

# A CONTRIBUTION TO THE PATHOLOGICAL ANATOMY OF CHOREA WITH THE REPORT OF A CASE.

BY CHARLES L. DANA, M.D., NEW YORK.

*Visiting Physician to Bellevue Hospital.*

THE present paper deals chiefly with the pathological anatomy of the nervous centres in chorea. The changes elsewhere, particularly those in the heart have been often described, and there is a pretty definite agreement that the most uniform condition in patients dying of chorea or with chorea is fibrinous deposits on the valves of the heart, usually the mitral. Osler thinks that this occurs in 90 per cent. of cases.

I shall not take up this particular point, but turning to the nervous side of the question, I will give first the report of my own case.

Wm. G., Swiss, single, aged eighteen. Family history unknown. Admitted December 15th, 1888. Patient was always weak and sickly as a child. Has no clear remembrance of having any of the ordinary children's diseases; gives no rheumatic, venereal or alcoholic history.

Patient began to have choreic movements twelve years ago, *i.e.*, at the age of six years; cause unknown. The movements were not severe and when at the age of twelve he came to this country he was able to work and be useful.

The patient has had so-called epileptic attacks at occasional intervals for many years. The attacks used to occur at night only, but of late they have come on during the day also.

*Physical Examination.*—The patient lies in bed and is unable to walk or help himself on account of the violence of the choreic movements. He is somewhat emaciated and anæmic. His face is dull and the expression stupid, but he answers questions intelligently. The speech is slow and jerky on account of the move-

ments of the lips and tongue. Over the left parietal bone is a hole the size of a half-dollar made by a trephine in an operation performed in San Francisco fourteen months ago. No report of any hemiplegia or other form of paralysis. There are no heart murmurs, lungs normal, as are also the abdominal viscera. Urine yellow, clear, neutral, sp. gr. 1021, no albumin; microscopical examination negative. Patient's movements are so great that he cannot feed or help himself. He has several epileptoid attacks daily and nightly with tonic, and clonic and also with co-ordinate movements, throwing himself about, screaming, and frothing at the mouth. The fits are of a hysteroid character. Ordered chloral hydrate and frequent feeding with stimulants.

*December 20th*, five days later, hysteroid attacks are less numerous and only at night; choreic movements less, so that patient can feed himself. He is stupid from the chloral. Temp.  $100\frac{1}{2}$ , pulse 80, res. 20.

*December 28th*.—Thirteen days after admission, is much brighter, sits up, talks and reads quite well; chorea better. Ordered ext. physostigma gr.  $\frac{1}{4}$ . Diminished chloral. Patient improved considerably, the fits ceasing altogether, until January 6th, 1889, when he developed pneumonia and died January 8th.

*Autopsy*.—Rigor mortis well-marked, body considerably emaciated, left lung shows beginning pneumonia, heart normal; no vegetations on valves, liver and spleen normal, kidneys were small, capsule adherent and thickened; markings fairly plain, skull was extremely thick, measuring 14 ctm. ( $\frac{3}{4}$  in.) on section through occipital bone. Brachycephalic in shape. Antero-post diameter 18, transverse diameter 16 ctm., giving a cephalic index of 88<sup>1</sup>.

The old trephining hole lay over the left supra-marginal gyrus. The dura mater was not very adherent, the pia mater was thickened and congested, but not markedly adherent to the cortex. There was no excess of cerebro-spinal fluid. The brain looked normal, except for a very superficial softening seen on the under surface of both temporal lobes. The cord was apparently normal; the brain, cord, pieces of sciatic, musculo-spiral nerve and biceps were saved for further examination.

