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CONTRIBUTIONS TO THE PATHOMORPHOLOGY OF PULMONARY INNERVATION

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There is extensive evidence in the literature *(Sturm)* to demonstrate the paramount role played by pulmonary innervation in pathological and normal processes.

The pathomorphology of pulmonary innervation has not, however, kept pace with functional experiments and has been unable to solve many a clinical problem. There is a large number of publications by various authors, all dealing with some aspect of the pathohistology of the autonomous nervous system under various pathological conditions of the lungs. In a comprehensive study, Yarugin reviewed the observations of nearly 40 Russian and Soviet scientists on the pathological changes of the central and autonomous nervous systems in tuberculosis. Guseinov described the pathohistology of the interneuronal synaptic connections of the autonomous nervous system in acute and chronic conditions covering such subjects as the cervical and thoracic ganglia and the solar plexus of patients who had died of pulmonary sclerosis. Filatova reports on the impairment of the laryngeal and cervical nerve elements in pulmonary tuberculosis.

Owing probably to technical difficulties the available literature on the pathohistology of the intramural nerves of the lung is far less adequate. Linberg, among others, has found destruction of intramural nerves in peribronchial sclerotic processes and in acute and chronic hilar inflammation. Miller demonstrated by staining with haematoxylin eosin, round cell infiltration of the intramural ganglia in a case of pulmonary tuberculosis.

In the present paper we wish to contribute some new data to the pathohistology of pulmonary innervation. The observations were made on two patients who had died of congestive heart failure.

(i) John's Hospital, Prot. No. 679, a female patient of 63. Postmortem diagnosis, relapsing verrucous endocarditis of the bicuspid valve with insufficiency of the bicuspid valve and stenosis of the left venous ostium (buttonhole stenosis). Brown induration and fibrosis of the lungs, hypostatic pneumonia.

The left ventricle of the heart was atrophic, the venous ostium hardly passable to the little finger. A high degree of induration in the lung, and in some places massive scar-formation could be noted. Anthracosis and fibrosis were found in the hilar lymph nodes and in the periarterial and peribronchial lymphatic tissues. There were some acinous fibrotic tuberculous foci, especially in the lymph nodes, but also in the lung parenchyma near the hilum. In one of the main arteries the media showed sclerosis of the adrenaline type.

(ii) John's Hospital, Prot. No. 703. A 25 years-old woman. Postmortem diagnosis, chronic fibrous endocarditis with insufficiency of the bicuspid and the aortic valves. Stenosis of the left and right venous ostia and of the aorta. Brown induration and pulmonary fibrosis.

Marked congestion, fibrosis and anthracosis of the lung, the deeper parts oedema, were observed. There was a great nomber of haemosiderin-containing phagocytes in the alveoli. Fibrosis was most marked in the septa.

In order to study the neurohistology of these two congestive fibrotic lungs, suitable slices taken from the hilum and from the periphery were fixed in neutral formaldehyde for about 4 weeks and frozen sections impregnated according to Bielschowsky—Gross—O. Schultze.

The publications of Larsell and Dijkstra give ample information on the normal innervation of the human lung. The pulmonary nerves mainly run in the periadventitial tissue of the blood vessels and in the peribronchial connective tissue. As a matter of course they also penetrate the bronchial and vascular walls, terminating in various of their structural elements. Along the peri- and intrabronchial nerves a series of ganglia is intercalated.

The intramural ganglia of the lung showed well-defined changes. The capillaires in the ganglia were dilated in places. The processes of the ganglion cells failed to present the usual consistent aspect. They were thickened, homogenized, showed a tortuous course and marked impregnation. In some places the processes showed a rich arborization and curving and formed intricate windings. At other places they were irregular, distorted, some of them were swollen, others filamentous (Fig. 1).

The dendrite-plates were thickened and sometimes displayed characteristic curves, forming so-called window-structures.

The changes described, corresponding to Stöhr's dendritic disharmony, may also be found in old age, yet according to Stöhr and Feyrter they are the result of increased or pathological activity.

