

THE MORBID HISTOLOGY OF THE CARDIAC NERVOUS  
GANGLIA.\*

JOSEPH MCFARLAND, M.D., AND ANDREW ANDERS, M.D., PHILADELPHIA.

In the year 1911 our attention was called to a patient in the Philadelphia General Hospital, whose most interesting clinical manifestation was a remarkably slow pulse, for which no adequate cause could be found.

There was no jaundice, and a careful study of the radial and jugular pulses made by the clinicians in charge failed to show any abnormality of the auriculo-ventricular contractions. The pulse which for some time had been beating at about thirty-six became slower and slower, as death came on, until shortly before death it was only twenty in a minute.

The autopsy, which was conducted with thoroughness, also failed to explain the bradycardia. The record book in the hospital in which the patient died gives the following summary, beyond which it seems, for the present purposes, unnecessary to go:

H. A. L. White man. Aged 70 years.

Clinical diagnosis: Myocarditis; pulmonary congestion; interstitial nephritis.

Pathological findings: Arterio-sclerosis; chronic interstitial nephritis; senile pulmonary emphysema.

In discussing the findings and in an attempt to account for the bradycardia, it was suggested that the disturbance might have had something to do with the intrinsic nervous mechanism of the heart, and that an examination of the nervous ganglia might afford a clue to the nature of the condition.

To this end the heart, which had been preserved in formaldehyde, was brought to the laboratory, and what turned out to be a very tedious and not very profitable piece of work was begun. The details of this work were carried out

---

\* Received for publication Dec. 6, 1912.

with great patience by Dr. Anders, and it is unfortunate that the results have been so disproportionate to the amount of work actually performed. That so little seems to be known about the cardiac ganglion is our apology for the present publication, if any apology is required.

It is well known that the heart receives its innervation through branches of the vagus nerves, and through the cardiac branches of the sympathetics.

The former act as inhibiting, the latter as accelerating influences.

But in addition to these, the heart is provided with certain nervous ganglia, whose exact office is less well understood, but which are generally supposed to be connected with its sensory mechanism.

The nerves imbedded in the heart muscle and in the furrows are richly supplied with ganglia, which have been designated the automatic motor centers of the heart. The heart contains a circle of nerves, richly supplied with ganglia, at the edge of the inter-auricular septum, and another at the junction of the auricles and ventricles. Whenever the two meet they exchange fibers.

The ganglia are for the most part near the pericardium. In mammals the two larger ganglia are situated close to the orifice of the superior vena cava, in birds the largest node of nerve-tissue, containing thousands of ganglia, occupies the posterior part of the decussation of the longitudinal and transverse sulci.

These nodes of nerve tissue send smaller branches into the muscular walls of the auricles and ventricles, and these branches, in turn, are the seat of smaller ganglia.

In the frog, a large collection of ganglia — Remak's ganglion — is situated, together with the vagus fibers, within the wall of the sinus of the vena cava (the dilated orifice of the vena cava in the right auricle, whose independent movement precedes that of the auricle).

From this ganglion the vagus fibers pass to the anterior and posterior septal nerves, each of which is provided with a ganglion at the auriculo-ventricular junction, the ventricular

ganglion of Bidder. The motor fibers terminate in slightly clubbed extremities in each muscle cell; the sensory, which are derived from the medullated fibers, in flat expanded terminal plexuses which are quite abundant in the endocardium and pericardium. All ganglion cells are bipolar or multipolar. In the frog most of them are surrounded by a network of fibers; in Bidder's ganglion, spindle-shaped cells with two processes, one at each end, preponderate. In the rabbit and in the frog the ganglionic cells belonging to the sympathetic system have two nuclei, while the vagus ganglia have only one.

After division of the vagus branches (in the frog) the spiral process and the pericellular network from which it originates undergo degeneration.

The straight process gives off the muscle nerves. The bulb of the aorta contains numerous nerves for its muscle-fibers; but whether it contains ganglia also is doubtful (Landois).