#### MICROSCOPICAL EXAMINATION.

The brain, cord, and nerves were placed in Müller's fluid, frequently changed, and at the end of three months (for cord,

<sup>1</sup> I am indebted to my house-physician, Dr. Alex. Lambert, for the above carefully taken notes of this case.

bulb and nerves), and five months (for brain) placed in alcohol. Pieces of the motor convolutions, temporal, and parietal convolutions, as well as sections of the corpus striatum and optic thalamus were cut and stained. Sections through the pons, bulb and cord were also made. The stains used were Weigert's, the ordinary hæmatoxylin, carmine, and Congo red and Golgi's nitrate of silver. By the latter method very beautiful sections were obtained.

*Convulsions and subcortical White Matter.*—There is a slight amount of lepto-meningitis, the gray matter is considerably injected, the neuroglia cells are not excessively increased. The pyramidal cells are for the most part normal. Occasionally one finds a cell undergoing pigmentary degeneration. The outlines and processes and lymph paths come out beautifully by Golgi's stain. The nerve fibres can be seen running up into the cortex; the transverse fibres are also present. The chief changes are just beneath the cortex. Here the white matter is in some sections honeycombed with little spaces, round, oval, or like long slits. The spaces are either empty or partly filled by blood vessels (which latter are shrunk by the bichromate). The blood-vessel walls are somewhat thickened, but not strikingly so. There is no real arteritis. They have, however, been tensely distended, and exudates, including red blood cells poured out. This has distended and eroded the perivascular spaces, forming large dilatations, similar to those described by Dickenson. (See illustration.)

The process, though chronic, cannot be looked upon as inflammatory, and it can only be explained by assuming a flabbiness and loss of tonus of the vessel walls (due to prolonged distension) and allowing abnormal dilatation and filtration of the vessels' contents. There is no hyperplasia of connective tissue shown by Weigert or logwood stains, nor any amyloid bodies. At the base and tip of the temporal lobe, where the surface of the brain was softened a severer grade of meningitis or chronic meningeal thickness was present and the superficial layers of the cortex showed evidences of disintegration; the ganglion cells could be seen, but the white matter beneath was more extensively honeycombed and slit, while there was evidently increase of neuroglia cells.

*Basal Ganglia and Internal Capsule.*—These parts did not appear to the naked eye so much involved as did the subcortical tissue. However, the middle portions did not harden well, and only the optic thalamus, the lower part of the internal capsule and the anterior part of the caudate nucleus could be examined

microscopically. These parts showed the same honeycombed appearance from vascular dilatation, though less marked than in sections higher up. Here also it could be seen that the small arterioles formed varicose dilatations, which were full of blood. The internal capsule showed microscopically the more serious disorganisation. Its fibres were split up by interlacing and dilated vessels, whose walls were thin, degenerated and often seemed actually falling to pieces. Here I noticed, first, a varicosity of the nerve-fibres, caused by bulging of the myeline sheath, as described by Berkley. Cross sections of the capsule stained badly with Weigert, and seemed to be full of fibres swollen or partly disorganised. There was also a decided hyperplasia of connective tissue in the capsule, which was not noted in the thalamus or caudate nucleus.<sup>1</sup>

*The corpora quadrigemina* were dotted and streaked with dilated capillaries, but showed no large perivascular spaces.

*Crura Cerebri* and III. *Nerve Level*.—There is a less degree of vascularity than at higher levels; cells of III. N. nucleus are normal, so also are the fibres of the crus and the cells of the substantia nigra

Descending root of V. N. normal.

*Pons Varolii*.—The nucleus of the IV. N. contains few cells and some of these seem degenerated. The fourth nerves appear to have more degenerated fibres. The cells of the motor nucleus of the V. seemed to be normal in size and number, without pigmentation or vacuolation. The blood vessels are numerous and dilated, and their walls are thicker than those seen in the brain.

*Upper Medulla*.—A neuro-fibroma, the size of a pea, is seen just at the exit of the acoustic nerve on the left side, the fibres of the acoustic pass around it, a few passing into it. The only nerve nuclei in which I could detect signs of degeneration were those of the vagus (including the anterior nucleus) and accessories. The gray matter of the floor of the fourth ventricle was much honeycombed with very small cavities made by dilated arteries. There was apparently some increase of connective tissue in the pyramidal tracts. The neuro-fibroma referred to had not destroyed any parts by pressure.

