

**The significance of the typhoid serum reaction in the offspring of patients suffering from enteric fever / by Charles Bolton.**

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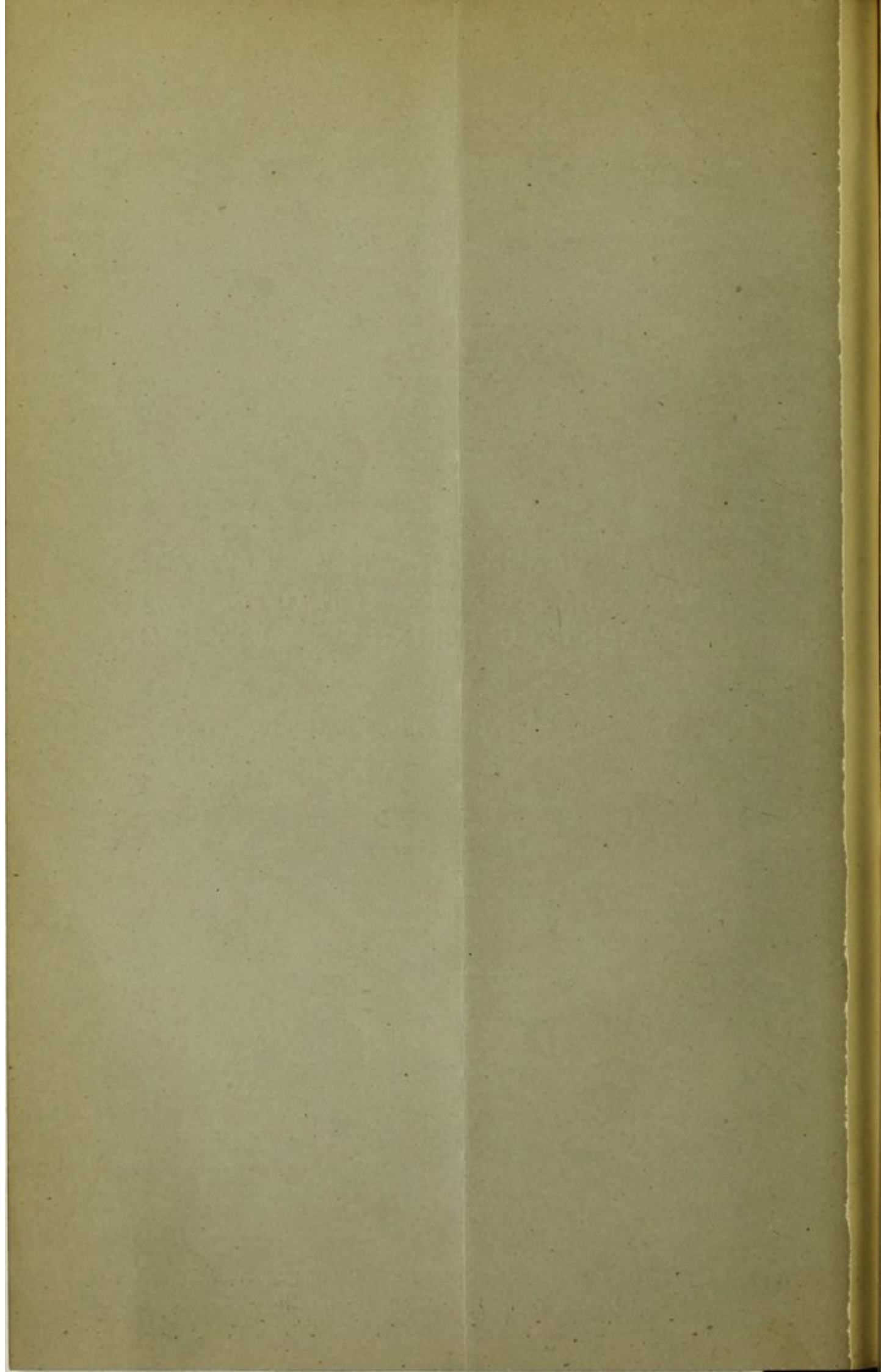
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THE SIGNIFICANCE OF THE TYPHOID  
SERUM REACTION IN THE OFFSPRING  
OF PATIENTS SUFFERING FROM ENTERIC  
FEVER.

By CHARLES BOLTON, M.D., B.Sc. (Lond.).







## THE SIGNIFICANCE OF THE TYPHOID SERUM REACTION IN THE OFFSPRING OF PATIENTS SUFFERING FROM ENTERIC FEVER.

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It has been shown that the serum reaction may or may not occur in the foetus of a patient suffering from enteric fever who reacts to the test herself. The significance of this, however, has not yet been clearly worked out, owing, no doubt, in great part to the difficulty of obtaining the necessary material, and also to the fact that the child must be dead in order that a complete examination may be made.