In the past this elaborate nervous mechanism was looked upon as originating and governing the contractile movements of the heart, but one by one physiologists have abandoned the idea that the cardiac movements are neurogenic and, with the single exception of Kroneker, now adhere to the opinion that the cardiac movements are myogenic and originate in the inherent tendency of the cardiac muscle to rhythmical contraction — the myogenic theory. With this change in the theory of origin of the cardiac contractions has come about a change in the opinions that have been held in regard to the office of the cardiac ganglion cells, and it is now generally conceded that these cells have no motor influence but are purely sensory in function.

The ganglia, which are so large and so easily found in amphibians, in reptiles, and in birds, become numerous, small, widely disseminated, and, especially in man, difficult to find.

It was the small size and disseminated character of these ganglia in the human heart that was the chief cause of the great tedium of the present piece of work. In order to find

the ganglia at all, numerous pieces of the tissues of the heart had to be examined, and, in order that comparative studies could be made, pieces of tissue from as nearly as possible the same parts of all of the various hearts had to be examined, in order that, as nearly as possible, the same ganglia were compared. We made numerous attempts to find the homologues of Remak's ganglion in the inter-auricular groove, and of Bidder's ganglion in the inter-ventricular groove at the auriculo-ventricular junction, with little success. After the study of many sections from different hearts, we were at length obliged to narrow our efforts down to the study of the sub-epicardial areolar tissue in the deep fossa or pit between the right auricle and the base of the aorta. Disseminated throughout this tissue, a number of small ganglia and isolated nerve cells could usually be found.

In the study of these ganglia and of the scattered nerve cells that accompanied them we endeavored to determine the following :

- 1, The histological character of the ganglionic nerve cells.
- 2, The frequency with which the cells were diseased.
- 3, The relation of disease of these cells to physiological disturbance of the cardiac action.
- 4, Whether the condition of the ganglia in the case of bradycardia was sufficiently different from the condition of the ganglia in other hearts to explain the bradycardia.

In all fourteen hearts, taken at random from autopsies in two hospitals, and representing a miscellaneous variety of diseases, and ages varying from a few days to eighty years, were studied. In some cases we were fortunate enough to find a number of ganglia, but in others we could find but one.

The material was as good as that usually obtained from the autopsy table — no better, no worse. Some of it was hardened in formaldehyde, but for the most part it was fixed in Zenker's solution. The embedding and cutting was done in paraffine. The stain employed was thionine, the method

being that used for the demonstration of the Nissl's granules.

In material collected as ours had to be, we were naturally on the lookout for artefacts that might have arisen through post-mortem change, but we believe that we have excluded them from any important part in the deductions we have made. The changes that we describe were observed in cells that were very often side by side with normal cells in the same ganglion, and that we think a fairly safe guarantee that they were not the result of autolytic or other post-mortem change.

The ganglia were all quite small, scattered, and in close relation to medullated nerve fibers, sometimes lying in the nerve itself.

1. The histological character of the nerve cells.

We found one isolated nerve cell that was multipolar in shape, and resembled the motor nerve cells. All of the other nerve cells that we studied were distinctly of the sensory cell type. It seemed, however, that there were certain peculiarities about these cells that were not exactly as we expected.

Thus the nuclei of the cells of the cardiac ganglion do not seem to correspond in position with those seen in other nerve cells, for instead of occupying a central position in the cell, they were so commonly excentric that after the examination of a large number, we were constrained to abandon the idea that this was a sign of disease, and came to regard it as normal.

We also came to the conclusion that the Nissl's granules in these cells are less perfectly formed and distributed than in other nerve cells, and commonly much smaller.

There was scarcely a ganglion, among all those that we studied, in which the cells were uniformly normal. In many of the ganglia every cell was distinctly abnormal; in most of them more cells were diseased than normal.

The criteria by which we determined normality and abnormality were: (1), the position of the nucleus in the cell; (2), the staining quality of the nucleus and the bodies of Nissl; (3), the loss of the nucleus; (4), the solution and

diffusion of the chromaphilic bodies; (5), the shrinking and puckering of the cytoplasm; (6), the occurrence of vacuoles in the nucleus and cytoplasm; (7), the apparent dissolution of the cytoplasm which was reduced to a mere shadow possessing the outline of a cell, but totally without a nucleus and without any granules.

2. The frequency with which the cells were diseased.

We were astonished to find the presence of diseased cells so universally prevalent in our material. In only three out of fourteen cases were there normal cells—normal except for slight changes in the bodies of Nissl, as has been noted already. In one other case two ganglia were found, one in which the cells were nearly all diseased, one in which they were nearly all normal.