*Spinal Cord*.—The pia mater was thickened, somewhat adherent and filled with distended vessels. The spinal cord showed some congestion, the distended and thickened vessels being most

<sup>1</sup> I could find no hyaline bodies such as are described by Dickenson and others.

numerous in the lateral columns. There was none of the honeycombed appearance as found in the brain and pons. In the lumbar cord a double canal was present, and for a short distance a third canal; a slight increase of interstitial tissue was observed in the lateral columns. The anterior and posterior roots showed no degenerated fibres.

*The Nerves.*—Sections of the anterior tibial nerve showed no inflammatory or degenerative changes whatever.

*SUMMARY.*—Brain, chronic leptomeningitis, non-adhesive, and therefore not severe. Diffuse and varicose dilatations of the small arteries, especially of the deeper sub-cortical matter and capsule. Degenerative changes in arterial walls; no arteritis. Perivascular lymph-spaces greatly dilated. Cortical cells in most regions normal. The severest changes, vascular, interstitial and degenerative were in the under surface of the temporal lobes in the internal capsule and adjacent parts of corpus striatum (especially lenticular nucleus), and optic thalamus (antero-internal part). Varicose nerve fibres were here noticed.

*Pons Varolii and Medulla.*—Same condition but much less marked. Cell degeneration in some cranial nerve nuclei. Slight connective tissue increase in pyramidal tracts.

*Spinal Cord.*—Slight lepto-meningitis, congestion of cord, especially in lateral tracts. Double central canal.

The record of the foregoing case naturally leads one to turn to previous accounts of autopsies for comparison. We here notice, first of all a curious distribution of these records.

The mortality from chorea seems to be much greater in England than anywhere else. In no other country have so many autopsies been made.<sup>1</sup> Of the English hospital cases 3 or 4 per cent. die. The Collective Investigation Committee found a mortality of over 2 per cent from chorea. Some years ago French physicians saw a good deal of fatal chorea, but few reports are made by them now. In Germany, there have been very few contributions to the pathological anatomy of chorea. In America I know of only three cases reported in detail.

The English observers have almost always examined acute cases, and their findings chiefly pertain to the vascular system; subinflammatory states, exudations, embolisms, &c.,

<sup>1</sup> Stuges collects eighty fatal cases reported by six English hospital physicians.

being noted. The Germans have seen more in the connective and nerve tissues, and note hyperplasia of the former with degenerative changes of the ganglion cells.

The French have as yet contributed few autopsical records of positive value.

I have examined and tabulated the *post-mortem* records in over eighty cases.

Raymond collected and tabulated (*Dict. Encyclopæd. de Sc. Med.*) seventy-nine cases. Seé in 1850 (*Mémoire de l'Acad. de Med.*) collected eighty-four reports of autopsies. Eliminating the duplicated cases, I find that there are on record nearly 200 reports of autopsies made upon patients dying of, or with acute or chronic chorea.

The large majority of these are of no value whatever, so far as the observations on the nervous system are concerned. In some in which careful examinations were made, the chorea was accompanied with mania, as in Golgi's case, or was symptomatic as in Froriep's case, or was of the hereditary type, as in Macleod's.

From a critical analysis of the list of reports, I can find only thirty-nine cases which give a satisfactory account of the nervous system. Even here, in some instances, the examination is not perfectly complete.

