PATHOLOGY OF MALARIAL SPLEEN.

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

The spleen is an organ which has been known for a long time past as pre-eminently suited to deal with the effete products which find their way into the blood stream which is thus restored to its original purity. It has also been definitely established that it is one of the most important places in the body where injurious products of all descriptions are effectively dealt with when the latter are brought to it. Furthermore, the spleen has lately gained considerable importance as the principal centre for the production of antibodies which are absolutely important for the defence of the animal body against micro-organismal invasion. For the performance of all the above-mentioned functions, the organ has to depend on certain special groups of cellular elements which form a very characteristic structural unit in the anatomy of the spleen, i.e. the cells of the reticulo-endothelial system. These cells are always available in sufficiently large number to cope with the usual needs of the animal under normal conditions. But under abnormal circumstances either brought about by infection or by the presence of foreign particulate matters resulting therefrom, as in malaria, or introduced into the system by artificial means, as in vital staining, a large amount of extra work is thrown on the spleen which meets the increased demand by putting forth a larger number of its vital cellular elements. Such increased output of cells of the reticulo-endothelial system is only possible because of their enormous potentialities of rapid multiplication and in developing a larger amount of cytoplasm in their bodies. While these cells struggle hard to cope with the abnormal situation, an adequate supply of nourishment, including oxygen, and an equally adequate removal of the products of cellular metabolism must be ensured, and these are brought about by a greater flow both in the arterial and venous systems as well as by dilatation of the existing vascular channels peculiar to the spleen. The net result of all the above changes is an increase in the volume of the organ which is manifested clinically by an enlarged spleen.

It will thus be seen that the essential underlying basis of splenic enlargements, in the majority of cases, is a work hypertrophy to start with modified by such changes as may intervene from time to time under varying circumstances. Such a hypothesis, however, precludes all those conditions where the enlargement is due to gross involvement of the organ by neoplastic and other growths, i.e. lymphosarcoma, lymphadenoma, leukæmia and cystic formations. Coming back to the discussion of the above hypothesis, it may

be seen that all the changes enumerated previously may come upon the organ suddenly but last for a comparatively short period, as in any acute infective process. The resulting enlargement therefore lasts only for a short time and as soon as the infective process is over, the organ gradually resumes its normal size and structure. If, on the other hand, the above factors continue to operate either continuously or repeatedly at frequent intervals, the resulting pathological alterations will *pari passu* not only take place in increasing intensity but will become more or less of a permanent nature. Such splenic enlargements, therefore, do not disappear or take a very long time to do so after the stimulus to activity has ceased to exist.

In such chronic conditions, other factors are superimposed sooner or later and these no doubt are responsible for additional pathological alterations in an already enlarged organ. For instance, when the infective process is a long continued one the resulting cellular accumulations in the spleen also become more or less of a permanent nature and these must require some stroma to support them. This demand is met by an increased formation of reticulum which often becomes thickened. Another important feature in these cases is the marked thickening of the capsule and the trabeculæ which therefore, particularly the latter, become very numerous and prominent. In the chronically enlarged spleens, these thickenings consist mainly of fibrous tissue and very little of involuntary muscle fibres. As a result the periodic and rhythmic contractions of the organ are very feeble and the blood in the pulp and sinuses cannot be emptied as efficiently as in a spleen under normal conditions. The inevitable result of this change is that the organ remains constantly in a state of turgescence, stretching the capsule and the trabeculæ, which *pari passu* undergo further thickening due to the deposit of additional connective tissue. This high degree of engorgement is noticed during the time of surgical operations for splenectomy when the quantity of blood which may be recovered from the splenic vein, after the organ is removed from the abdomen, may be as much as one-third of the total weight of the spleen. The last but not the least important condition which may supervene is a diffuse fibrosis of the entire parenchyma producing a very hard and tough spleen which cuts with difficulty and with a grating sensation. The pulp cannot be broken down with the tip of the thumb. Such a change results when the poisons brought to the organ work for a long time and are sufficiently strong to cause destruction of the pulp which is subsequently replaced by connective tissue. When this stage is reached, the organ may undergo some diminution in size and its capsule is thrown into wrinkles. For obvious reasons, such a spleen becomes useless to the body.

With a preliminary discussion like the above regarding the pathogenesis of the common enlargements of the spleen, it will be a comparatively simple matter to describe the changes which take place in the organ in the most common tropical malady, viz. malaria.

