*Bull. Org. mond. Santé*
*Bull. Wld Hlth Org.* } 1962, 27, 709-715

# Serological Reactions in Rhesus Monkeys Inoculated with the 17D Strain of Yellow Fever Virus*

HERNANDO GROOT [1]

*Haemagglutination-inhibition tests, which depend on the appearance of haemagglutination-inhibiting antibodies in the serum in virus infections, are in common use in the study of arthropod-borne diseases. This paper contains the results of an investigation into the appearance and pattern of haemagglutination-inhibiting antibodies in the serum of rhesus monkeys inoculated intracerebrally with the 17D strain of yellow fever virus during the testing of seed lots of yellow fever vaccine. These antibodies appeared on the tenth day after inoculation, and were still demonstrable four years later. In all of the eight monkeys tested complement-fixing and neutralizing antibodies against yellow fever antigens also developed, and in six out of the eight heterologous antigens developed.*

The extensive use of haemagglutination-inhibition (HI) tests in the study of arborvirus infections has made it desirable to examine the appearance and pattern of haemagglutination-inhibiting antibodies in the blood serum of rhesus monkeys inoculated with the 17D strain of yellow fever virus, during the testing of seed lots of yellow fever vaccine. This article reports the results of such a study, using seven antigens, with a concomitant study of complement-fixing and neutralizing antibodies.

## MATERIAL AND METHODS

This study was carried out with 8 *Macaca mulatta*, 7 of which were used for testing a secondary seed lot of yellow fever vaccine prepared in 1957 from a primary seed lot of 17D (No. 1290) supplied by the Yellow Fever Laboratory of The Rockefeller Foundation in New York in January 1943. These 7 monkeys had not been inoculated previously with any virus. The remaining animal, No. 8, had been inoculated two years before with Guaroa virus by the subcutaneous route. Guaroa virus has been classified in the Bunyamwera group and is not immunologically related to yellow fever virus.

The monkeys were inoculated in two groups on different dates. One group (A) comprised 6 monkeys (No. 1-6) that received an intracerebral inoculum of 10 500 $LD_{50}$ on 31 August 1957. The other group (B) comprised 2 monkeys (No. 7, 8) that received an intracerebral inoculation of 2350 $LD_{50}$ on 8 November 1958. For serological studies all monkeys were bled before inoculation and on days 10, 20 or 21, and 30 after inoculation. In addition the monkeys in group B were bled on days 5 and 15 after inoculation. Finally the monkeys were bled several months after inoculation as follows: No. 8 on day 204, No. 7 on days 402 and 739, No. 6 on day 486, No. 2 on day 610, No. 4 on days 878 and 1215, No. 1 on days 580, 878 and 1488, and No. 3 and No. 5 on days 878 and 1488. After the bleedings the sera were promptly separated from the clot and stored at about −20°C until the serological tests were performed. The monkeys were kept in a common cage outside the laboratory building in Bogotá, altitude 2640 m above sea level. Furthermore, all animals were bled several times during the first 9 days after inoculation in order to test for circulating virus. The sera were inoculated into infant mice (undiluted), and into 3-week-old mice (undiluted, and diluted 1 : 3).

The specimens for serological tests were submitted to the neutralization test as specified in the proposed recommendations on minimum requirements for yellow fever vaccine (World Health Organization, Expert Committee on Yellow Fever Vaccine, 1957) with the French neurotropic (FN) strain of yellow fever virus; to HI tests with yellow fever Ilheus,

* This work was supported by the Colombian Government and the Pan American Health Organization.

[1] Director, Laboratory of the Carlos Finlay Institute, Bogotá, Colombia.

St Louis and dengue-2 antigens; and to complement-fixation (CF) tests with yellow fever and Ilheus antigens, using the methods described by Clarke & Casals (1958), and Casals & Palacios (1941). For HI and CF tests, acetone-ether extracted brain tissue from infant mice inoculated with the corresponding virus was used. In the HI test, 8 units of antigen were used, and non-specific inhibitors in the sera were removed with kaolin. The sera were tested in serial twofold dilution commencing at 1 : 10. The titre of a serum was taken as the highest dilution giving complete inhibition of hemagglutination, and was recorded as the exponent of the power of 2 which, multiplied by 5, gave the denominator of the dilution. Thus, 1 equals a titre of 1 : 10, 2 a titre of 1 : 20, and so on. In the CF test, 8 units of antigen and 2 units of complement were used; the sera were tested in serial twofold dilutions beginning at 1 : 10, and the titre was expressed as the denominator of the highest dilution which showed at least 3 plus fixation.