The list of valuable records, so far as I can find them, is as follows:—

1. ROKITANSKY, *Sitz. ber. der. Wien. Akad. der. Wiss.*, 1837.
2. STEINER, *Prag. Vierteljahrsch.*, 1868, 25 Bd. iii.
3. MEYNERT, *Wien. Med. Presse*, 1868, pp. 194.
4. OPPOLZER, cited by Rosenthal; *Wien. Med. Presse*, 1868, p. 195.
5. TUCKWELL, "St. Barth. Hosp. Rept.," vol. v., p. 86.
6. RUSSELL, *Med. Times and Gazette*, 1865, p. 88.
7. E. L. FOX and R. S. SMITH, *Med. Times and Gazette*, 1870, p. 423.
8. AITKEN, *Glasgow Med. Journal*, 1853, vol. i., p. 92.
9. L. CLARKE.
10. NAUNYM, SCHMIDT's *Jahrbüch*, Jan. 15, 1889.
11. ELISCHER, *Virch. Archiv*, vols. lxi., p. 485 and lxiii., p. 104.

- 12 to 18. DICKENSON, *Medico-Chirurg. Trans.*, 1876, vol. xli.
19. J. H. HUTCHINSON, *Phil. Med. Times*, 1876.
20. DONKIN and HEBB, *Med. Times and Gazette*, 1884, Nov. 1.
21. GOLGI, *Rivista Clinica*, 1874, p. 361.
22. BERKLEY, *Medical News*, Aug. 25, 1883.
23. ROSS, "Diseases of Nervous System," vol. ii.
24. BURY, quoted by Ross (*loc. cit.*)
25. KELLY, *Trans. Path. Society of London*, vol. xxiii., p. 94.
26. CL. DE BOYER, *Bull. Societ. Anat.*, 1875, t. xx., p. 551.
27. M. GUINON, *La France Medicale*, Jan. 19, 1886.
28. F. ROLAND, *La Progres Medicale*, 1886, vol. iv. p. 893.
29. HANDFORD and POWELL, "Brain," July, 1889.
30. Ditto ditto ditto.
31. DANA.
32. PATELLA, *Gazz. degli Ospital*, Sept., 1888.
- 33 to 39. JAKOWENKO, *Wiestnik psichiatrii i. nervopatol*, 1889, ii.

In excluding from my table so many records made, in many instances by careful observers, I do not mean to deny their value. These observations have shown in a general way that in death from chorea, congestions, extravasations, embolisms, and softenings, exist in the nervous centres. They have also proved the great uniformity of heart lesions. It is, however, only by a very minute and careful microscopical study of cases that any light upon the neuro-pathology of chorea can be obtained. For it does not follow because the cord is often found soft, or the walls of the central ventricles pultaceous, or that clots are found in the central arteries in fatal chorea that any such change occurs in the ordinary type of the disease. And the large number of incomplete autopsies upon chorea has simply confused our notions of it.

This confusion as to the pathological anatomy of chorea has been increased by the fact that systematic writers

