

Deecke (Thes)

On the Perivascular Spaces

In the Nervous Centers.

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BY THEODORE DEECKE,

SPECIAL PATHOLOGIST OF THE NEW YORK STATE LUNATIC ASYLUM.

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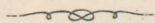
[From the *American Journal of Insanity*, for January, 1874.]

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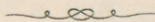
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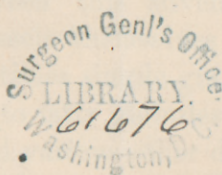


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On the Perivascular Spaces in the Nervous Centers.

BY THEODORE DEECKE,

Special Pathologist of the New York State Lunatic Asylum.

It is well known to those who, in the past ten years, have been interested in the progress of the microscopical anatomy of the nervous centers, that the existence of perivascular spaces, of a system of canals surrounding the vessels which penetrate the substance of the brain, has been a subject of discussion not yet satisfactorily terminated.

Virchow,¹ who first of all touched upon this subject in a paper, "On the Dilatation of Smaller Vessels," gave us the description of a homogeneous tunic, a sheath surrounding the arteries, the veins, the arterioles and ducts even of a capillary character, and observed in the spaces between this adventitious tunic and the walls of the vessels themselves different kinds of cell formations, sometimes simple granulated cells, sometimes transformed into fatty globules intermingled with lymph-corpuscles and various other deposits.

In 1859, Robin,² who apparently had no knowledge of the discovery made by Virchow, with the exactness of a genial interpreter, supplied us with an ample description of the adventitia of the cerebral vessels, the contents of the space formed by this involucreum,

(1) *Archiv.*, 1851, III.

(2) Robin: Recherches sur quelque particularités de la structure des capillaires de l'encephale. *Journal de la Phys. de l'homme et des animaux*, 1859, II.

and his illustrations leave no doubt concerning the correctness of his observations in every respect.

After Robin, 1865, His¹ took up the question and was the first who applied the injecting method to the examination of these canals. Fromman,² 1867, called our attention to the contradictions in the observations and conclusions made by His, and considered the so-called perivascular spaces, or *canals outside* the adventitious tunic of Robin, as *artificially* produced by the injected liquid.

Roth,³ 1869, observed, in sections made through the hardened brain substance, the existence of fine filaments transversely connecting the brain tissue and the walls of the contracted vessels; and Obersteiner,⁴ 1870, maintaining the views of His, proved the existence of spaces of a similar kind around the nerve tubes as well as the ganglion cells themselves.

The first then, who cleared up these somewhat complicated conditions, was Golgi,⁵ 1871, in his excellent researches on the "Microscopical Anatomy of the Nervous Centers," who exposes in a most convincing manner the inadmissibility of the views of His and his followers; and his interpretations have been confirmed by Boll,⁶ in their utmost extent.

A somewhat peculiar position has recently been taken by Batty Tuke,⁷ a most careful English investigator in "The Morbid Histology of the Brain and the

(1) Ueber ein perivasculares Canalsystem in den nervösen Central-organen und ueber dessen Beziehungen zum Lymphsystem. *Zeitsch. f. wiss. Zoologie*, XV.

(2) *Untersuchungen*, Th., II.

(3) Zur Frage der Bindesubstanz in der Grosshirnrinde Virchow: *Archiv.*, XLVI.

(4) *Wiener Academie-Berichte*, Bd., LXI, Abth., I.

(5) Contribuzione alla fina anatomia degli organi centrali del systema nervoso. *Revista Clinica*, Nov., 1871.

(6) *Archiv. für Psychiatrie*, IV., I.

(7) *British and Foreign Medico-Chirurgical Review*, CII.: April, 1873.

Spinal Cord observed in the Insane," a position which again threatens to complicate the question.

Batty Tuke, abandons the former theory of His, regarding the perivascular canal.

"But as the existence in health of a space between the brain substance and the vessel is now more than doubtful, this term must be departed from, and the following experiments and observations are put forward to indicate that the existence of a canal around a vessel is an abnormal condition."

"In every section I have examined, in which blood has remained in the vessels, there is no evidence of the existence of a perivascular canal."

"Even supposing the actual existence of a small lymph space around a cerebral artery, it is difficult to understand how the backward flow of its contents could be carried on against the constant counter-impulse of the blood. His himself has abandoned the theory, and Rey and Retzius confirm him in his departure from it. A 'perivascular canal' must be regarded as a morbid condition, and in this indicative sense the term will be in future employed by me."—10 *Ibid.*

However, at the same time, he denies the existence of a lymphatic sheath around the vessels of the brain and the spinal cord, and gives us the description of "a thin hyaline membrane, as thrown out by the tunica adventitia, which invests the vessel in many forms of cerebral disease."

