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ON THE MECHANISM OF LYMPHOCYTARY LESIONS
CAUSED BY ADRENALIN AND TYPHIC ENDOTOXIN

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(Report Delivered by Mr. Gaston Hamon to the 20 December 1948 Session)

In an earlier communication (Comptes rendus, 227, 1948, p. 695) we showed how we can bring about cellular lesions and major conjunctive reactions in the lymphoid tissue either with adrenalin or with typhic endotoxin. Later on we will have an opportunity to try to determine the cause of these reactions and to spell out the nature of the chemical elements that bring about these reactions. But today we only want to study the manner in which these cellular necroses are produced.

There are two major mechanisms which we must consider here, a priori. First of all, we can think of a direct toxic action, with the adrenalin and the endotoxin behaving like real poisons (cytoplasmic poison or nuclear poison) as far as the lymphocytes are concerned. However, all of the experiments which we conducted so far, in an effort to establish a toxicity of this kind, have failed: Thus, isolated lymphocytes survive for several hours, in vitro, when they are kept in fresh guinea pig serum, even if the latter includes large quantities of adrenalin or endotoxin.

For these experiments, we usually employ the following technique. The cervical ganglia are removed from guinea pigs who have fasted for 24 hours and they are then chopped up in physiological water. After they have been filtered on gauze, we added to this cellular suspension a trace of neutral red and then an equal quantity of fresh guinea pig serum which either did or did not contain either adrenalin or typhic endotoxin (1-4 µg per ccm). One drop of these various preparations is then deposited between glass slides and it is observed for 8 hours at 37°. The various examinations which we

made all showed that, under these conditions, the cells remain intact in the vast majority, regardless of the composition of the medium in which they are washed. In particular, they continue to reveal these pretty neutral red granulations which we usually consider as a sign of vitality -- even in the presence of adrenalin or endotoxin. Undoubtedly, this kind of examination method is not very precise. For example, it does not indicate any possible changes that might have occurred in the cell metabolism. We think, however, that, if these changes did take place, they were quite small since they did not bring about the rapid death of the lymphocytes.

This is why we do not believe that adrenalin or endotoxin can be considered as real lymphocytary poisons, and we think that it is necessary to involve another mechanism if we want to explain the so-very intensive lesions which are produced when these substances are introduced into the organism.

On several occasions (see above), we had already an opportunity to indicate the nature of the mechanism involved here, in our opinion. We were dealing here with vascular disorders of various kinds, disorders which however all resulted in a disturbance of the cell metabolism; this phenomenon appeared to be particularly serious in the case of lymphocytes which, as in the case of cancerous cells, are very fragile elements. To support our assumption, we would like to report here the result of experiments which we think are rather demonstrative here.

Let us take some cervical ganglia, removed from a guinea pig, and let us cut them very finely into a homologous serum; let us then filter this preparation in order to get a homogeneous cell suspension; let us inject it, in a volume of 0.5 ccm, into the skin of new [young] guinea pigs and then, at variable time intervals (ranging from 10 minutes all the way to 24 hours), let us make a biopsy of the tissue injected. The examination of the sections enables us to make the following observations. First of all, in the sub-epidermic conjunctive tissue we only find lymphocytes which were experimentally introduced at this point. A little later (1 hour after the injection), we have a diapedesis of the polymucleates whose size increases progressively and becomes quite considerable after 24 hours. The lymphocytes disappear gradually in the environment of cells which have come from the blood but so long as we can indeed find them (about 15 hours), we do note that they keep their normal structure. Let us now inject, under the skin of new guinea pigs, lymphocytary suspensions prepared as above, but mixed with a sufficient dose of adrenalin (that is to say, 50 mug) in order to disturb the local circulation quite definitely (Comptes rendus, 227, 1948, p. 314). As our histological sections show, the diapedesis of the polymucleates, under these conditions, does not occur (which, by the way, makes the entire examination much easier), but the lymphocytes do not remain intact for a long time. After a few hours, they reveal obvious signs of degeneration; the nucleus breaks up into irregular balls of chromatin (pyknosis), etc. Finally, and this is the fact which we think is of the utmost importance here, looking at the sections, we can observe lymphocytary lesions that are absolutely comparable to those which we see in the thymus or the spleen of animals which were given an intraperitoneal injection of adrenalin or endotoxin.

The rapid degeneration of the cells observed in ~~this case~~ can only be a result of the vascular disorders. ~~because~~ the adrenalin turns out to be incapable of directly harming the lymphocytes. The fact that it manifests itself, histologically, through lesions identical to those which we find in the lymphoid organs of animals treated with the same hormone or with endotoxin, in our opinion, constitutes almost decisive proof supporting the vascular origin of these [lesions].