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The Cellular Reaction in Experimental Syphilis. Supravital and Fixed Material.

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The blood and tissues of rabbits inoculated with *Treponema pallidum* have been studied from the standpoint of the cellular reaction at different periods of the disease. The evidence from successive weekly blood counts on 5 groups of rabbits, 40 animals in all, indicated that the various classes of cells were numerically affected. A striking finding was the increase in the numbers of circulating monocytes[1] associated with actively developing lesions. The increase was very much more pronounced than the spontaneous rises of monocytes noted in groups of normal rabbits, the blood of which was examined at similar intervals over prolonged periods of time.[2]

Similar experiments have been carried out in which various tissues involved by the disease process were examined, both in supravital and in fixed preparations, in order to study the relationship between the blood picture and the types of cells concerned in the tissue reaction. Supplementary observations were also made on a large number of syphilitic rabbits in which the blood was not examined systematically; every instance of tissue examination, however, was immediately preceded by a blood count. Standardized pipettes were used and the differential counts were made with the supravital technique. Scrapings of fresh tissue were examined by the supravital method, using neutral red and Janus green dyes, and fixed preparations of the tissues were made with various fixatives and stains. In all experiments, special attention was paid to the clinical character of the disease. The particular lesions studied and the time selected for their examination was largely determined by the general course of the infection, and it should be emphasized that an essential feature of the study was the examination of lesions at different stages of development. The lesions studied included the primary orchitis and periorchitis resulting from testicular inoculation as well as the metastatic orchitis of the uninoculated testicle, generalized lesions of the periosteum, cutaneous lesions of metas-

[1] Pearce, L., *Trans. of the VIII International Congress on Dermatology and Syphilology*, 1930, in press.

[2] Pearce, L., and Casey, A. E., *J. Exp. Med.*, 1930, **51**, 83; **52**, 23, 39, 145, 167.

tatic origin and those resulting from scrotal implants, and inguinal and popliteal lymph nodes.

The results at present show that during the phase of an early orchitis or of an early scrotal chancre when a peripheral monocytosis is beginning to appear, the most conspicuous cell observed in the fresh tissue preparations of these lesions is one that cannot be distinguished from a blood monocyte on the usual morphological grounds. A few clasmatocytes are seen but they are far less numerous. With more advanced testicular and chancre lesions, the clasmatocytes become increased and in addition, the number of lymphocytes is increased. Regressing lesions are characterized by a large proportion of clasmatocytes and lymphocytes. In spite of the difficulties of examining fresh preparations of early generalized lesions because of their small size, the observations which have been made are in keeping with those of an early orchitis and chancre. The findings with respect to well developed generalized lesions of the periosteum and skin in various parts of the body correspond to those of the testicle and scrotum. A study of fixed material has confirmed the results obtained with preparations of fresh tissue with respect to the large mononuclear cells in early lesions. It should be stated, however, that the numbers of lymphocytes and plasma cells appear to be greater in fixed than in supravital preparations. As far as the inguinal and popliteal lymph nodes are concerned, comparatively large numbers of monocytes were found during actively progressing phases of lesions in their drainage areas.

In supravital preparations of tissues of early lesions, particularly of an orchitis, the large mononuclear cells have a variable appearance. The majority appear to be typical blood monocytes of the proper size with the characteristic indented nucleus and a rosette of neutral red, but there are also many cells with various modifications leading to a type which is ordinarily classified as a clasmatocyte. In cutaneous lesions, the number of eosinophiles seen in supravital preparations is quite striking.

It seems highly probable that the large numbers of monocytes present in the tissues of syphilitic lesions furnish the source for the peripheral blood monocytosis, and from this standpoint, the monocyte appears as an important and perhaps one of the most essential participants in the cellular reaction to *Tr. pallidum.* The participation of the clasmatocyte, on the other hand, particularly in association with older lesions, may be referable to secondary factors, such as degenerative changes or necrosis. In Morgan's[3] opinion, the clas-

[3] Morgan, H. J., *Trans. Am. Phys.*, 1930, **45**, 69.

matocyte is the important cell in the cellular pathology of testicular and scrotal lesions of acute experimental syphilis.

The observations on other aspects of the cellular reaction in experimental syphilis will be presented in future communications.

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Amytal on Smooth Muscle.

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While using sodium amytal (sodium iso-amyl-ethyl barbiturate) as a routine laboratory anesthetic, it was observed that some of the dogs seemed to show certain signs of increased intestinal motility. Gruber[1] found the tone of isolated intestine, uterus and ureter diminished by the barbituric acid derivatives (uterus by 1:10,000 or stronger amytal solution). Drabkin *et al.*[2] reported maintenance of the rhythmic contractions and of response to the oxytocic principle of pituitary by the isolated uterus following large doses of amytal (1:1,000).[3] Swanson[4] obtained only a depression of the tone of all smooth muscle structures (by 1:25,000 sodium amytal or stronger).

As these observations are somewhat in conflict, a series of experiments was done with smooth muscle tissues from various animals. The animals were killed by exsanguination and the desired parts removed at once and placed in iced Tyrode's or Locke's solution, where they were kept 2-4 hours. (In one or two instances where ether had been used a longer cold waiting period was found to improve the behavior.) The physiological bath chamber contained 200 cc. Precautions were observed as to constancy of temperature, oxygenation and pH.

The first experiments showed only depression by sodium amytal. On using smaller and smaller doses of the drug, however, a consistent "reversal effect" was obtained with every specimen that offered a uniform and dependable activity. Concentrations of 1:100,000-1:40,000 caused a prompt and vigorous increase in tone,

1 Gruber, Charles M., *J. Pharm. and Exp. Ther.*, 1927, **30**, 149.

2 Drabkin, D. L., Ravdin, I. S., and Hirst, J. C., *Am. J. Med. Sci.*, 1929, **178**, 379.

3, 4 Personal communications.