"There exists," he continues, "some discrepancy in the description of this membrane by various authors, some speaking of it as a cellular fibroid secondary sheath, others as a hyaline fibroid, and others as a purely hyaline membrane, homogeneous and clear, which at first is non-fibrillated, but as it goes on contracting becomes less hyaline and more fibrous, like a sheath."

"The examination of a very large number of prepared sections and of recent specimens has convinced me of the existence of a membrane *outside the adventitia* to which the two latter descriptions are applicable. *I believe it is continuous with the sheath of pia mater* surrounding the vessels as they enter the substance of the brain, and *that it exists around every artery as its normal sheath*, although in perfect health it is not easy of demonstration. Robin found it in every subject he examined, and Clarke demonstrated it

in the brain of a healthy young man who had been accidentally killed, and I can show its presence in the medulla oblongata of a cat killed by cut throat. In health it is exceedingly thin, perfectly homogeneous, non-fibrillated; in fact, a pure hyaline membrane, forming a somewhat loose envelope to the vessel. At bifurcations it is not intimately applied to the angle, but forms a triangular sac, and becomes again continuous a short distance beyond it. In the same way it ensaculates abnormal tortuosities and kinks. Judging from the fact that it is invariably demonstrable in empty perivascular canals, it would appear that it is rendered thicker by being subjected to lymph exudation. It also becomes more apparent in advanced age. When in this condition it is easily recognizable in the *pia mater*, which has been treated with water only for the purpose of cleaning, and in squeezed-out fresh brain which has received no treatment at all. It is true that glycerine, camphor-water and other agents render it more obvious, but their employment is by no means necessary. In the highest form of morbid development it is to be seen intimately attached to the brain-wall of a perivascular canal. So closely does it adhere at times, that it can be seen lying on the surface of the section, having been dragged out by the knife, but still clinging to the edges of the canals."—Page 454.

It is apparent in these expositions, we have to deal with quite a new interpretation. Batty Tuke makes a clear distinction between the *hyaline membrane* of Robin, Lockhart Clark, Rokitansky, Wedl, Koelliker, Sankey, Rindfleisch, &c., and the *adventitious tunic* of Virchow, Robin, Fromman, His, Golgi and others, but he does not claim the presence of this *fourth* membrane itself, lying *outside the adventitia*, as a morbid product but only the thickened condition of the same in certain cases.

In regard to the investigations since my connection with the Asylum, they embrace nineteen brains of insane persons, and one of a young man in full health, suddenly killed on the railroad. Of these I would state the following anatomical facts.

In every case examined carefully, a covering surrounding the vessels which penetrate the brain substance,

could be made visible, a sheath inclosing the vessels sometimes more and again less distended, and sometimes closely adherent to the inner coats. The contents of this sheath, when still expanded in its natural condition, were invariably recognized as consisting principally of lymph, and the direct communications of these ducts with those which surround the vessels of the *pia mater*, were easily demonstrated by injections of the lymph ducts of the *pia mater*.

What are these ducts and what is the nature of the membrane, forming the sheath, in an anatomical and physiological point of view? I can not but adhere to the opinions of the first discoverers, Virchow and Robin. It is evidently nothing more or less than the adventitious coat of the vessel itself, destined to carry away the overflow of the blood, the plasm which has exuded from the capillaries into the tissues, and which has not been taken up again into the venous current.

Besides the homogeneous tunics, there are no other membranes visible but the two in a close connection form the walls of the vessels themselves. I have never observed, either in sections, or in carefully insulated specimens of larger vessels with numerous branches, after removing the sometimes very delicate tunics, any traces of another which could be regarded as an adventitious coat of the vessels. But the peculiarity that even ducts of a true capillary character also show the presence of these membranes and in direct communication with those of larger branches, renders it more than probable that they represent nothing more or less than the very adventitious coat itself.

That the spaces enclosed by this membrane and the media of the vessels may be found more or less distended, and in morbid affections of the vascular system sometimes in an extraordinary state of expansion, is a very well known fact. Also deposits of foreign ma-

terials, the exudation of fat globules, pigment bodies, crystals, etc., have been noticed by various authors. The presence of such deposits does not always indicate a morbid condition, as I have demonstrated them in specimens taken from a sound brain, as well as from a diseased one. But the extent to which they appear, is undoubtedly a matter of more or less importance, and in cases of general paresis, I have observed these spaces, here and there, entirely filled by cell formations of an irregular and spongy texture, apparently new formations, sometimes surpassing three or four times the inner caliber of the capillary vessels.

