SCIENTIFIC GRANTS COMMITTEE

OF THE

British Medical Association.

REPORT LXXXIII.

SOME EXPERIMENTS ON ENTERICA, SCARLET
FEVER, AND MEASLES IN THE
CHIMPANZEE.*

[A PRELIMINARY COMMUNICATION.]

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THE bacillus described by Eberth in 1880 and isolated by Gaffky in 1884 has been very generally accepted as the causal agent of enteric fever, although it was not then possible to fulfil Koch's third postulate, and to produce with the bacillus lesions in animals similar to those resulting from the disease in man. Additional evidence was forthcoming as to the probable responsibility of the Eberth-Gaffky bacillus for enteric fever in 1896, when I was able to show that the serum of human beings, in either the acute or the convalescent stage of the disease, was often able, even in considerable dilution to agglutinate emulsions of the bacillus. But this observation does not amount to actual proof, as Balthazard¹ thinks, for we know that the serum of patients suffering from typhocoloid (paratyphoid) fever, while agglutinating the typhocoloid bacillus in, say, 1 in 2,000 dilution, may nevertheless agglutinate the typhoid bacillus in 1 in 100 dilution—that is, in greater dilution than the serum of many patients with genuine enterica. It does not therefore follow, although it may be probable, that a bacillus agglutinated in considerable dilution by the patient's serum is the causative agent of the disease; but it is certainly a corroborative fact when other indications point that way.

Various investigators have tried to produce the typical intestinal lesions in animals; but in those cases in which successful results have been obtained it has been necessary to give excessive doses of the bacillus. Thus Remlinger² fed rabbits and rats for four to ten days on cabbages contaminated with *B. typhi* abd.; of eight animals, four showed no symptoms. The other four had the typical variations in temperature accompanied by the serum reaction and intestinal lesions characteristic of enterica. Chantemesse confirmed these experiments and obtained similar results in monkeys.

In ordinary monkeys I have not seen any effect beyond a transitory diarrhoea and the subsequent appearance of the serum reaction follow the administration of a single dose of typhoid bacilli by the mouth, even when accompanied by virulent streptococci. Nor indeed has infection occurred when the organisms were introduced directly into the small intestine, or under the dura mater, or into the knee-joint. But I do not lay much stress on these negative results.

Macacus Rhesus ♀

July 30th, 1901.—*B. typhi* abd. given in milk. Blood—no agglutination 1:2.

August 7th.—Blood agglutinates 1:8 in 30 minutes.

" 8th.—	"	"	1:16	"
" 10th.—	"	"	1:32	"
" 12th.—	"	"	1:8	"
" 14th.—	"	"	1:16	"
" 15th.—	"	"	1:32	"
" 16th.—	"	"	1:16	"
" 19th.—	"	"	1:20	"
" 22nd.—	"	"	1:40	"
" 28th.—	"	"	1:100	"
" 30th.—	Killed under CHCl ₃ . No evidence found of enteric lesions.			

The blood was examined daily, with few exceptions.

The variation in strength corresponds with what is also seen in man.

* The experiments on enterica were made in part during my tenure of the Ernest Hart Memorial Scholarship. To my regret the Scientific Grants Committee did not see its way to letting me extend them to "paratyphoid" fever. The investigation of scarlet fever and measles was undertaken with the aid of the Research Scholarship of the Grocers' Company.

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Chimpanzee A. ♀ (Fig. 1).

July 15th, 1901.—1 c.cm. 24 hours culture in broth of *B. typhi* abd. (Laboratory culture, unknown origin) given in milk. Blood; no reaction, 1:2.

July 21st.—Blood reacts slightly, 1:10 in 60 minutes.

July 25th.—Blood reacts slightly, 1:20 in 30 minutes.

July 27th.—Necropsy. Peyer's patches enlarged and swollen. Mesenteric glands and spleen enlarged. *B. typhi* abd. obtained from broth culture of spleen.

Fig. 1.—Chimpanzee A; lower portion of ileum.

Chimpanzee B. ♂ (Figs. 2, 3, and 4.)

May 21st, 1902.—1 c.cm. culture of *B. typhi* abd. per os. Blood reacts 1:10 in 30 minutes.

May 24th.—Blood reacts 1:30 in 30 minutes.

May 26th.—Blood reacts 1:30 in 30 minutes.

May 31st.—Blood reacts 1:60 in 30 minutes.

June 1st.—Blood reacts 1:80 in 30 minutes.

June 2nd.—Necropsy. Appearances as above.

The chimpanzee, although not every individual, is susceptible to *B. typhi* abd., but the virulence of my cultures was not sufficient to produce a fatal result in the two instances in which they were given the opportunity of so doing. In the other two cases the animals were killed under chloroform on the twelfth day after infection. The clinical symptoms were but slightly marked; a dirty tongue and diarrhoea were the most prominent. In one instance general malaise was fairly evident; headache was apparently not present. No rose spots were seen nor was the spleen felt. The initial dose is often

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followed, both in the chimpanzee and in the lower monkeys, by a slight and temporary rise of temperature accompanied by diarrhoea. The temperature curves were not very characteristic. One of the charts is appended. I am not inclined to lay much stress on the atypical character, because the temperature of the chimpanzee is normally subject to rather wide variation partly according to the surrounding temperature. The serum reaction did not always become strong although it almost always appeared. Before infection the blood generally did not agglutinate *B. typhi* abd. at all.

The chief evidence of infection is found in the characteristic intestinal lesions (of which photographs are given) and the recovery of the bacillus from the spleen tissue after death.