There are three sources from which the serum reaction in a child or foetus may be derived. The offspring may have been infected with the *Bacillus typhosus* by the mother through the placental blood, the foetus then developing its own agglutinin, or the agglutinin of the mother may have passed into the blood of the foetus from the placental blood, or it may be assimilated by the foetus from the mother's milk.

There is clinical evidence that the foetus may be directly infected with typhoid bacilli through the placental blood. Etienne <sup>(1)</sup> has published a case of abortion on the twenty-ninth day of the fever, in which typhoid bacilli were found in the placenta, ventricular blood, liver, and spleen of the foetus. Speier <sup>(2)</sup> has also found the bacillus in the placenta, peritoneal fluid, liver, and kidney of a 4-months foetus, the abortion taking place during an attack of enteric fever.

The possibility of the passage of agglutinin from the maternal to the foetal blood has been experimentally proved by Widal and Sicard <sup>(3)</sup>. They state that the passage of agglutinin is inconstant and generally incomplete, and that the reaction obtained from the offspring is less marked than that from the mother. Their experiments were performed on rabbits. Achard <sup>(4)</sup> also, experimenting on guinea-pigs, has found that the agglutinating property is transmitted to the foetus, but only in a minute quantity. In his positive cases the mothers had been repeatedly inoculated, and their blood possessed considerable agglutinating power, whilst in the negative cases they had only been inoculated once or twice.



From the clinical side, numerous cases of enteric fever occurring before, during, and after a pregnancy have been reported. Unfortunately, however, in most of the cases the investigation has been limited to an examination of the blood for the serum reaction, whereas, in order to determine the source of the agglutinating power of the blood, a bacteriological examination of the organs of the foetus is necessary. This, of course, is frequently impossible, as the child may not die.

Where the attack of enteric fever occurs after the birth of the child, any agglutinating power possessed by the blood of the latter must have been obtained from the milk of the mother. This has been shown actually to occur by Talamon and Castaigne (<sup>5</sup> and <sup>6</sup>). These observers, in a case of enteric fever occurring four months after delivery, obtained a marked positive serum reaction from the mother's milk. The child, whilst taking the breast, gave a positive reaction, and after weaning a negative reaction. The reaction, however, reappeared four days after recommencing breast feeding. They also quote a case of the fever three months after delivery, in which the blood of the suckling did not react, although the mother's milk gave the reaction. They state that in the former case the child had enteritis, and thus explain the absorption of the agglutinin, as it has been stated that the agglutinating substance is not absorbed by mucous cavities unless a lesion is present.

On the other hand, if the attack of enteric fever has occurred a considerable time before the pregnancy, the infant, if its blood gives the serum reaction, has probably obtained the agglutinin from the milk of the mother; it may possibly have obtained it before birth from the placental blood; and it is highly improbable that it could have contracted typhoid bacilli from latent infection in the mother, and manufactured its own agglutinin. The only instances which I can find in the literature which has been published on the subject, in which the serum reaction has been made use of under these circumstances, are three cases recorded by Kasel (<sup>7</sup>). In the first case, the mother, during the third week of enteric fever, gave the reaction (1 in 30). Fifteen months later, shortly before her confinement, she still gave a positive reaction (1 in 50 in half an hour), but the child after birth gave a negative reaction in spite of repeated tests. In the second case the mother had an attack of enteric fever fifteen years before pregnancy. When the child was *æt.* 3 months the mother gave a positive reaction (1 in 50), but the child gave a negative reaction (1 in 1). In the third case, the mother had enteric fever twenty-one years before the pregnancy. When the child was *æt.* 9 the blood of the mother gave a positive reaction (1 in 50), but the child gave only a doubtfully positive reaction (1 in 1). He consequently concluded that the agglutinin in the blood of a child, born of a mother who had had enteric fever some years before conception,



is minimal in amount, and that if the agglutinating power in the mother does not exceed 1 in 50 the agglutinin either does not pass during the pregnancy to the foetus, or it disappears shortly after the birth of the child.