That on the other hand, frequently reported congestions, the overflow of blood and increased exudations will produce a dilatation of the brain substance itself, surrounding the vessels, is a presumption which may be admitted, although the histories of them can not be obtained. But that such dilatations really exist is an indisputable fact, and that after the reabsorption of the superabundant liquids by the absorbing ducts, these, when relieved from the pressure and contracted again to a uniform caliber, may leave a space between their membranes and the altered tissue of the brain substances, will be easily conceived, as the fact is in numerous cases observed. But I have never found in these spaces of a morbid development, any traces of organized lymph, nor any deposits similar to those demonstrable in the adventitious spaces as above mentioned. The only microscopical elements visible in these spaces, are fine filaments transversely crossing the space and forming a connection between the dilated tissue of the brain and the enveloping sheath of the vessels.

The question arises, what is the nature of these filaments? For a long time I was unable, from the apparently conflicting facts, to form a judgment. However, more recently, I subjected these formations to careful

comparisons with similar conditions observed in specimens of hardened brain, and with the application of highly magnifying powers, have solved the question to my full satisfaction.

In preparations taken from hardened brain, as the hardening process depends upon a deprivation of water, the vessels will be found always in a more or less shriveled and contracted condition. The really existing physiological space enclosed by the adventitious tunic will very rarely be visible even in the thinnest sections. And the more the action of the hardening agent advances, the less distended will these spaces appear; and in most of the cases we may find the thin adventitious membrane so closely adherent to the media, that neither a separating space nor the membrane itself seem demonstrable by our optical instruments. It is for this reason that in so many cases the natural condition has been overlooked. The space produced by the contraction of the adventitia was accepted as a true canal around the vessels. The fact that it was possible to fill these canals by an injection, especially by the use of the puncturing method, could only confirm this theory. In other cases in which the still expanded, adventitious covering was seen containing the organized lymph, this state was confounded with the former one. And, Batty Tuke and others, in the belief that the one false interpretation had to fall with the other, created the new theory of this hyaline membrane. Nevertheless, he is indebted to Virchow and Robin for the explanation of what he himself calls the adventitious coat.

Although in all specimens of hardened brain, as above mentioned, the true adventitious membrane of the vessels is only with difficulty demonstrable, it is virtually always existing. In a closer examination of the external surfaces, such vessels will never show the smooth appearance of the medium coat or of the

simple membrane of a capillary. They are uneven, shaggy and trimmed with small bunches of twisted fibres, when insulated, and in sections, there are in these artificial spaces the same transversely crossing filaments observable, as in the above described spaces of a morbid origin. The application of higher and well defining powers will leave no doubt as to the determination of their nature. They represent the so-called Deiter's cells of the connective tissue of the brain substance, these peculiar brush-like or radiant-like cells which, adherent to the adventitious coat of the vessels, in consequence of its contraction, appear as drawn out from the molecular mass, which composes the parenchyma of the nervous centers.

There remains at this time no other question to solve. The great diversity of the opinions are undoubtedly, for the most part, due to the various methods of investigation employed by the authors. The injecting method so valuable in its results, may, even when applied with the utmost care, in combination with the puncturing method, produce artificial ducts, especially in tissues altered by some morbid affections. In consequence of the action of such hardening agents as alcohol, chromic acid, bichromate of potash and ammonia, osmic acid and others, we have to deal with so many changes of the normal structure, that the true anatomical conditions are demonstrated, sometimes only with great difficulty. The examination of the fresh tissues, however, in indifferent liquids, as water, albumen, gelatine, blood-serum, &c., should never be neglected, as it is by the employment of as many different methods of examination as possible, and by the application of theories carefully deduced therefrom, that we will be able to throw further light on regions so attractive to the student of histology.

THE
AMERICAN JOURNAL OF INSANITY.

THE AMERICAN JOURNAL OF INSANITY is published quarterly, at the State Lunatic Asylum, Utica, N. Y. The first number of each volume is issued in July.

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The JOURNAL is now in its thirtieth year. It was established by the late Dr. Brigham, the first Superintendent of the New York State Lunatic Asylum, and after his death edited by Dr. T. Romeyn Beck, author of "Beck's Medical Jurisprudence;" and since 1854, by Dr. John P. Gray and the Medical Staff of the Asylum. It is the oldest journal devoted especially to Insanity, its Treatment, Jurisprudence, &c., and is particularly valuable to the medical and legal professions, and to all interested in the subject of Insanity and Psychological Science.