The lesions are more advanced than in man at the corresponding date; perhaps on account of the larger infecting dose.

Fig. 2.—Chimpanzee B; lower portion of ileum.

Various modes of infection by scarlet fever were tried; by clothes, skin peelings, swab from throat of patient, culture of streptococcus conglomeratus, and the heart blood removed shortly after death with a syringe. With the last only rhesus monkeys and rabbits were infected. The streptococcus isolated proved very fatal to the latter; in the monkey it merely caused suppuration. Some of the material was from a very malignant case described by de Boinville.³ In the chimpanzee the only positive result was obtained when the throat was rubbed with the swab from a patient's throat.

Fig. 3.—Chimpanzee B; lowest portion of ileum. Natural size.

Fig. 4.—Chimpanzee B; section through lowest Peyer's patch.

A scarlatinal tonsillitis ensued, but no rash or extensive desquamation.

Chimpanzee C. ♀ (Chart 1).

January 4th, 1903.—1 loop agar culture B. typhi abd. (Fisher). Blood: no reaction, 1:2.

January 8th.—Blood reacts trace 1:30.

January 14th.—Blood reacts well 1:30.

The blood never reacted in higher dilution. This animal died 13 months later on February 20th, 1904, of pneumonia.

Chimpanzee D. ♂.

May 21st, 1903.—Portion of typhoid stool given in water. (B. typhi abd. could not be isolated.) Blood gave no reaction; nor did it at any time later.

June 4th.—Distended abdomen. Yellow stools.

June 8th.—Since there has been no rise of temperature some culture of B. typhi abd. is given in milk.

June 22nd.—The temperature curve has been quite erratic, and has come down to normal.

This animal was probably not infected. It died on August 10th, 1903, of diarrhoea, due to colitis—a common and fatal disease of the chimpanzee. From the faeces was isolated a bacillus closely resembling B. dysenterica Gray).

Chimpanzee. ♀ (Chart 2.)

June 25th, 1902.—Clothed in nightgown from scarlet fever case. No result.

July 6th.—Swab from case of scarlet fever applied to throat.

July 10th. Doubtful roseola.

July 11th.—White specks on both tonsils; not on uvula.

July 12th.—Exudate covers both tonsils. The roseola, mostly on abdomen, has not a scarlatiniform appearance.

July 14th.—Still exudate on left tonsil only. (The temperature chart is given below.)

Streptococcus conglomeratus was isolated from the throat. Own blood agglutinates it.

Similar methods of infection were tried for measles and also the injection of blood taken direct from the median basilic view of measles cases. It had no effect: it may even have conferred immunity rather than conveyed infection.

Chimpanzee. ♀

May 22nd, 1902.—Clothed in nightgown from case of measles. No effect.

June 5th.—Swab from case of measles applied to nose and throat. Temperature, 100.2° F.

June 7th.—Coryza. Temperature, 99.6° F.

June 11th.—Slight roseola. Temperature, 102° F.

June 15th.—Rash gone. Temperature, 99.2° F.

It remains doubtful whether this animal was really infected with measles. Coryza is not uncommon in the chimpanzee, although here it seemed to have a causal relation to infection.

Chimpanzee. ♂

January 29th, 1902.—Injected 2 c.cm. measles blood. No effect.

February 8th.—Injected 4 c.cm. measles blood. No effect.

February 22nd.—Clothed in measles nightgown. No effect.

Of these experiments I think that those on enterica assist in fulfilling Koch's third postulate as applied to Eberth's bacillus.

I have called these remarks a preliminary communication to indicate my sense of their incompleteness; but anthro-poids are scanty and costly, so that the completion of the investigation may be a matter of years.

It only remains for me to acknowledge my indebtedness to the British Medical Association and to the Grocers' Company, who to a large extent made the investigation financially possible, and to thank many friends and colleagues who, often at much trouble and inconvenience to themselves, provided me with material (21 cases of scarlet fever and 25 cases of measles) and laboratory facilities.

REFERENCES.

¹ Balthazard, *Toxine et Antitoxine Typhiques*, p. 2. ² Remlinger, *Ann. de l'Inst. Pasteur*, 1897, p. 829. ³ De Boinville, *Lancet*, 1902, vol. ii, p. 359.

REPORT LXXXIV.

EXPERIMENTAL NEPHRITIS FOLLOWED BY
DECAPSULATION OF THE KIDNEY.

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WHEN Edebohls first suggested the decapsulation of the kidney as a reasonable method of treatment in chronic nephritis, he based his proposal upon the urinary and general improvements which followed the fixation of a movable kidney by the removal of its capsule. In one of his cases which died four months after decapsulation, he observed "enormously dilated and enlarged blood vessels which penetrated from the fatty capsule through the capsule proper into the kidney substance." This access of additional blood he considered would provide increased nutrition, stimulate an extensive regeneration of the secreting cells, and consequently produce a more efficient excretion of waste products. Whether decapsulation yields better results than the simpler reni-puncture of Reginald Harrison, which has been so widely and successfully employed, is a question which the available clinical data have not yet satisfactorily answered. We must wait from two to five years before making any definite conclusions as to the value of this operation. Meanwhile, we may with advantage investigate the anatomical aspect of the procedure, and thus the present inquiry has for its main object the observation of the tissue changes which follow the decapsulation of kidneys in which nephritis has been induced.

Claude and Balthazard, and Albarran and Bernard already in 1902 published short notes on the changes following renal