EXPERIMENTAL MEASLES IN MONKEYS (Macacus Rhesus)

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During a recent epidemic of measles in Porto Rico the authors infected a series of monkeys with citrated blood from early cases of the disease. The purposes of this study were (1) to determine the incubation period of measles in this experimental animal; (2) to study the character of the symtoms produced and (3) to culture the blood of the measles patients selected and the blood of the experimental animals after symtoms of the disease had appeared.

It is well known that experimental measles can be produced in monkeys. Goldberger and Anderson(1) succeeded in producing experimental measles in Rhesus monkeys and state that the eruption appeared in from ten to twenty-six days following inoculation. In the experiments of Goldberger and Anderson blood serum from cases of measles was diluted three times with saline and filtered through a Berkefeld filter after which monkeys were inoculated with this material. Blake and Trask(2) were also able to induce the disease in monkeys with material obtained from the naso-pharynx of active cases of measles and further demonstrated that the virus is filterable. Nevin and Bittman(3) have induced symptoms of measles in rabbits and monkeys following the injection of blood from active cases. Duval and d'Aunoy(4) have reported similar results in guinea pigs. It seems amply confirmed then that this human malady can be transmitted to monkeys and possibly to other laboratory animals although the evidence here is not at all conclusive since a definite rash has not been produced in rabbits and guinea-pigs.

In view of the recent reports of Tunnicliff(5), Ferry and Fisher (6), Hibbard and Duval(7), and others on the cultivation of a non-hemolytic streptococcus from the blood of measles cases the authors thought it would be of value to again study the experimental disease in monkeys and make an attempt to cultivate this organism from both the human cases of measles and animals used in the experiments. Should a non-hemolytic streptococcus be cultivated from active cases of this disease and the same microbe be found in the inoculated animal showing definite symptoms of the disease, the evidence would appear more convincing that measles is caused by a streptococcus and not by a filterable virus as so many investigators have believed. Fur-

thermore if the streptococcus appeared in the experimental animal showing symptoms of measles it might be possible to reproduce symptoms of the disease in other monkeys by passage of the streptococcus from animal to animal.

Cases of measles were selected in the Municipal Hospital, San Juan, for study. All of the cases selected were in the first or second day of eruption. Blood cultures were made from each case in blood-broth tubes, blood-broth flasks and on blood-agar of pH. 7. 6. These cultures were examined daily for one week. In no case (six cases in all) was a streptococcus cultivated. In case No. 6 a Gram-positive coccus was cultivated which was undoubtedly due to contamination.

Five monkeys were inoculated with citrated blood from cases one to five. Each monkey was given five cubic centimeters of infected blood intraperitoneally. All of the monkeys developed a measles-like rash in from fourteen to seventeen days. This rash was accompanied by a rise in temperature of from one to two degrees C. The fever was highest at the time of full development of the rash and quickly subsided as the rash disappeared. The rash first appeared on the ears and over the forehead and then extended to the face, neck, chest and groin. In monkey 3, denuded of hair, the rash was also visible over the entire scalp. This eruption persisted for five to seven days but was fully developed on the third day after onset. Blood-cultures from these animals taken during the first three days of the rash were entirely negative. Two additional monkeys were given blood from infected monkeys on the second day of the eruption. In both instances the monkeys developed what we believe to have been a typical measles rash as it occurred in the other experimental animals. Blood-cultures from these two monkeys also proved to be entirely negative for streptococci or other bacteria.

In the experience of other workers the incubation period of experimental measles in monkeys has been extremely variable. Blake and Trask report an incubation period of eight to twelve days; Goldberger and Anderson report an incubation period ranging from ten to twenty-six days while Nevin and Bittman, in the two monkeys successfully inoculated by them, the incubation period was five and ten days. In each case the incubation period is given from the time of inoculation until the first appearance of the rash. In our series the incubation period was fairly constant ranging from fourteen to seventeen days. The temperatures of the animals were recorded each day beginning with the normal taken for several days before inoculation. A definite rise in temperature preceded the appearance of the rash by one or two days. It should be pointed out, however, that

false temperature readings in monkeys may easily be obtained if the animals are unduly excited. When the animal is quieted the temperature more nearly approximates the normal. Because of this we do not regard the temperature records of very much significance and so in every instance we have relied upon the appearance of the rash as the first definite indication of the disease.

Two monkeys were also given intraperitoneal injections of 5 cc. of normal human citrated blood as a control to determine if they would develop a rash as a result of the injection of these proteins. In neither case did a rash develop and blood cultures from these animals proved to be negative as might be expected.

SUMMARY

Six cases of measles in the first and second day of eruption were carefully cultured for the non-hemolytic streptococcus reported to be present in measles cases by other investigators. In no instance was this organism found.

Monkeys injected with 5 cc. of citrated blood from five of these cases developed a measles-like rash on the fourteenth to seventeenth day following inoculation intraperitoneally. Coincident, and shortly preceding the appearance of the rash, there was a rise of one to two degrees C. in temperature. Blood cultures made from the blood of monkeys during the first three days of eruption were entirely negative for the streptococcus and other bacteria.

Two monkeys (controls) injected intraperitoneally with 5 cc. of normal citrated human blood did not develop a rash. Blood cultures from these animals were also negative. Citrated blood from measles cases was injected intraperitoneally into two of the monkeys which had previously received measles blood and had developed a rash. Both monkeys were immune to the second injection of measles blood.

CONCLUSIONS

We believe that our failure to find the streptococcus in human cases of measles and in monkeys following the injection of infected blood from these cases is direct evidence against the streptococcus etiology of measles. In the tropics streptococcus infections are not so common as in temperate climates. Scarlet fever, for example, is practically never found in Porto Rico and when present is usually discovered in persons recently arriving from the North. Measles, on the other hand, is extremely common in Porto Rico. We believe that in temperate climates where streptococcus infections are so common

extreme conservatism should be exercised in assigning to this microbe the etiologic role in this disease.

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