The yellow fever antigens used in the HI tests were prepared as follows: one with the pantropic JSS strain; one with the FN strain; one with 17D; and one with strain 36701. Strain 36701 is a yellow fever strain recovered by chance from the blood of a man in Villavicencio, Colombia, who had been vaccinated with 17D one week before the bleeding which yielded the strain. This is presumably a "humanized" strain of 17D. The remaining antigens were prepared as follows : Ilheus, with Laemmert strain; dengue 2 with Tr 1751 strain ; and St Louis with an unspecified laboratory strain. These three strains were kindly supplied by the Rockefeller Foundation Virus Laboratories, New York. The antigens used in the CF tests were prepared with yellow fever, FN, strain, and Ilheus, Laemmert, strain.

For neutralization tests, all the sera from each one of the two groups of monkeys were tested simultaneously. For HI tests, all sera from a given monkey were tested simultaneously with the different antigens, except for antigen 36701. This antigen was used in another test in which all the sera were examined. All the HI tests were repeated at least once. In the retests, however, not all sera from a given monkey were tested at the same time. For CF, all the sera were tested simultaneously with both the antigens used.

## RESULTS

None of the animals developed paralysis or died. Table 1 shows that in 6 monkeys yellow fever virus was demonstrable in the circulating blood. In the 2 remaining specimens no viraemia was demonstrated. The titre of the circulating virus was low—only traces in No. 1, 4 and 7; and 40 $LD_{50}$ per ml of serum in monkey No. 3; 57 $LD_{50}$ per ml of serum in monkey No. 8; and 67 $LD_{50}$ per ml of serum in monkey No. 6 on the third day. In this monkey, however, there is evidence that the titre was higher on the second day. Assuming that all the deaths of the mice inoculated with the monkey sera were due to 17D virus, it appears that virus circulated in the monkeys up to the fifth or sixth day. Regarding monkey No. 2, one of the mice inoculated with serum taken on the eighth day died, but proof that this death was due to 17D virus is lacking because no specificity test was performed.

In these animals the virus that was recovered between the second and the fourth day was identified by neutralization test as yellow fever virus by means of specificity tests performed with monovalent yellow fever immune sera.

### *Neutralizing antibodies*

Of the two sera obtained on the fifth day after inoculation one (from monkey No. 7) gave a survival ratio of 4/6; the other (from No. 8) gave a negative result.

As shown in Table 2, on the tenth day after inoculation 6 monkeys exhibited evidence of neutralizing antibodies for yellow fever, but only 2, No. 7 and No. 8, gave survival ratios of 6/6. The 2 animals which gave negative results, No. 2 and No. 5, had no demonstrable viraemia. The sera of all 8 monkeys taken on the 20th or 21st day showed complete protection.

### *HI antibodies*

Table 3 presents the results of the tests performed with the 52 monkey serum specimens. These results were obtained in tests in which all the sera from a given monkey were tested simultaneously with the different antigens, except for antigen 36701. As shown in Tables 3 and 4, all monkeys developed HI antibodies for the four yellow fever antigens used. In 3 animals, however, 17D HI antibodies were demonstrated before those to JSS. Antibodies to 17D, FN and JSS were still demonstrable in all 4 monkeys bled between 3 ½ and 4 years after inoculation. Antibody titres, which reached a peak on days 20-30 after inoculation, had already decreased on days 204 and 402. Later on they remained at a rather constant level. Antibody