No.	Reporter.	No. of Cases.	Age.	Sex.	Cause.	Duration.	Type & Complications.	Findings.
1	ROMTANSKY	...	...	...	...	...	...	Increase of connective tissue in brain and cord.
2	STEINER	...	...	...	...	...	...	Increase of connective tissue in spinal cord, with serous exudation and effusion of blood in spinal canal.
3	MEYER	...	16	F.	...	...	Chorea of Sydenham.	Congestion and sclerotic changes in brain, colloid bodies. Degenerative changes in cells of spinal cord.
4	OPPOLZER	...	...	M.	...	...	...	Increase of connective tissue in cord, softening in its upper dorsal and lower lumbar parts.
5	TUCKWELL	...	13	F.	Preceded by rheumatism.	3 weeks.	Chorea of Syd.	Embolism both posterior cerebral arteries and partial softening in under surface of temporal lobes. Spinal cord normal.
6	RUSSELL	...	14	M.	Rheumatic.	About 1 month.	Chorea of Syd.	Brain atrophy, increased subarachnoid fluid. Pial echymoses.
7	E. L. FOX	...	17	F.	Fright.	1 month.	Chorea of Syd.	Brain vessels empty, cord and corpus striatum examined only. Meningeal hemorrhage, small vessels of corpus striatum engorged with blood. Other parts not examined.
8	AITKEN	...	17	F.	...	10 days.	Sub-acute chorea, imbecility.	Varicose dilatation of blood vessels of gray matter of brain. Lessened spec. grav. of basal ganglia.
9	L. CLARKE	...	17	F.	...	6 years.	Severe type of chronic chorea.	Oedema of brain and cord. Brown-red coloration of pia in fissure of Sylvius and at base, caused by fungi growing along the vessels.
10	NAUNYM	...	...	...	...	...	Chorea of pregnancy.	Diffuse irritative process causing increased proliferation of nuclei of neuroglia and of vessel walls. Signs of degenerative process in nerve cells.
11	ELISCHER	...	23	F.	3rd attack.	4 months.	Chorea of pregnancy.	Hyperemia of parts of brain and especially of cord. Hydro-myelia, especially of lower cord (congenital?) Hematomyelia of upper part of cord.
12	DICKENSON	...	10	F.	Rheumatic.	3 days.	Chorea of Syd.	Dilatation of arteries and veins and effusion in perivascular spaces. Congestion of cord.
13	Ibid	...	10	F.	Fright, 3rd attack.	3 weeks.	Chorea of Syd.	Dilatation of arteries and veins, especially of optic thalamus, congestion and extravasation in cord.
14	Ibid	...	7	F.	?	24 days.	Chorea of Syd.	Congestion of brain and cord.
15	Ibid	...	8	F.	Fright.	2 months.	Chorea of Syd.	Congestion of corp. striatum and in the white matter of one of the convolutions with signs of small embolisms?
16	Ibid	...	11	M.	Rheumatism.	6 weeks.	Chorea of Syd.	Congestion of brain with old spots of so-called sclerosis (arterio-sclerosis?) especially in basal parts and corpora striata.
17	Ibid	...	13	F.	Rheumatic, 3rd attack.	3 weeks.	Chorea of Syd.	Congestion of basal parts of brain and old spots of sclerosis? especially in motor convolutions. Congestion of cord.
18	Ibid	...	54	M.	?	4 years.	Chronic chorea.	Congestion of brain with old spots of so-called sclerosis (arterio-sclerosis?) especially in basal parts and corpora striata.



