

in their periphery. They have likewise always revealed typical epithelioid cells with the characteristic arrangement of neutral red. These epithelioid cells have at times progressed to the stage of degeneration which is seen so commonly in tuberculosis and which is indicated by the decrease in the amount of the neutral red and by the accumulation of large numbers of refractive droplets. From time to time a moderate reaction on the part of the granulocytes has also been evident and typical clasmatocytes have been present, but always the striking observation has been the massive number of monocytes in all stages of development, modification and degeneration into epithelioid cells.

The element that time plays in these various changes, the determination of the variety of substances which are capable of producing these changes, the question as to whether such substances have a chemical similarity or only one of a physical nature (*i. e.*, in this specific action) are still being investigated. In brief, the essential aim of these studies is the determination of the character of the stimulus which brings about an increase in monocytes and the formation of epithelioid cells in disease processes.

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Production of Epithelioid Cells in Lymph Glands by Injection of Non-Tuberculous Substances.

DUNCAN C. HETHERINGTON. (Introduced by R. S. Cunningham.)

From the Department of Anatomy, Vanderbilt University Medical School.

Until the introduction of certain dyes permitting the staining of cells in the living condition, the epithelioid cell was a rather vague cytological entity. However, it is now possible to define it morphologically (as seen supra-vitally stained with neutral red) as a relatively large cell having a great number of very fine granules or vacuoles, arranged in a rosette, which assume with this vital dye a salmon pink to a brownish red tint. Such an appearance furnishes neither definite nor conclusive evidence regarding the origin or function of this cell, but does, on the other hand, very clearly define it as a cell of distinctive characteristics. This specific characteristic staining quality was first noted by Sabin (1923) in cells obtained from tuberculous lymph nodes, and similar cells have since been observed by other investigators in tuberculous tissues generally. As it had been found that epithelioid cells are very numerous in tuber-

culous involvement of the lymph nodes, it seemed that these structures would be a favorable location for the study of the possible effect of non-tuberculous substances.

Rabbits were used for these experiments. They were subjected to laparotomy and the mesenteric lymph nodes were exposed. By means of small glass pipettes, material was removed from various parts of the nodes, the experimental materials were then injected into the substance of the nodes, and the incision closed. The substance used in these experiments have been sterile macerated rabbits' brain, olive oil (with and without phosphorous), cod liver oil (unphosphorated), and mineral oil. All of the aspirated material was studied on supra-vitally stained slides.

In the material from the normal nodes, a few monocytes were usually, but not invariably, found, but in none of them were any epithelioid cells seen.* The animals were sacrificed 72-120 hours after the injection of the experimental material and many supra-vital preparations were carefully studied. In the rabbits which had been given macerated brain, examination brought to light an abundance of typical epithelioid cells and a large number of monocytes. A similar but not as marked production of monocytes and epithelioid cells was found in the animals injected with the other substances mentioned above.

It is impossible at the present time to fully evaluate these observations. Since Cunningham and Sabin¹ believe that the epithelioid cell may be a transformed or modified monocyte, and since Lewis and Lewis² have described the formation of epithelioid cells from monocytes, attention must be called to the coincidental increase in the monocytes and epithelioid cells in these experiments. Regardless of any interpretation which it may be possible to put upon these observations, it seems wholly clear that typical epithelioid cells (indistinguishable by the methods used from those found in tuberculous nodes) can be produced in lymph nodes *in vivo* by factors other than an active infection by the tubercle bacillus.

* It is important to note that a large number of normal mesenteric lymph nodes have been studied both by the puncture method and by scraping the cut surface of the node and in none of these have typical epithelioid cells been found.

¹ Cunningham, R. S., Sabin, F. R., Sugiyama, S., and Kindwall, J. A., *Johns Hopkins Hosp. Bull.*, 1925, xxxvii, 231.

² Lewis, M. R., and Lewis, W. H., *J. Am. Med. Assn.*, 1925, lxxxiv, 798.