

value in prognosis. It has been shown that in those cases in which the leucocytic reaction is not marked there is a strong tendency to chronicity, terminating in fixed delusions and dementia; and conversely, that those in whom the leucocyte reaction is high most frequently recover.

(8) That with regard to treatment by the artificial stimulation of the leucocytosis, the mental illness is often considerably shortened, and that an impending attack may be aborted.

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The Histological Evidence that Toxins reach the Spinal Cord via the Spinal Roots; with Special Reference to Plasma-Cells. By DAVID ORR, M.D., and R. G. ROWS, M.D.

IN May, 1907, we published the results of our first series of experiments dealing with the question of toxic absorption along the lymphatic paths of nerves and the effects upon the spinal cord, medulla, and pons.

The experiment consisted in placing a celloidin capsule containing a broth culture of an organism underneath the sciatic nerve or under the skin of the cheek of rabbits and dogs, and we held from the microscopical examination of the

tissues that toxins travelled upwards in the perineural sheath. On reaching the cord they induce degeneration of the myelin, commencing at the point where the fibres lose their neurilemma sheath and become incorporated in the central nervous system.

We have continued our investigations into the above question, and naturally many side-issues have arisen, but what has engaged our attention most has been the observation of the histological changes in the nerve between the toxic focus and the spinal cord. We thought that, once the histological reaction had been observed and its character noted, our original thesis would rest on the more secure basis of confirmatory evidence, and so we would be free to enlarge the scope of our investigations.

Our experimental work is by no means complete. There are several points which require careful control, and so we can only show one part of the investigation on hand. Our method is precisely the same as formerly, with this exception, that in this section of our experiments we endeavour to obtain a toxic effect of a subacute or chronic nature. In this demonstration, then, we hope to show the histological evidence for believing that the toxins gain the perineural lymphatic system, spread between the fasciculi of the nerve along the septa, and into the nerve-bundles to some extent, and, it will be seen, pass upwards over the spinal root ganglia to reach the cord by both anterior and posterior nerve-roots. The toxins while travelling towards the cord affect the non-nervous elements, especially the vessels, to a much greater degree than the fibres of the nerve or the cells of the root ganglia; and the reaction is of an irritative or subacute nature. The changes in the perineurium are most intense at the site of the capsule. One important fact to be noted is the early reaction around the capillaries and the veins, a fact which seems to point to these structures being the channel by which the lymph makes its way back into the general circulation rather than to any selective action on the part of the toxin.

The capsule with the inflammatory reaction around it was cut in transverse section. The organisms inside stained well. Outside, in the immediate neighbourhood of the capsule, there were some small groups of organisms. The exudate surrounding the capsule was composed of three layers: (1) a layer of degenerated polymorphonuclear leucocytes, and cells

with a large nucleus and a considerable quantity of protoplasm which stained imperfectly and showed marked regressive changes; (2) a fibrous layer in whose meshes were many fairly well stained round mononucleated cells; (3) a layer composed of mononucleated cells and typical plasma-cells.

On examining the nerve the most striking feature was the large collection of plasma-cells lying in the meshes of the perineural sheath. Many of these lay loose in the spaces, but they were for the most part collected in groups round the veins, which were dilated, and infiltrated their adventitial wall.

In the sciatic nerve, root ganglia and spinal roots, there were proliferative changes in the smallest vessels, the earliest of which consisted in the presence of small round cells in the adventitial sheath. The more advanced irritative phenomena consisted in the development of a periarteritis bearing a striking resemblance to that found in a chronic encephalitis such as is seen in general paralysis of the insane. At this stage the proliferation in the adventitial sheath is composed of adventitial cells, some mononucleated cells, and typical plasma-cells. Many of the finest capillaries show only plasma-cell formation in the adventitial sheath.

In the posterior root ganglion the nerve-cells showed a mild degree of degenerative change, but the capsular cells around each nerve-cell were greatly increased in number, and in many instances had invaded the nervous elements. Plasma-cells in large numbers were still met with in the lymph-spaces of the sheath of the ganglion, and at the proximal pole of the latter there was often a large collection of typical plasma-cells situated in the interval between the anterior and posterior spinal roots.

In the anterior and posterior spinal roots the reaction around the small vessels was, as indicated above, very marked, and plasma-cell formation was a prominent feature. Some veins in this situation showed at times large collections of small round cells in the adventitial lymph-spaces. Occasionally one observed small circumscribed areas in which the myelin was atrophied, leaving the axis-cylinder bare. In the space so formed there were, not infrequently, typical reticulate cells, the "Gitterzellen" of Nissl. Finally, it is worthy of note that no proliferation or cell grouping has been seen around the arterioles.

In the histological changes which we have shown you one

has no difficulty in recognising the results of irritation, and owing to the nature of the experiment and the distribution of the lesions the reaction cannot be otherwise than due to lymphogenous toxicity. The lesions must map out the course of the toxic lymph, and therefore pathology teaches us, in this instance, the path of lymph-flow in nerves.

But we are inclined to go one step further, and apply our results to the pathology of general paralysis of the insane, in which the irritative vascular phenomena and those of the supporting tissues of the brain are a constant, marked, and progressive feature. Just as in this series of experiments, so in general paralysis of the insane the adventitial lymph-space infiltration, composed of proliferated adventitial cells and plasma-cells, is one of the most striking histological findings. Clinical and pathological investigations point clearly to the fact that general paralysis of the insane is a toxi-infective encephalitis of a subacute or chronic nature, and the changes found are not comparable to those seen in blood infection or intoxication. We suggest, therefore, that whatever may be the exciting agent in the causation of this disease, its primary and even its later effects are exerted *via* the lymph-channels connected with those of the central nervous system, and that absorption of toxins along nerves is worthy of attention.

Ependymal Alterations in General Paralysis. By
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A GRANULAR condition of the ventricular ependyma, especially that of the fourth ventricle, has long been recognised as one of the most important of the *post-mortem* lesions of general paralysis. In the opinion of the writer it is present in at least 90 *per cent.* of the cases, and the more carefully the examination of the ependyma is made, the greater will be the percentage of cases showing granulation in asylum *post-mortem* books. In the *Journal of Mental Science*, July, 1905, the writer (1) recorded the frequency of this condition in an analysis of 131 consecutive *post-mortems* on male paralytics at Wakefield