TABLE 1

RESULTS OF TESTS FOR CIRCULATING VIRUS IN 8 RHESUS MONKEYS INOCULATED INTRACEREBRALLY WITH 17D VIRUS

| Monkey No. | $LD_{50}$ inoculated | Dilution of sera | Mortality ratios of adult mice after inoculation with sera taken on day: 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 10 500 | undiluted | 2/6 [a] | 2/5 | — | 0/5 | 0/5 | 0/5 | 0/4 | 0/6 |
| | | diluted 1/3 | 0/5 | 0/6 | — | 1/6 | 0/6 | 0/5 | 0/6 | 0/6 |
| 2 | 10 500 | undiluted | 0/6 | 0/5 | — | 0/3 | 0/6 | 0/6 | 1/6 | 0/6 |
| | | diluted 1/3 | 0/5 | 0/6 | — | 0/5 | 0/6 | 0/6 | 0/6 | 0/5 |
| 3 | 10 500 | undiluted | 3/5 | 1/6 [a] | — | 0/6 | 0/4 | 0/6 | 0/6 | 0/6 |
| | | diluted 1/3 | 0/6 | 0/5 | — | 0/5 | 0/5 | 0/6 | 0/6 | 0/6 |
| 4 | 10 500 | undiluted | 0/6 | 1/6 [a] | — | 1/5 | 0/6 [b] | 0/6 | 0/3 | 0/2 |
| | | diluted 1/3 | 0/5 | 1/6 | — | 0/6 | 0/5 | 0/6 | 0/6 | 0/6 |
| 5 | 10 500 | undiluted | 0/6 | 0/6 | — | 0/6 | 0/6 | 0/6 | 0/6 | 0/6 |
| | | diluted 1/3 | 0/7 | 0/6 | — | 0/6 | 0/5 | 0/5 | 0/6 | 0/5 |
| 6 | 10 500 | undiluted | 4/6 [a] | 5/5 | — | 2/5 | 0/6 | 0/6 | 0/6 | 0/5 |
| | | diluted | 4/5 | 1/5 | — | 0/5 | 0/5 | 0/4 | 0/6 | 0/5 |
| 7 | 2 350 | undiluted | 0/5 | — | 1/6 [a] | 0/6 | 0/5 | 0/6 | — | — |
| | | diluted | 0/4 | — | 1/6 | 0/6 | 0/4 | 0/6 | — | — |
| 8 | 2 350 | undiluted | 4/5 [a] | — | 0/6 [b] | 0/5 | 0/6 [b] | 0/6 | — | — |
| | | diluted 1/3 | 1/6 | — | 0/5 | 0/5 | 0/5 | 0/6 | — | — |

[a] The specificity for yellow fever performed with this isolate was positive.
[b] Infant mice inoculated with this serum died but no specificity for yellow fever was performed.

TABLE 2

RESULTS OF NEUTRALIZATION TESTS [a] IN MICE, USING THE FRENCH NEUROTROPIC STRAIN OF YELLOW FEVER VIRUS, ON THE SERA OF 8 RHESUS MONKEYS INOCULATED INTRACEREBRALLY WITH 17D VIRUS

| Monkey No. | Survival ratios of mice inoculated with mixtures of virus and sera taken on day: 0 | 10 | 20-21 | 30 |
|---|---|---|---|---|
| 1 | 0/6 | 4/7 | 6/6 | 5/5 |
| 2 | 0/6 | 1/6 | 6/6 | 5/6 |
| 3 | 0/6 | 4/6 | 4/5 | 6/6 |
| 4 | 0/5 | 3/6 | 5/5 | 5/6 |
| 5 | 1/5 | 0/6 | 6/6 | 6/6 |
| 6 | 0/5 | 3/5 | 6/6 | 6/6 |
| 7 | 0/6 | 6/6 | 6/6 | 6/6 |
| 8 | 0/6 | 6/6 | 6/6 | 5/5 |

[a] Virus dosage: 110 $LD_{50}$ for sera from monkeys 1-6; 64 $LD_{50}$ for sera from monkeys 7 and 8.

titres for JSS antigen were consistently lower than those for 17D and FN antigens, and, in most cases, lower than those for antigen 36701.

Six monkeys developed heterologous antibodies: 5 for Ilheus, St Louis and dengue 2; and one for Ilheus and St Louis. Antibodies for Ilheus and for St Louis were detected as early as the tenth day, but with titres well below those for 17D. The titres for Ilheus and dengue 2 were usually lower and never higher than those for JSS. The titres for St Louis were lower than, or equal to, those obtained with JSS in the majority of instances. The antibodies to St Louis, Ilheus and dengue 2, especially the latter, tended to disappear before the homologous antibodies; however, those for St Louis were still demonstrable at between 3½ and 4 years after inoculation in three instances.

An estimate of the degree of precision of the HI results may be obtained from the analysis of the results of the repeated tests. A total of 869 retests were made, each test meaning one serum tested with one antigen. When the test was repeated only once, the difference between the two titres was recorded.

