échantillon donné par F. Widal, toujours entretenu et que nous avons toujours employé pour nos recherches antérieures. Chez la mère le sang des cavités cardiaques présente un pouvoir agglutinatif de 150. Chez le fœtus, le sang des cavités cardiaques a un pouvoir agglutinatif de 200. Le liquide amniotique a également un pouvoir de 200.

The occurrence of agglutinins without bacteria in the fœtus appears to us contrary to expectation. It is a point requiring careful and repeated confirmation. If true, the deduction must be that a positive Widal's reaction in the fœtus is no proof that the fœtus has, or has had, typhoid fever. It further raises the question :—

4. *How does the fœtus acquire agglutinin?*—Since it is well established that typhoid bacilli are sometimes found in the fœtus it would be reasonable to expect that the fœtal tissues, reacting to the bacillary invasion, would produce their own agglutinins, the fœtus behaving as though it were an independent individual. If bacilli were always found in the fœtal tissues when the fœtal serum gave a positive reaction, as in Fordyce's and in Bolton's cases (Nos. 5 and 14), there would be ground for presuming that the fœtus always produced its own agglutinins in this way. Etienne's case, if true, seems to support the opposite view—namely, that the serum reaction can occur in the fœtus without bacilli being present. It is a most important case but it needs confirmation. If confirmed it would show that agglutinin may occur in the fœtus without bacillary infection. If this be the case there are two possibilities : either the fœtus receives the agglutinin directly from the mother across the placenta ; or, the fœtus reacts to the maternal bacillary infection, producing its own agglutinins in response to stimulation by maternal toxins.

The passive transmission of the agglutinin from the mother to the fœtus would seem possible, since we know that the virus of measles,[1] of variola,[2] and of syphilis can pass, and also soluble drugs[3] such as mercury, potassium iodide, alcohol, and chloroform. If, however, this be the usual method by which the fœtus obtains its agglutinins it is difficult to explain (1) why the fœtal serum reactions should be absent in so many cases (viz., Nos. 2, 3, 4, 7, 12, 13, 15, 16, 17, 18, 19, and our own), in all of which the maternal reactions were positive ; (2) why, in a case such as that given by Batty Shaw (No. 17), the fœtus, which remained in utero for four months after the maternal attack of typhoid fever, should give a negative reaction when the mother's serum gave a strong reaction both at the time of the fever and also at the time of the child's birth.

We would further draw attention to the fact that the negative fœtal results have nearly all occurred in the cases in which early delivery had taken place. In the negative cases the times were: ninth day, fourth day, thirteenth day, tenth day, tenth day, eighth day, third week, and third week of the fever; whilst positive results were obtained at the sixth week, third week, third month, and twenty-fifth day. The times were appreciably the longer when a positive result was obtained. It is difficult to see why there should be this delay in the passage of agglutinins if the fœtus receives them from the mother; unless the placenta can be supposed to exert a temporary "barrier-action" [27] against the passage across it of agglutinins but ultimately allows them to pass. It seems equally reasonable to suppose that the fœtus produces its own agglutinins. It is a matter of regret that all the cases of positive serum reaction in the fœtus have not been bacteriologically examined.

The effect of pregnancy upon the mother who has typhoid fever.—Typhoid fever occurring during pregnancy does not affect the prognosis or alter the course of the disease. The results in the seven cases that have occurred in Guy's Hospital over a period of 28 years are given in Table II.

TABLE II.

Age of mother.	Month of pregnancy.	Fate of mother.	Fate of fœtus.
24	8	Died.	Born alive at eighth day of fever. Died in three-quarters of an hour.
26	5	Recovered.	Went to term. Born alive and lived.
21	2½	,,	Abortion on seventeenth day of fever.
24	3½	,,	,, twenty-sixth ,, ,,
24	4	,,	,, fourteenth ,, ,,
20	8½	,,	Labour on fourth day of fever. Child lived.
31	4	,,	Abortion during fourth week of fever.

