SPLEEN AND RESISTANCE TO MALARIA AND HÆMOGLOBINURIA.

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(*Read at Symposium, August 27-28, 1937.*)

The importance of the spleen in the defence mechanism of the body against infections has been fairly extensively studied. The mass of evidence that has accumulated shows that in certain infectious diseases the importance of the spleen in resistance is unquestionable while in others it is not quite so pronounced. As regards malaria, although it has long been suspected that the spleen probably plays an important part in resistance to the disease, its exact rôle was not clearly worked out till recently. Within the last five years, investigations were conducted on the rôle of the spleen in resistance to *P. knowlesi* infection in monkeys chiefly through splenectomy, which is a recognized method of experimental study. In order to understand the significance of the results correctly and for purposes of comparison the effect of splenectomy on the course of *L. donovani* infection in monkeys and mice was also studied. The results showed that, while splenectomy in monkeys intensifies markedly the course of *P. knowlesi* infection and destroys completely both natural and acquired resistance, it has little or no influence on the course of *leishmania* infection in monkeys or mice. The following is a brief summary of the results obtained.

THE EFFECT OF SPLENECTOMY ON THE NATURAL IMMUNITY OF DIFFERENT SPECIES OF MONKEYS TO HOMOLOGOUS STRAINS OF PLASMODIUM.

The course of *P. knowlesi* infection varies greatly in different species of monkeys. Ordinarily in *Silenus rhesus* it causes an acute fatal infection, while in *S. irus* and *S. radiatus* it produces a low grade, non-fatal infection. In splenectomized animals these differences due to natural species immunity completely vanishes; all three species suffer alike from acute and rapidly fatal infections.

EFFECT OF SPLENECTOMY ON THE NATURAL IMMUNITY OF DIFFERENT SPECIES OF MONKEYS TO HETEROLOGOUS STRAINS OF PLASMODIUM.

The host parasite specificity in plasmodium infections is recognized to be fairly rigid and cross infection experiments have generally given negative results. For example, attempts to infect monkeys with the human plasmodium or *vice versa* (except in a few instances) have mostly been unsuccessful. Therefore attempts were made to find out if this natural resistance of monkeys

to heterologous strains of plasmodium could also be broken down by splenectomy. Although seven monkeys were experimented upon (4 *rhesus*, 2 *irus*, and 1 *radiatus*) and two species of malarial parasites (*P. falciparum* and *P. vivax*) were used, none of the animals could be infected even by repeated massive doses of infection. This shows that the natural resistance of monkeys to the human plasmodium is not influenced by splenectomy.

Effect of Splenectomy on Latency.

The usual history of monkeys after infection with *P. knowlesi* and treatment is as follows. The acute primary attack gets cured in about a week and the parasites disappear from the peripheral blood, for a time. Then, for a period of about 4 to 8 weeks, relapses occur to be followed by a long period of latency extending over several months. If splenectomy is done during the latent period of infection, a severe relapse follows. Splenectomy seems to be the best method for inducing a relapse in monkeys in which the infection is latent. Out of 42 monkeys splenectomized during latency 34 relapsed and 8 did not. In the latter, the presumption is that there was no residual infection. The correctness of this supposition was proved by the fact that every one of the 8 monkeys on being given a small dose of *P. knowlesi* developed a severe fatal infection.

Effect of Splenectomy on Acquired Immunity.

It is generally found that monkeys that had once been infected and treated exhibit a certain degree of acquired immunity to re-infection. In some animals this immunity is so great that they cannot be re-infected at all even after repeated massive doses of infection. After the completion of our studies on immunity, there were 11 monkeys that had acquired complete refractoriness to re-infection. Extirpation of the spleens of these immune monkeys resulted in the disappearance of this acquired immunity in all cases. Some of them showed a relapse and the others were proved to be susceptible to re-infection. In the above experiment it is interesting to note that all the *rhesus* monkeys proved to have acquired immunity, relapsed without exception, showing that in the susceptible species the primary infection does not get completely cured and that acquired immunity is associated with the presence of a residual focus of infection, whereas in the resistant species (*irus* and *radiatus*) the infection, in about 50 per cent of cases, gets completely cured and even in the absence of a residual focus of infection a high degree of acquired immunity may be present.

The Effect of Splenectomy on Specific Treatment.

Studies on the value of quinine in the treatment of malaria in splenectomized and non-splenectomized monkeys showed that in splenectomized animals (*a*) larger amounts of quinine were required to cause complete disappearance of all parasites from the peripheral blood, (*b*) the drug had to

be administered for a much longer period, (*c*) the cure rate was distinctly less, and (*d*) the death-rate was markedly higher than in non-splenectomized monkeys. Commencing treatment of primary attack when parasite rate was 10%, 1 gr. of quinine by injection and 4 grs. by mouth per day for 7 days were enough to make all parasites disappear from the peripheral blood in over 80% of non-splenectomized animals. The same treatment in splenectomized animals was able to cause the disappearance of all parasites in 40 per cent of the animals only ; but by continuing the treatment for 2 weeks the percentage could be raised to 60.

In the case of *irus* and *radiatus* complete sterilization could be effected in over 50% of the non-splenectomized monkeys through efficient treatment with quinine only, whereas in splenectomized animals only 16% could be completely sterilized ; others showed a latent infection for a considerable period of time. The death-rate in the treated series for splenectomized *rhesus* varied from 20 to 30 per cent, whereas in the non-splenectomized group it was invariably less than 10 per cent.

The Effect of Splenectomy on the Incidence of Hæmoglobinuria.

Several workers have recorded that hæmoglobinuria occurs as a complication of *P. knowlesi* infection in *S. rhesus* monkeys in about 30 to 60% of cases and that it does not occur at all in *S. irus* or *S. radiatus*. It was found that when the animals are splenectomized prior to infection with *P. knowlesi* the incidence of hæmoglobinuria is greatly increased. In 90 to 100% of splenectomized *rhesus* and in about 30 to 50% of splenectomized *irus* and *radiatus* hæmoglobinuria is met with. This stresses the importance of the spleen in hæmoglobinuria of monkeys.

The Effect of Splenectomy on the Course of Leishmania Infection.

The effect of splenectomy on the course of *leishmania* infection was studied both in mice and in monkeys. The normal picture of experimental infection in mice is as follows :—

½ c.c. of a standardized dose of infective material produces in 6 weeks heavy infection in about 20 to 30%, moderate infection in 20 to 30%, mild infection in 20 to 30%, and no demonstrable infection in 10 to 20%. Splenectomy before or after infection did not alter this picture in any way.

Four *irus* monkeys infected with *leishmania* were splenectomized. This operation failed to affect the course of *leishmania* infection, although the animals were observed for over three months.

From these studies it is concluded that the presence of the spleen plays a part of great importance in the resistance to malaria, but there is no evidence to show that splenectomy influences the course of *leishmania* infection in any way.