In the intramural ganglia examined there occurred clublike formations of varying structure, impregnating very intensively and homogeneously. Appearing in inter- or epicellular position, they varied in size. They took the shape of drops, pears, circles or clubs and were in all cases connected with a thin nerve fibre. De Castro has described such changes in the superior cervical ganglion of patients with Korsakoff's disease, Herczog in the coeliac ganglion, Lavrentiev and Lasovszky in one of the ganglia of the posterior longitudinal plexus, Guseinov in the cervical ganglia and in the solar plexus of patients suffering from chronic conditions, Gasparini in the ganglia of the pulmonary plexus. Ábrahám, who studied these structures, found them in the 1st and 2nd lumbar ganglia of patients suffering from gangrene, while Conti discovered them in the ganglia of the heart and the lung, ans studied them thoroughly. According to Guseinov, these clublike formations correspond to synaptic terminal plates, which in consequence of a functional stress have become swollen, homogeneous and have lost their fenestration. In the ganglia examined a whole range of such clublike

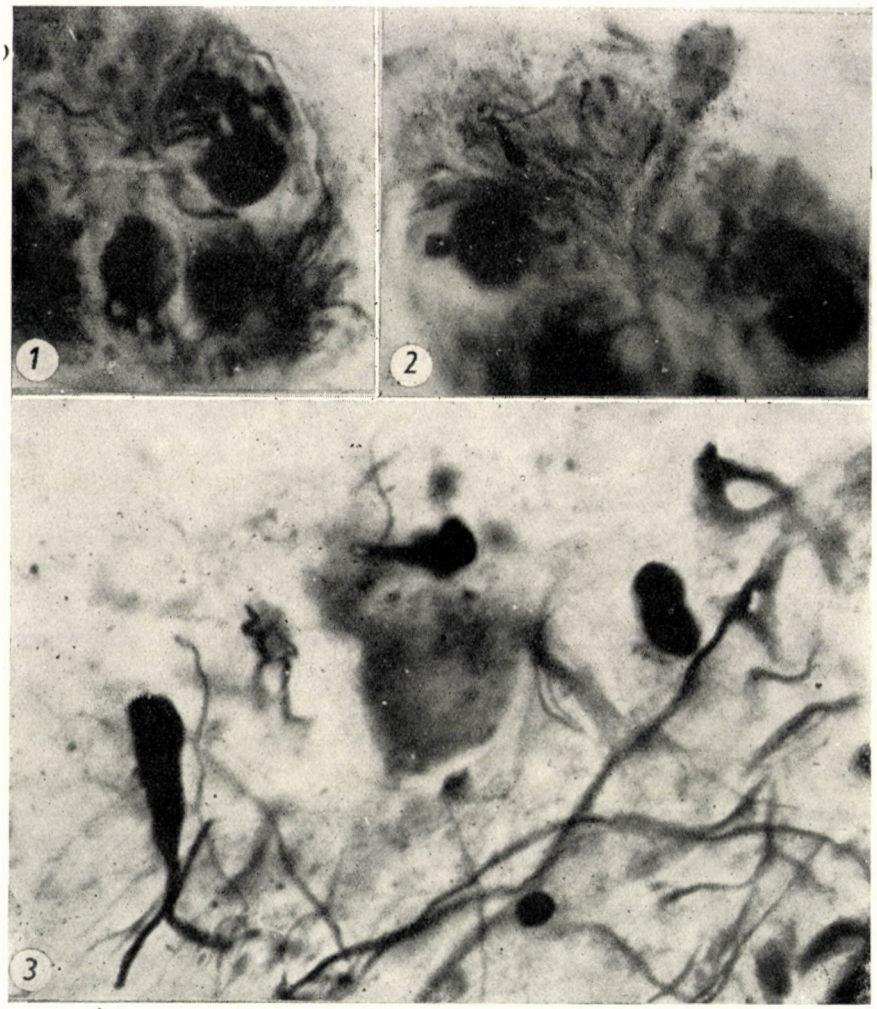


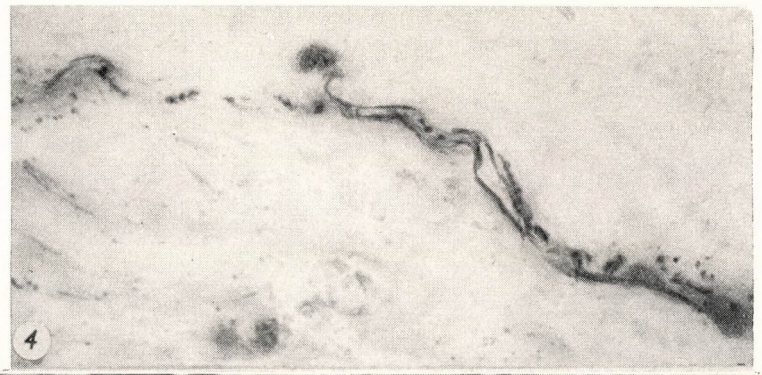
Fig. 1. 25-year-old female patient. Stenosis of the left venous ostium. Intramural ganglion in the congested lung. Dendrit disharmony and window-structure in ganglion cells. Bielschowsky—Gros—O. Schultze's silver impregnation. ×300.

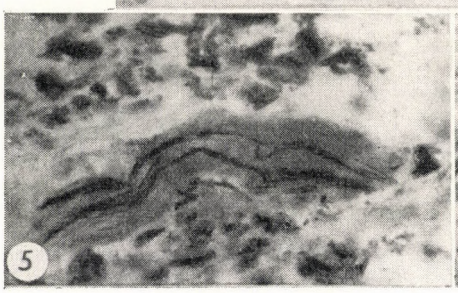
Fig. 2. 25-year-old woman. Stenosis of the left venous ostium. Intramural ganglion in the congested lung. Inter- and epicellular clublike formations. Silver impregnation according to Bielschowsky—Gros—O. Schultze. ×300.