TABLE 3

SEROLOGICAL REACTIONS IN 8 RHESUS MONKEYS INOCULATED INTRACEREBRALLY WITH 17D VIRUS

| Monkey No. | Days after inoculation | HI titres | | | | | | | CF titres | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 17D | 36701 | FN | JSS | Dengue 2 | Ilheus | St Louis | YF | Ilheus |
| 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 4 | 2 | 1 | 1 | 0 | 0 | 2 | 0 | 0 |
| | 21 | 7 | 7 | 6 | 5 | 1 | 4 | 4 | 80 | 0 |
| | 30 | 7 | 8 | 6 | 4 | 1 | 3 | 3 | 80 | 0 |
| | 580 | 4 | 1 | 4 | 2 | 0 | 1 | 2 | 0 | 0 |
| | 878 | 3 | 2 | 3 | 2 | 0 | 1 | 1 | 0 | 0 |
| | 1488 | 3 | 2 | 3 | 2 | 0 | 0 | 1 | — | — |
| 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 3 | 2 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 21 | 5 | 6 | 4 | 3 | 0 | 0 | 0 | 40 | 0 |
| | 30 | 6 | 8 | 5 | 3 | 0 | 0 | 0 | 40 | 0 |
| | 610 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | — | — |
| 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 5 | 4 | 4 | 3 | 0 | 1 | 3 | 0 | 0 |
| | 21 | 6 | 8 | 5 | 3 | 1 | 2 | 3 | 80 | 0 |
| | 30 | 5 | 6 | 5 | 3 | 2 | 2 | 4 | 40 | 0 |
| | 878 | 3 | 2 | 3 | 3 | 0 | 2 | 2 | 0 | 0 |
| | 1488 | 3 | 2 | 3 | 2 | 0 | 0 | 1 | — | — |
| 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 3 | 4 | 3 | 2 | 0 | 0 | 1 | 0 | 0 |
| | 21 | 8 | 9 | 7 | 5 | 3 | 5 | 5 | 320 | Tr |
| | 30 | 6 | 8 | 5 | 3 | 1 | 3 | 4 | 80 | 0 |
| | 878 | 3 | 3 | 4 | 3 | 0 | 0 | 1 | 0 | 0 |
| | 1215 | 3 | 3 | 4 | 3 | 0 | 0 | 1 | — | — |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 3 | 2 | 3 | 2 | 0 | 1 | 1 | 0 | 0 |
| | 21 | 5 | 7 | 4 | 2 | 2 | 2 | 4 | 40 | 0 |
| | 30 | 5 | 7 | 4 | 2 | 0 | 1 | 2 | 40 | 0 |
| | 878 | 3 | 1 | 3 | 2 | 0 | 0 | 0 | 0 | 0 |
| | 1488 | 3 | 1 | 3 | 1 | 0 | 0 | 0 | — | — |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 2 | 3 | 1 | 1 | 0 | 1 | 1 | 0 | 0 |
| | 21 | 7 | 9 | 6 | 3 | 1 | 2 | 4 | 160 | 0 |
| | 30 | 6 | 8 | 6 | 3 | 1 | 2 | 3 | 80 | 0 |
| | 486 | 1 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| 7 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 4 | 2 | 0 | 0 | 0 | 0 | 0 | 10 | 0 |
| | 15 | 5 | 8 | — | 3 | 0 | 0 | 0 | — | — |
| | 20 | 6 | 7 | 4 | 3 | 0 | 0 | 0 | 40 | 0 |
| | 25 | 5 | 6 | 5 | 2 | 0 | 0 | 0 | 20 | 0 |
| | 30 | 5 | 5 | 5 | 3 | 0 | 0 | 0 | 20 | 0 |
| | 402 | 4 | 4 | 3 | 3 | 0 | 0 | 0 | 0 | 0 |
| | 739 | 3 | 1 | 3 | 2 | 0 | 0 | 0 | — | — |
| 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10 | 4 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 15 | 6 | 5 | 3 | 3 | 0 | 2 | 3 | 40 | 0 |
| | 20 | 7 | 6 | 5 | 5 | 0 | 2 | 3 | 40 | Tr |
| | 25 | 7 | 6 | 5 | 4 | 0 | 2 | 3 | — | — |
| | 30 | 7 | 6 | 5 | 3 | 0 | 2 | 3 | 40 | 0 |
| | 204 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |

TABLE 4

SUMMARY OF RESULTS OF HI TESTS WITH 7 ANTIGENS ON THE POST-INOCULATION SERA FROM 8 RHESUS MONKEYS INOCULATED INTRACEREBRALLY WITH 17D VIRUS

| Days after inoculation | 5 | 10 | 15 | 20-21 | 25 | 30 | 204-402 | 486-610 | 739-879 | 1 250-1 480 |
|---|---|---|---|---|---|---|---|---|---|---|
| Numbers of monkeys tested | 7,8 | all | 7,8 | all | 7,8 | all | 7,8 | 1, 2, 6, | 1, 3, 4, 5, 7 | 1, 3, 4, 5 |
| Antigens | Number of monkeys that showed antibodies | | | | | | | | | |
| YF (17D) | 0 | 8 | 2 | 8 | 2 | 8 | 2 | 3 | 5 | 4 |
| YF (36701) | 0 | 7 | 2 | 8 | 2 | 8 | 2 | 3 | 5 | 4 |
| YF (FN) | 0 | 7 | 1 [a] | 8 | 2 | 8 | 2 | 3 | 5 | 4 |
| YF (JSS) | 0 | 5 | 0 | 8 | 2 | 8 | 2 | 3 | 5 | 4 |
| Dengue 2 | 0 | 0 | 0 | 5 | 0 | 4 | 0 | 0 | 0 | 0 |
| Ilheus | 0 | 3 | 1 | 6 | 1 | 6 | 0 | 1 | 2 | 0 |
| St Louis | 0 | 6 | 1 | 6 | 1 | 6 | 0 | 1 | 3 | 3 |
| | Average titre of the sera with antibodies | | | | | | | | | |
| YF (17D) | 0 | 3.5 | 5.5 | 6.4 | 6.0 | 5.9 | 2.5 | 2.7 | 3.0 | 3.0 |
| YF (36701) | 0 | 2.4 | 6.5 | 7.4 | 6.0 | 7.0 | 2.5 | 1.7 | 1.8 | 2.0 |
| YF (FN) | 0 | 2.1 | 3.0 | 5.1 | 5.0 | 5.1 | 2.5 | 2.7 | 3.2 | 3.2 |
| YF (JSS) | 0 | 1.8 | 3.0 | 3.6 | 3.0 | 3.0 | 2.0 | 1.3 | 2.4 | 2.0 |
| Dengue 2 | 0 | 0 | 0 | 1.6 | 0 | 1.3 | 0 | 0 | 0 | 0 |
| Ilheus | 0 | 1.0 | 2.0 | 2.8 | 2.0 | 2.1 | 0 | 1.0 | 1.5 | 0 |
| St Louis | 0 | 1.5 | 3.0 | 3.8 | 3.0 | 3.1 | 0 | 2.0 | 1.3 | 1.0 |

[a] Only 1 monkey tested.

When the test was repeated more than once, the differences between each titre and the mode or the median were recorded. For example, if the first test gave a titre of 3, the second a titre of 4, and the third a titre of 4, one difference of 1 and one difference of 0 were recorded. Similarly, if in three tests the titres were respectively 5, 4 and 6, two differences of 1 were recorded. In this manner the following differences were observed: no difference in 516 cases (59.4%); difference of 1 in 290 cases (33.4%); of 2 in 55 cases (6.3%); and of 3 in 8 cases (0.9%). Thus it is evident that differences of 1 in the HI titres (actually one tube more or less in twofold serial dilutions of serum) are not significant.

*CF antibodies*

All 8 monkeys developed CF antibodies for yellow fever: in one (No. 7) on the tenth day; and in the remaining 7, within 15 to 21 days after inoculation. These findings are in agreement with previous observations by Lennette & Perlowagora (1943). The yellow fever antibodies, however, were not demonstrated in the sera taken 204 or more days after inoculation. Furthermore, 2 animals, No. 4 and No. 8, showed traces of antibody to Ilheus on the 20th or 21st day, but this appeared to be a transient phenomenon.

## DISCUSSION

In general, in the 8 monkeys inoculated with 17D, the first antibodies demonstrated were the HI antibodies for 17D. Shortly afterwards HI antibodies for the other yellow fever antigens appeared; then CF antibodies for the FN strain developed, and, in the majority of the cases, HI antibodies for Ilheus, St Louis and dengue 2. The HI titres for the heterologous antigens were lower than those for 17D. Neutralizing antibodies for yellow fever were demonstrable in the majority of cases on the 10th day, but it was not until the 20th-21st day that all sera showed complete protection. The pattern of this serological response is quite similar to that

observed by Theiler & Casals (1958) in cases of yellow fever infection occurring in individuals considered not to have been previously infected with any Casals Group B virus.