The death-rate was 14 per cent. Vinay [31] gives the mortality at 17 per cent. Duynot [10] gives six deaths in 36 cases, a mortality of 16 per cent. These figures do not differ widely from those given by the Metropolitan Asylums Board for all cases.

The effect of typhoid fever in the mother on the pregnancy.—The effect of enteric fever on the pregnancy is bad. In the majority of the cases abortion or premature labour takes place. This was so in six of the seven cases in Guy's Hospital—i.e., 85 per cent. Vinay gives two-thirds

of abortions. Martinet's figures are 66 abortions in 109 cases. Penot[25] gives 65 per cent. of abortions. The delivery is most often easy and the patient experiences considerable relief. The uterus involutes just as if there were no maternal illness. The fœtus, even if viable, is often born dead or dies soon after birth. As we have suggested, it is possible that this heavy mortality amongst viable fœtuses might be reduced by the induction of premature labour in the earliest stage of the fever. Such induction would seem to be justifiable in the interests of the child when the prognosis for the mother is apparently so little influenced by labour.

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Bibliography.—1, 2, and 3. Ballantyne: Archiv Pediatr., vol. x., 1893, p. 301; Antenatal Pathology and Hygiene, vol. i., p. 188; ibid., p. 156. 4. Batty Shaw: THE LANCET, August 28th, 1897, p. 539. 5. Bolton: Journal of Pathology and Bacteriology, vol. vii., 1901, pp. 137–41. 6 and 7. Chambrelent: Journal de Médecine de Bordeaux, vol. xxvii., 1896, pp. 245–57; Revue Mensuelle de Gynécologie, d'Obstétrique, et de Pédiatrique, Bordeaux, February, 1900. 8. Dogliotti: Gazzetta Medica di Torino, 1897, p. 821. 9. Durk: Münchener Medicinische Wochenschrift, vol. xliii., 1896. 10. Duynot: THE LANCET, May 10th, 1902, p. 1334. 11. Eberth: Fortschritte der Medicin, vol. vii., 1889, p. 889. 12. Ernst: Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie, vol. viii., 1890, p. 188. 13 and 14. Etienne: Presse Médicale, 1896, p. 465; Comptes Rendus de la Société de Biologie, 1899, p. 860. 15. Fordyce: Transactions of the Edinburgh Obstetrical Society, vol. xxiii., 1898, p. 90. 16. Fraenkel and Kiderlein: Fortschritte der Medicin, vol. vii., 1889, p. 641. 17. Frascani: Riv. Gen. Ital. di Chir. Med., vol. iv., 1892, pp. 282–348. 18. Freund and Levi: Berliner Klinische Wochenschrift, 1895, p. 539. 19. Giglio: Centralblatt für Gynäkologie, vol. xiv., 1890, p. 819. 20. Griffiths: Medical News, May 15th, 1897. 21. Hildebrandt: Fortschritte der Medicin, vol. vii., 1889, p. 889. 22. Janiszeski: Münchener Medicinische Wochenschrift, vol. xl., 1893, p. 705. 23. Kirton: Medical Supplement of the Metropolitan Asylums Board, 1897. 24. Mosso and Danic: Comptes Rendus de la Société de Biologie, vol. x., 1897, p. 238. 25. Penot: Thèse de Paris, 1899, Epitome, Brit. Med. Jour., 1900, vol. i., No. 27. 26. Planchu and Gallavardin: Lyon Médicale, vol. lxxxviii, 1898, pp. 479–83. 27. Porak: Archives de Médecine Expérimentale et d'Anatomie Pathologique, vol. vi., 1894, p. 192. 28. Resinelli Annali di Ostetrica e Ginecologia, vol. xviii., 1896, p. 695. 29. Rous and Lacroix: Presse Médicale, Paris, 1902, pp. 315–17. 30. Stengel: New York Medical Journal, vol. x., 1898, p. 338. 31. Vinay: Lyon Médicale, Dec. 3rd, 1893.

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