Fig. 3. 63-year-old woman. Stenosis of the left venous ostium. Intramural ganglion in the congested lung. Inter- and epicellular clublike formations. Bielschowsky—Gros—O. Schultze's silver impregnation. ×600.

formations could be observed (Figs. 2 and 3). Similarly to the foregoing, these changes most probably also result from pathological processes.

In our sections the most common finding was the destruction of the bronchial and peribronchial nerves. In the myelinated fibres segmental thickening, homogenization, sometimes swelling and disintegration occurred. The thin unmyelinated sympathetic motor fibres were apparently fewer in number but displayed hardly any pathological change. Pathological changes in nerve fibres were mainly found in the subchondrial areas. Among the degenerated forms of nerve fibre we also encountered such types as only appear in certain periods of the degenerative processes (disintegration of the nerve fibre into argentophil granules (Fig. 4). In view of this fact we may assume that the pathological nerve function in these lungs has been examined in its dynamism.





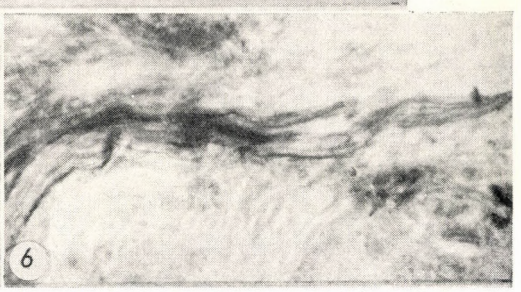


Fig. 4. 25 year-old woman. Stenosis of the left venous ostium. Myelinated fibre-degeneration in the congested lung. Bielschowsky—Gros—O. Schultze's silver impregnation. × 150

Fig. 5. 63 year-old woman. Stenosis of the left venous ostium. Intramural nerves in the lung. Normal myelinated and nonmyelinated fibres in fibrotic, anthracotic areas. Bielschowsky—Gros—O. Schultze's silver impregnation. × 300

Fig. 6. 25 year-old woman. Stenosis of the left venous ostium. Intramural nerves in the lung. Normal nerve fibres in hyaline areas. Bielschowsky—Gros—O. Schultze's silver impregnation, haematoxylin-eosin after-staining. × 150

