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CONTRIBUTIONS TOWARDS THE STUDY OF THE MECHANISM

ACQUIRED IMMUNITY IN P. KNOWLESI INFECTION

INTENTIONALLY INDUCED IN MAN.

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Research undertaken by one of us¹⁾ in collaboration with BALIF and CHELARESCO has shown that specific acquired immunity to the three species of plasmodium which cause malarial infection can be experimentally established in man. Such immunity becomes effective only after a certain number of repeated infections with one of these species. In our conclusions we put forward the hypothesis that such acquired immunity did not exclude the intervention of other defensive factors of the organism, apart from those of simple premunition.

The explanation of the mechanism of immunity in malaria has been carried a step forward as a result of the studies on the pathogenesis of P. knowlesi in man and the acquired immunity that has been found to develop.²⁾

Research on M. rhesus by SINTON and MULLIGAN³⁾, MALAMOS⁴⁾, M. EATON, L. COGGESHALL and H. KUMM, L. COGGESHALL and M. EATON⁵⁾ seem to indicate that antibodies are present in the serum of animals suffering from chronic infection.

1) Rivista di Malariologia, A.XIV, 1935.

2) Indian Medical Gazette, 1932, 67, No.6, 301. Archives Roumaines de Pathol. expérim. et de Microbiol. Vol.10, 1937, No.1. Bull. Soc. Pathol. exotique, Vol. XXX, No.4, 1937, 305.

3) Records of Malaria Survey of India, Vol. III. 3 and 4, 1932; 323, 524; 809.

4) Archiv F. Schiffs-u. Tropenhygiene, Vol.41, H.1, 1937, S.162.

5) The Journal of Experim. Medicine, V.67, No.6; V.68, No.1; 1938; 857; 17; 30.

The facilities afforded by malaria-therapy to study acquired P. Knowlesi immunity in man and the circumstances that a test animal highly sensitive to this infection - M. rhesus - is available, provide a unique opportunity for research on the mechanism of this immunity.

Our observations relate to a group of 35 paralytics who have been repeatedly inoculated with blood containing virulent P. Knowlesi. After a first inoculation, usually followed by a spontaneous cure, only 5 per cent of these cases showed an abortive clinical form on the occasion of a second intravenous inoculation of virulent blood; 20 per cent showed only temporary parasitic infection; 77 per cent had neither fever nor parasites after this trial inoculation (10 to 50 cc. of blood containing a very large number of parasites).

We first tested a number of immune cases, to see whether they were not in a state of premunition, by inoculating M. rhesus with 5 to 10 c.c. of their blood. The results of observation of the animals and of a daily thick-drop examination of the blood of our M. rhesus were negative throughout the 20 to 25 days following infection; the subsequent control inoculation showed us that the animals were susceptible to infection. In view of the experience of the authors mentioned above as to the high receptivity of M. rhesus and of our own experience of over 100 of these animals inoculated in the most varied conditions, we came to the conclusion that in our cases acquired immunity in man was not necessarily connected with premunition requiring the presence of the parasite in the organism in a latent form.

To obtain a better idea of what was happening to the parasite in the blood of an immunised patient on the one hand and in the blood of two new patients on the other, we tested our patients' blood for its power to infect M. rhesus, the immunised patient having been given an intravenous inoculation of 50 c.c. of virulent blood, and the new patients only 10 c.c. The blood for inoculating M. rhesus was obtained at intervals of 6 hours, 12 hours, 24 hours, 48 hours, and 7 days.

The results were as follows: the immunised patient, D.I., had neither fever nor parasites after this transfusion of virulent blood (3rd inoculation).

None of the M. rhesus contracted the infection through inoculations of the immunised patient's blood made as from the 6th hour after the patient had himself received his infection of virulent blood.

A subsequent test infection of 3 of these M. rhesus with virulent blood showed, as usual, high susceptibility to P. Knowlesi infection.

The blood of the new control patients, who had received only one-fifth of the quantity of virulent blood, was infectious for M. rhesus. In addition, it so happened that one of the two patients passed through a very short period of incubation.

These facts entitle us to affirm that the blood of a man immunised by repeated inoculations of P. Knowlesi contains protective principles which would clearly appear to destroy the parasite.

CONCLUSIONS.

Acquired immunity in man after one or more P. Knowlesi inoculations of virulent blood is constant, and may occur regardless of premunition. The existence of protective principles in the blood of an immune man is demonstrated by the fact that the blood of a man reinoculated with a large quantity of virulent blood is not infectious. The parasite would seem to be destroyed during the first few hours after reinoculation.

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