In these studies it is evident that the HI antibody response for the 4 yellow fever antigens used is not the same, much lower titres being obtained with the JSS antigen than with the 17D, 36701 and French neurotropic antigens. The titres obtained with the latter three antigens are similar. These findings in rhesus monkeys are in agreement with our findings in human sera not only from people vaccinated against yellow fever with 17D, but also in survey sera. In such sera, a larger proportion of specimens react with the 17D antigen, and the titres for 17D are higher than those with JSS antigen. We have no satisfactory explanation to offer for the lack of sensitiveness observed with JSS antigens. The results obtained with the regular 17D antigen and with that prepared with the strain 36701, isolated from a man vaccinated with 17D one week earlier, are very similar in spite of the fact that they are not strictly comparable, because the two tests were not performed simultaneously. The only exception is monkey No. 8 in which no antibodies for 36701 were detected on the 10th day.

The heterologous antibodies for other Group B viruses which developed in 6 of the monkeys were of lower titre than those for 17D and tended to disappear earlier. There seems to be a correlation between homologous titres for 17D and heterologous titres for Ilheus and St Louis, those for 17D being approximately three tubes higher in the majority of instances. Of the three heterologous antigens used, St Louis appears to be the most sensitive.

It is believed that our results were not influenced by any intercurrent arborvirus infection of the monkeys. The animals were kept outside the laboratory, and although their cages were not mosquito-proof, there is no evidence of the natural existence in Bogotá of any Group B arborvirus.

The amount of circulating virus observed in the monkeys is well within the WHO requirements. However, this does not mean that other substrains of 17D producing higher amounts of circulating virus are not entirely safe for human use.

The reactions observed in the one monkey, No. 8, previously inoculated with Guaroa virus were not significantly different from the results in the rest of the group. However, the results with this monkey were not used in making the evaluation of the secondary seed lot.

## ACKNOWLEDGEMENT

Grateful acknowledgement is made to Dr J. Austin Kerr for his advice and for the revision of the manuscript.

## RÉSUMÉ

L'usage généralisé du test d'inhibition de l'hémagglutination pour étudier les infections dues aux virus transmis par les arthropodes a rendu nécessaire l'étude du développement des anticorps inhibant l'hémagglutination dans le sérum des singes rhésus, inoculés par le virus amaril 17D, lors de l'évaluation de l'activité des lots primaires de vaccin antiamaril. L'auteur donne les résultats de cette étude, qui a porté sur 7 antigènes, avec étude complémentaire des anticorps neutralisants et fixateurs du complément.

En général, chez les 8 *Macaca mulatta* inoculés par le vaccin 17D les anticorps inhibiteurs de l'hémagglutination (IHA) pour 17D apparurent les premiers, suivis peu après des anticorps IHA pour les autres souches de virus amaril; ensuite ce furent les anticorps fixateurs du complément pour la souche française neurotrope, et, dans la plupart des cas les anticorps correspondant aux virus Ilheus, St Louis et dengue-2. Le titre des anticorps hétérologues était inférieur à celui des anticorps 17D. Les anticorps neutralisant le virus amaril étaient décelables, dans la plupart des cas, le 10e jour. Ce schéma est semblable à celui qui a été décrit dans le cas d'infections amariles survenus chez des personnes n'ayant jamais été infectées auparavant par l'un des virus du groupe B.

Les anticorps hétérologues pour les autres virus du groupe B, que produisirent 6 des singes, avaient un titre inférieur à celui des anticorps anti-17D, et avaient tendance à disparaître plus rapidement. La quantité de virus décelée dans le sang des singes était dans les limites des normes établies par l'OMS.

## REFERENCES

Casals, J. & Palacios, R. (1941) *J. exp. Med.*, **74**, 409

Clarke, D. & Casals, J. (1958) *Amer. J. trop. Med. Hyg.*, **7**, 561

Lennette, E. H. & Perlowagora, A. (1943) *Amer. J. trop. Med.*, **23**, 481

Theiler, M. & Casals, J. (1958) *Amer. J. trop. Med. Hyg.*, **7**, 584

World Health Organization, Expert Committee on Yellow Fever Vaccine (1957) *Wld Hlth Org. techn. Rep. Ser.*, **136**