The question arises what might be the cause of the continuous degeneration of nerve fibres in congested lungs. Sosunov found in cases of bronchiectasis the branches of the vagus nerve around the larger bronchi compressed and destroyed by the increase in the volume of peribronchial connective tissue. It could accordingly be supposed that congestive induration and fibrosis would produce a mechanical lesion of the nerve fibres. After examining a considerable number of sections it seemed remarkable that fibrosis due to congestion and anthracosis, though high in degree and destructive to the blood vessels, should leave the nerves relatively intact. In many of the preparations there were normal myelinated and nonmyelinated fibres running in anthracotic, fibrotic tissue and also normal ganglion cells and fibres crossing the very centre of hyaline foci, probably the residue of a tuberculotic process (Figs. 5, 6). Weiss and Röhlich provided experimental evidence that epi- and perineural tissue possesses a protective and eliminant capacity against dye particles injected into the nerve fibre. Our morphological examinations also lead us to suppose that the intact nerves crossing the destroyed lung parenchyma are actively protected by the protective, eliminant power of the nerve interstitium.

Since, in the cases described above, the destruction of nerve fibres mostly occurred in anatomically intact areas and since we have found normal fibres and nerve bundles in areas with fibrosis, anthracosis and hyaline degeneration, we believe in congested lungs it is not so much the contact pressure of the connective tissue as a toxic effect or a continuous neuroreflectory stimulus, i. e. an increased nervous activity, which destroys the intramural nerve elements of the lung.

It takes further investigations to decide how far the above morphological changes are influenced by congestion, advanced age and alternative factors. Nevertheless, we have thought it necessary to give an advance account of our observations, emphasizing that all the changes described were present alike in both the young and the old female subject examined and that it is felt that these changes must have a decisive part to play in the functional defensive processes of the lung.

Summary

The intramural nerves of congested lungs were studied in two subjects who had died of heart failure. Disharmony and hypertrophy of dendrites and clublike formations in the intramural ganglia were found, in addition to an extensive continuous degeneration of myelinated fibres. Nerve fibres passing through anthracotic, fibrotic, hyaline areas were found comparatively normal. This leads to the conclusion that morphological changes in the nerves are caused by toxic effects and pathological reflex stimuli rather than by mechanical compression due to induration and fibrosis.

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ДАННЫЕ К ПАТОМОРФОЛОГИИ ИННЕРВАЦИИ ЛЕГКИХ

И. Куруц и И. Оштьени

Резюме

Авторы исследовали интрамуральные нервы двух больных, погибших вследствие тяжелого порока рседца. С патолого-анатомической точки зрения в легких было установлено выраженный застой, индурация, фиброз, особенно вокруг сосудов и бронхо, и антракоз.

В интрамуральных нервных узлах авторы нашли морфологические изменения, говорящие за функциональную перегруженность: так на пример дисгармониюотросток нервных клеток, гиперплазию дендритов, и кроме того гомогенно импрегнирующиеся, разположенные между целлюлярно и надцеллюлярно пуговицо-видные образования различной величины, соответствующие по всей вероятности и по данным исследований Гусейнова увеличенным синаптическим пуговкам, утратившим свою фенестрацию. В нервных стволах наблюдается прежде всего дегенерация мягкотных волокон.

На основе исследования изменений нервов и взаймного отношения этих изменений с пролиферирующей и измененной соединительной тканью, авторы предполагают, что нервы, проходящие через рубцевые, фибротические участки легких стоят под активной защитой интерстиции нервов. Это предположение основано на том, что в многочисленных срезах бросается в глаза, как массивный фиброз будьто избегает нервные стволы, и даже в средине не содержащих сосудов гиалинизированных узлов встречаются неповрежденные мягкотные и безмягкотные нервные волокна.

Из своих наблюдений авторы сделают вывод, что нейрогистологические изменения, наблюденные ими в застойной легочной ткани, не являются настолько следствием механического давления со стороны пролиферирующей соединительной ткани, как следствием токсических воздействии и патологических рефлекторных раздражений.