No.	Reporter.	No. of Cases.	Age.	Sex.	Cause.	Duration.	Type & Complications.	Findings.
19	J. H. HUTCHINSON	1	12	M.	Fall. ...	8 weeks.	Chorea of Syd.	Congestion of brain with some plugging? of arteries of corpora striata; cord is soft, 3rd to 5th dorsal. Brain very soft, walls of vessels disintegrated, cord showed congenital abnormalities, blood vessels full of micro-organisms. Pachy and leptomeningitis, atrophy of cerebral convolutions. White matter hyperaemic, spots of softening and gray degeneration, corpora striata softened, cord soft, membranes thick, ganglion cells atrophied, varicose axis cylinders, hyperplasia of connective tissue in cord and cell pigmentation. Dilatation and thickening of arterioles with necrotic areas about them, degenerative changes in ganglion cells, varicosities of nerve fibres, amyloid bodies. Same changes very much less marked in bulb. Same changes quite marked together with sclerotic changes in cord, no emboli.
20	DONKIN & HEBB	.....	20	F.	Fright. ...	7 days.	Chorea of Syd. (?) with mania.	
21	GOLGI ...	.....	42	M.	.....	10 years.	Chronic symptom-atic, with mania.	
22	BERKLEY...	.....	41	F.	Fright. ...	7 years.	Chronic chorea, imbecility.	
23	ROSS...	...	...	...	.....	.....	Chorea of Syd.	Hyperaemia of spinal cord, especially of anterior and anterior lateral arteries. Degeneration of accessory nerve cells. Periaxial exudations and erosions; and lesions in general like those described by Dickenson. Soft spots and small extravasations of blood in corp. striat. Fatty degeneration of capillaries and small arteries. Marked meningo-encephalitis and cerebral atrophy, other parts normal. Microscopical examination (?) Nothing. Very great cerebral hyperaemia, two pseudo cysts of the choroid plexus. Intense cerebral hyperaemia, thromboses and minute hemorrhages in pons and upper cord. Same as No. 29.
24	BURY ...	.....	...	...	.....	.....	Chorea of Syd.	
25	KELLY ...	.....	9	F.	?	15 days.	Chorea of Syd.	
26	CL. DE ROYER	.....	7	F.	.....	4 months.	Chorea of Syd.	
27	GUINON ...	.....	19	F.	.....	2 months.	Chorea of Syd.	Vascular dilatations and perivascular erosions. Softened areas subcortical, especially in occipital lobes. Hyperaemia, emboli (?) Small hyaline bodies in globus pallidus lying about vessels, vide Meynert, Dickenson, Berkley.
28	ROLAND ...	.....	7	F.	Scarlet fever.	Acute.	Chorea of Syd.	
29	H. HANDFORD & E. POWELL	.....	19	M.	.....	21 days.	Chorea of Syd., with insanity.	
30	H. HANDFORD & E. POWELL	.....	20	F.	.....	2 weeks.	Chorea of Syd., with insanity.	
31	DANA ...	.....	19	N.	.....	12 years.	Chronic with epilepsy.	Vascular dilatations and perivascular erosions. Softened areas subcortical, especially in occipital lobes. Hyperaemia, emboli (?) Small hyaline bodies in globus pallidus lying about vessels, vide Meynert, Dickenson, Berkley.
32	PATELLA...	.....	11	...	.....	.....	Chorea of Syd.	
33	JAKOWENKO ...	6	...	...	.....	.....	Chorea minor, later delirium acutum.	

have usually cited all the various findings in fatal cases as evidence of the lack of any definite anatomical basis of the disease. In fact the records in sub-acute cases, in chronic cases, in juvenile or adult cases, and in complicated cases, should be studied separately, and compared together with the facts of the clinical history kept in view. In this way, it will be found that there is very much less discrepancy in results than is supposed.

In the lists of fatal cases collected are :—

1. Sub-acute chorea of Sydenham.
2. Chronic        ,,        ,,
3. Hereditary   ,,        (Huntingdon's).
4. Congenital   ,,
5. Symptomatic ,,

It is only the first two classes of cases that form the chorea as ordinarily met with. It is this disease whose pathology and anatomy is here specifically sought, and whose autopsical records I have collected.

I shall analyse my table with reference—

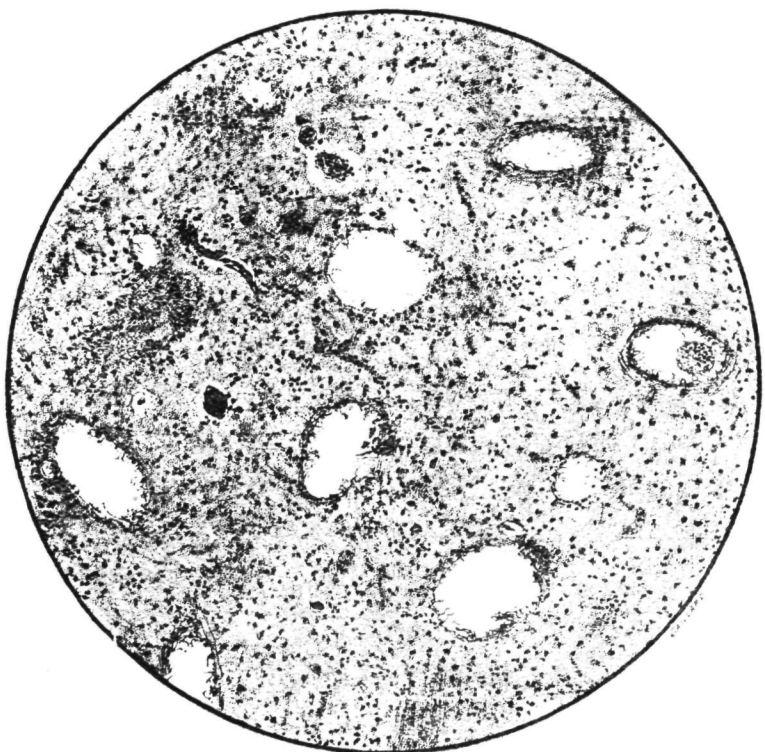
1st. To sub-acute chorea :