Lastly, as has been stated, an attack of enteric fever may occur during pregnancy. Of this type numerous instances have been recorded, and I propose to add three more to the list of cases already published. In some of these cases the blood of the child gave a negative and in others a positive result. The *negative* cases are the following:—The first was reported by Etienne <sup>(1)</sup> in 1896. It was a case of severe enteric fever, dying on the twenty-sixth day. A 4½-months foetus was removed from the uterus at the autopsy. The blood of this foetus gave a negative reaction, and its organs were sterile, and exhibited no evidence of enteric fever. The blood of the mother gave a positive reaction, and typhoid bacilli were found in her liver and spleen. Shortly afterwards, Charrier and Appert <sup>(8)</sup> obtained a negative result from a foetus of three or four months. In 1897, Shaw <sup>(9)</sup> published a case in which the child was born three months after the fever. It was healthy, it was fed at the breast, and it gave no reaction, or an extremely doubtful one, at the age of 5 weeks. Kirton <sup>(10)</sup> in the same year published two negative cases of foetuses, æt. 6 months and full term respectively. In both these cases the mothers gave positive reactions. Lastly, Stengel <sup>(11)</sup>, in 1898, obtained a negative result in a child born during an attack of enteric fever, the mother giving a positive reaction. The following *positive* cases have been published. In the paper already referred to Kirton also records a positive case, that of a child born at full term, the mother also giving the reaction. Chamberlent and Saint-Philipp <sup>(12)</sup> obtained a positive reaction in mother and child in a case of premature labour in 1896, and in the following year Griffiths <sup>(13)</sup> also obtained a positive reaction in the child, æt. 7 weeks, of a patient suffering from enteric fever. Lastly, Mosso and Daunic <sup>(14)</sup>, in 1897, recorded a case of normal labour three months after the fever, in which the placental blood at birth gave a positive (1 in 10) reaction, and the blood of the child, twenty-four hours after birth, also gave a positive reaction (1 in 1). The placenta was examined histologically, and no bacilli were found, but this cannot be held to prove their absence, as apparently no cultivations were made. Also, as the child lived, it was impossible to examine its organs for bacilli.

The cases which I myself have had the opportunity of examining whilst assistant medical officer at the Homerton Fever Hospital are the following:—

CASE 1.—*Enteric fever in the mother, without infection of the foetus.*—The patient was æt. 22, and three months pregnant. The disease was of a severe character, and she aborted during the third week, and subsequently died of perforation during a relapse. Before the abortion her blood (diluted to 1 in



20) gave at once a good serum reaction. The blood of the foetus gave no reaction whatever to the test, and its organs presented no post-mortem lesions. Cultivations were taken from the liver, spleen, gall bladder, and peritoneal fluid, but no growths were obtained from them.

CASE 2.—*Enteric fever in the mother without infection of the foetus.*—The patient was æt. 41, and eight months pregnant. Her attack of the fever was fairly severe, and she gave birth to a living child during the third week of the disease, subsequently recovering. Her blood (1 in 20) at once gave a good serum reaction. The child died twelve hours after birth. Its blood gave no reaction, and its organs presented no lesions. Cultivations were taken from the spleen, mesenteric gland, gall bladder, and kidney. From each organ the same growth was obtained upon agar. The growth consisted of very small, feebly motile, bacilli, which did not give any reaction on testing with enteric blood serum, and which were decolorised by Gram's method. The bacillus clotted milk and formed acid, fermented dextrose, formed a large amount of indol, and formed gas bubbles in shake-cultures of gelatin. The growths were evidently pure cultivations of the *B. coli communis*, as, on repeatedly making subcultivations on gelatin and agar plates, the same bacillus was invariably obtained.

CASE 3.—*Enteric fever in the mother, with infection of the foetus by the B. typhosus.*—The patient was æt. 19, and five months pregnant. On the twenty-fifth day of a relapse she gave birth to a stillborn child, subsequently recovering. Her blood (1 in 40) at once gave a good serum reaction. The blood of the child (1 in 20) reacted in a quarter of an hour. There were no lesions in its organs, and cultivations were taken from the gall bladder and spleen. The growth obtained on agar was in each case the same. It consisted of actively motile bacilli which gave the reaction with enteric blood serum, and also with the blood of the foetus. The bacilli were decolorised by Gram's method, and neither clotted milk nor formed gas from dextrose or in shake-cultivations of gelatin, but formed a little indol. The same bacillus was obtained from sub-cultures. Not having the opportunity of employing more extensive tests, I sought the aid of Dr. Bulloch, bacteriologist to the London Hospital, who very kindly examined a subculture from the gall bladder, and confirmed my opinion that the bacillus which I had found was the *B. typhosus*.

#### CONCLUSIONS.

In the only one of my own cases in which the foetus gave a serum reaction, it had been infected with typhoid bacilli, and had presumably formed its own agglutinin. With regard to the passage of agglutinin from the mother to the foetus through the placenta, although experimental evidence shows that on repeated inoculation of the mother a little agglutinin may pass to the foetus, I can find no clinical case on record in which the child gives a positive reaction to the serum test, and in which the organs have been proved free from *B. typhosus*. Until this is shown, the passage of agglutinin through the placenta in the human subject must be considered unproved.

On the other hand, as stated above, agglutinin has been proved to exist in the milk and colostrum of a woman whose blood gives the serum reaction, and it has also been proved that it is absorbed from the milk by the suckling child.

I desire, finally, to express my indebtedness to Dr. Bulloch for



his kind assistance, and to Dr. Goodall of the Homerton Fever Hospital for his kindness in allowing me to make use of the material required for this investigation.

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