The pathological changes in the spleen due to malaria will naturally vary according to whether the disease is acute or chronic. In the former condition, which is most characteristically seen in infection by *Plasmodium falciparum*, the spleen is found to be only moderately enlarged. The organ as a whole feels very much distended, its capsule is very tense and it has an intensely dark slaty colour. The tension on the capsule is so great that in some very acute pernicious cases I found it as thin as muslin and the slightest pressure of the knife to cut through it led to its rupture. Such a stretching and thinning of the capsule in acute malarial infection would explain the occurrence of rupture of the spleen either spontaneously or as a result of trauma of a very trifling character sometimes reported from hyperendemic areas. Although when felt over the abdomen during examination of the case clinically, one finds the organ fairly hard in consistence, it is entirely different when the same organ is examined on the autopsy table. As soon as the knife is placed on the surface and pressure exerted to cut through the tissues, the stretched capsule almost bursts and the splenic pulp at once bulges out. It looks like a soft, diffluent pulpy substance, intensely black in colour with a copious amount of equally dark, almost tarry, blood flowing out of it. One peculiarity which must have been noticed by every pathologist having a fair amount of experience of malaria is that it is extremely difficult, almost impossible, to cut a thin slice out of such a spleen as all the pulp tissues being very friable crumble into pieces. It is only possible to do so after the organ is hardened and fixed in formalin. When a contact smear of the spleen is stained and examined under the microscope, one finds plenty of red cells, some lymphoid cells, many large phagocytic mononuclear cells laden with hæmozoin pigment and an enormous amount of pigment in large or small masses freely scattered throughout the field. Curiously enough, parasites are found in very small number. In one case of which I have a personal knowledge, crescents were found in large numbers but hardly a single parasite in the trophozoit stage could be detected. Probably the infected red cells being damaged by the parasites are readily broken down when the latter are at once destroyed. In the histological picture the most outstanding features are the enormous amount of blood and hæmozoin pigment which have accumulated in the organ. This is so extreme in some cases, that the entire section appears like a mass of blood clot completely hiding the true picture of the spleen. Brownish black pigment may be seen strewn all over and mixed with the blood in small granules or in masses and also inside the reticulo-endothelial cells which are found in large numbers. The lymphoid follicles become small in size and are sometimes reduced so much that these can be recognized only in connection with the cross section of the arterioles.

Thus from what we generally see in acute malarial infection it is evident that the enlargement is entirely due to the extra burden suddenly thrown on the organ and to the concomitant vascular changes which inevitably follow such increased output of work.

When the infection is of a chronic nature the changes, though essentially of the same nature, do not present themselves in such an acute form. There is less vascularity but more cellular proliferation with increase in the reticular fibres. The capsule becomes fairly thickened and the trabeculæ get numerous and more prominent. The enlargement is always very much more than that in the acute infections but contrary to the usual conception it never assumes an unusually big proportion. In fact if the organ be found to be large enough to reach the pelvis, the suggestion of its being malarial in origin should be revised. I have been forced to arrive at this conclusion after a very careful study of the histological picture of a large series of unselected cases of splenomegaly obtained from the autopsy materials of the Medical College Hospital. The consistence of the chronic malarial spleen is firm and this perhaps is the origin of the term 'aguecake' applied to this type of spleen. During autopsy, the organ cuts well though with a little resistance and the cut surface shows a characteristic appearance, viz. a homogeneous black surface interspersed with minute whitish or greyish streaks. The substance cannot be broken with the pressure of the thumb unless a fair amount of force is exerted. Unlike the spleen in acute malaria one can cut even very thin slices from such an organ. The histological picture shows a diffuse pigmentation with marked cellular proliferation consisting mainly of large phagocytic mononuclear cells, their cytoplasm being filled with malarial pigment. There are also many cells of a lymphoid nature particularly aggregated in and around the Malpighian follicles. The vascularity, though obvious, is certainly less marked. Both the capsule and trabeculæ are considerably thickened. When stained with the Foot Bielschowsky's method, the reticulum is found in abundance. This type of splenomegaly which is the result of a chronic repeated malarial infection, although it diminishes in size to some extent, often persists for a very long time, sometimes throughout the greater part of one's life and this is so in spite of all the treatment given to the patient.

The types of splenomegaly described above are always accompanied by varying degrees of hepatic enlargement which is found to be due to the accumulation of pigments in the Kupffer's cells and marked engorgement of the liver capillaries. As in the spleen, these fixed reticulo-endothelial cells not only proliferate in number but also increase in their size. As it takes a very long time to dispose of their load of inert pigments which collect in large amounts, the hepatic enlargement also persists for a long period just like the splenic enlargement. The hepatic cells may contain hæmosiderin granules and also show some degree of fatty change but no hæmozoin pigments are ever found inside their cytoplasm. It must be definitely stated that inflammatory reaction of any kind is not met with in this organ, although in very chronic and long standing infections one may find collections of mononuclear cells limited only to the portal spaces. If we take such cellular accumulations as evidence of irritation, they might produce some fibroblastic reactions in these areas giving rise to thickening of the connective tissues, but even such a change

cannot be found always in the average chronic case of malaria met with in the autopsy room. Such a change, however, can neither produce an appearance of portal cirrhosis nor the clinical phenomena of the common cirrhosis of the liver. The hypothesis of cirrhosis of the liver of malarial origin, although advocated in older times, cannot be supported in view of the histological findings enumerated above.