Among the thirty-nine cases there are twenty-five in which the disease was the sub-acute chorea of Sydenham, uncomplicated with insanity, or other serious disorder. Leaving out the six cases of Jakowenko, which are published in Russian, and not accessible in detail to me, there remain nineteen cases, in which careful microscopical examinations were made. In sixteen of these there is a record of intense cerebral hyperæmia, periarterial exudations, and erosions, softened spots and minute hæmorrhages, and occasionally embolisms. The changes are most marked, not in the meninges, but in the deeper parts of the motor tract, the lenticular nucleus and inner parts of the thalamus.

In a few of the cases, only, is the cord affected somewhat similarly.

Of the remaining three cases, in one (Roland's) absolutely no changes are recorded. I cannot but think that they were overlooked, or that a mistake was made in some way.

In one case, only the corpus striatum and cord were examined, and here spots of softening were found ; and in one





case, the brain was very soft, the vessel walls were disintegrated, and full of micro-organisms.

In two cases of sub-acute chorea with insanity, there was intense cerebral hyperæmia with thrombosis and minute hæmorrhages, much as in uncomplicated cases.

In the six cases of Jakowenko, he says nothing about congestion, but describes minute hyaline bodies, found chiefly in the inner divisions of the lenticular nucleus (*globus pallidus*).

#### 2nd. Chronic chorea.

There are records of five cases of chronic chorea, lasting from four to twelve years.

Here we find dilatation and thickening of arterioles with necrotic and erosive changes about them, degenerative changes in ganglion cells, varicosities of nerve fibres, old spots of sclerosis, and hyaline bodies.

The cord is somewhat similarly involvea, but to a less extent.

There are no evidences of inflammation, or of continuous humoral irritations, such as eventually lead to decided arterial thickening.

Summing up we find that in the subacute types of chorea there is a hyperæmia of the brain and parts of the cord. In the brain this is not meningeal but subcortical and basal. The arterial walls are paralysed, dilated and badly nourished, so that exudations occur, and the lymph spaces become distended and eroded. There is sometimes stasis, thrombosis and spots of softening, or the walls give way, and there are minute hæmorrhages. The lymph spaces around the ganglion cells are not dilated.

In older cases, the vascular and neuro-degenerative changes are marked. The small arteries are permanently dilated, a little thickened and degenerated; perivascular channels may be more eroded and distended.

There is now some connective tissue proliferation, and signs of degeneration in the ganglionic cells. The nerve-fibres show a varicosity. (Berkley's case and my own). Hyaline bodies are seen.

In fine, we have in chorea, first a vaso-motor paralysis

and trophic disturbance, affecting certain areas of the brain, and to a less extent of the cord. Then we have this becoming chronic, with connective tissue, hyperplasia and degenerative changes in ganglionic cells and fibres.

As for the localisation of the lesion, the earlier English writers all looked for it in the basal ganglia, and their findings are, perhaps, a little biassed by the expectation of seeing something in these localities. In some autopsies only the cord and basal ganglia were examined. We cannot, however, locate chorea in these places exclusively, nor in the globus pallidus, nor in the cortex. It is rather a disease of the intracranial motor tract, including its starting point in the cortex, and especially in its co-ordinating adjuncts, the lenticular nucleus and thalamus