

UPON THE AGGLUTININ TEST IN THE DIAGNOSIS OF TUBERCULOSIS.

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IN 1898 Arloing and Courmont¹ published the results of experiments made by them on the agglutination produced by the serum of tubercular patients. For this purpose they used a strain of the tubercle bacillus isolated by the former, which produced a uniform turbidity when grown in glycerine broth. With this culture, serum from tubercular patients gave reactions at dilutions of 1 in 5, 10 or 20 in a large percentage of cases, and that from normal individuals only in a much smaller percentage and then not very strongly. From this they concluded that the agglutination reaction was likely to be of considerable use in the diagnosis of tuberculosis.

Other observers, however, who tested these results both with Arloing's culture and with various other preparations of the bacilli, came to the conclusion that the reaction was of no practical use. Koch² for instance showed that with most uninoculated animals similar reactions could usually be obtained, but that when inoculated they often gave agglutinations up to 1 in 200, 500 or even 2000. On investigation of a series of hospital patients and others, tubercular and non-tubercular, he found the following:—

Non-tubercular. 1 case reacted at 1 in 50, 5 at 1 in 25, 6 at 1 in 10, 19 gave practically no result.

Tubercular. 1 case reacted at 1 in 50, 4 at 1 in 25, 14 at 1 in 10, 59 gave practically no result.

¹ *Comptes rendus de l'Acad. des Sciences*, 19 Sept. 1898, and *Gazette des Hôpitaux*, 1 Dec. 1900, p. 1467.

² *Deutsche Med. Wochenschr.* 28 Nov. 1901.

At the same time in cases which had been treated with tuberculin he often obtained reactions up to 1 in 300.

Considering the difference of opinion on the subject, it seemed of interest to test the power of agglutination during the progress of a case of tuberculosis from the beginning to the end, in order to find out whether there ensued any marked alteration in the reaction. Monkeys were selected for the experiment as being animals which very quickly acquire intestinal tuberculosis on feeding with the bacilli. Accordingly two monkeys, both apparently normal, were fed with an emulsion of a virulent culture of human tuberculosis, and the serum of each before feeding, and at various times afterwards, was tested against a preparation of the same strain of *B. tuberculosis* as that with which they had been fed. The preparation of tubercle bacilli used for agglutination experiments was made by grinding in a mortar a culture of the bacilli grown on glycerine potato, and making a thick emulsion of the rubbed up mass in water. By centrifugalisation it was possible to drive all but the smallest masses to the bottom, and still leave a considerable number of fairly well separated bacilli in the fluid. This fluid when pipetted off showed very little deposit and no sign of the formation of flocculi, even after four or five days. The examinations were made by the macroscopic method, one part of serum being mixed with ten or more parts of the emulsion, and the formation of flocculi down the sides or at the bottom of the tubes noticed after standing at 37° C. over night. Microscopic examinations were also made, but in no case could agglutination be observed with certainty at as high a dilution.

Monkey "A" was never as lively as the other, rapidly became thin, and died in about a month. The post-mortem examination showed an advanced condition of pulmonary phthisis, with cavities and tubercular pneumonia in the left lung. There was no ulceration of the intestine or any sign that the tuberculosis had been caused by the feeding. From this it seems likely that it was suffering from tuberculosis before the feeding took place.

Monkey "B" on the other hand lived rather more than two months, and being then in a dying condition was bled to death. On post-mortem examination it showed marked general tuberculosis, with ulceration of the intestine, masses of matted mesenteric glands, and miliary tuberculosis of the whole body, pointing distinctly to the fact that the disease had originated from the feeding.

Before feeding, the serum from both monkeys completely agglutinated and cleared the emulsion of bacilli at a dilution of 1 in 10, and

showed a reaction up to 1 in 40, that from B showing a slight reaction at 1 in 50, and this result remained fairly constant, about 1 in 40 or 50, during the period in which the animals were under observation.

Table showing the reaction of agglutination of the two monkeys A and B, between the date of feeding and the time of death.

Dilution	Monkey A						Monkey B							
	Before feeding	6th day	11th	17th	26th	30th	Before feeding	6th day	11th	17th	26th	35th	64th	
1 in 10	+	+	+	+	+		+	+	+	+	+	+	+	
20	+	+	+	+	+		+	+	+	+	+	+	+	
25	+	+	+	+	+		+	+	+	+	+	+	+	
40	+	+	+	+	?	died	+	+	?	+	?	+	+	
50	-	-	-	+	-		?		-	+	-	+	?	
60	-	-	-	-	-		-	-	-	-	-	-	-	
100	-	-	-	-	-		-	-	-	-	-	-	-	

The value of the emulsion of tubercle bacilli used was tested by the reaction produced on it by the serum of goats; one, which was normal, giving a slight reaction at a dilution of 1 in 20, and two, which had been inoculated with the juices of ground tubercle bacilli, giving marked reactions up to 1 in 80. Considering the fact that animals inoculated with these tubercle juices give such a marked reaction, it is interesting that those which have acquired tuberculosis in the usual manner by taking in the living organisms through the mouth, either into the lungs, or into the intestinal tract, show such small variation from the normal.

The above observations show that during the progress of a tuberculosis infection in these monkeys, no agglutination titrate of any diagnostic value could be obtained in the early or late stages of the disease.

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