In nine out of the fourteen cases, there were abnormal cells in every ganglion found.

3. The relation of disease of the cells to physiological disturbance of the cardiac movements.

We experienced considerable difficulty in endeavoring to effect a correlation of these two conditions. The clinical notes of the individual cases were carefully read, but with the single exception of the case of bradycardia there were no evidences to show that the patients had any peculiarities of cardiac action, and in most of them nothing was said except a record of the pulse rate, and the statement that the "pulse was weak." We were therefore unable to show that such changes as we found were in any way associated with definite disturbance of the cardiac movements.

4. Whether the condition of the ganglia in the case of bradycardia was sufficiently different from that found in other ganglia to suggest any connection between the disease of the ganglia and the slow action of the heart.

We were not able to establish any connection between the two. More ganglia were found and studied in this than any other case, probably because the greater interest that attended it made us investigate it more carefully than we did any of the others, but in spite of this, we were not able to prove anything.

## CONCLUSIONS.

1. The nerve cells scattered over the surface of the human heart resemble the cells of the sensory type, and probably are a part of the sensory nervous mechanism of the heart.
2. These cells may differ from other sensory nerve cells in that an excentric position of the nucleus is normal to them.
3. The nerve cells of the cardiac ganglia are very frequently diseased.
4. The diseased cells occur in the ganglia side by side with normal nerve cells.
5. No disturbance of the cardiac movements seem to result from the disturbance of these cells.
6. The bradycardia in the case specially studied by us could not be referred to the diseased condition of the nerve cells of the cardiac ganglia.

## PROTOCOLS.

P. G. H. Vol. XXVI., p. 37. White man. Aged 79 years.

Autopsy findings: Arterio-sclerosis; chronic interstitial nephritis; senile pulmonary emphysema; cirrhosis of the liver.

Clinical memoranda: Bradycardia. Pulse 36 per minute, descending to 20 per minute shortly before death. The first sound of the heart apparently reduplicated at times. The second sound accentuated at the aortic cartilage. Both sounds short and without murmurs. Pulse regular, strong and full, not compressible. Systolic blood pressure 185; diastolic blood pressure 100. Dr. William Pepper made tracings of the radial and jugular pulses but found no heart block and no extra systolies.

Histological findings: Five ganglia were found and studied.

One contained twelve cells to the section. Two of these cells were fairly normal; one had a shrunken, badly staining nucleus; two were without nuclei and were badly vacuolated; three had the nuclei at the extreme edge of the cell, in one case actually projecting beyond the edge; four were puckered and going to pieces.

One ganglion contained eight cells to the section. One cell was normal, all of the others were puckered and vacuolated and either without nuclei or with shrunken or deformed nuclei.

One ganglion contained five cells to the section. All of these were badly diseased.

One ganglion contained four cells to the section. All of these were badly diseased.

One ganglion contained three cells to the section. One of these was

normal; one was slightly changed, one was enormously swollen, contained no chromophile bodies, and had a very pale and shrunken nucleus.

In addition to these ganglia, we found ten isolated ganglionic cells, all of which were badly diseased.

P. G. H. Vol. XXVII., p. 20. L. S. White man. Aged 45 years.

Autopsy findings: Hypertrophy of the heart; aortic sclerosis with calcification; cirrhosis of the liver with chronic passive congestion; chronic passive congestion of the kidneys; chronic passive congestion of the spleen; hypertrophy of the bladder; chronic adhesive pleuritis; edema of the lungs; hydropericardium.

Histological findings: The ganglia found were very small and few in number. The cells were nearly normal, but the Nissl bodies seemed to be disturbed so that the cytoplasm stained somewhat darkly and diffusely.

P. G. H. Vol. XXVII., p. 29. J. M. White man. Aged 35 years.

Autopsy findings: Chronic caseous tuberculosis of both lungs; cavitation at the apex of the right lung, metastatic tubercles in the lower lobe of the right lung; disseminated tubercles in the lower lobe of the right lung; chronic adhesive pleuritis of right and left pleura; chronic adhesive pleuritis; cirrhosis of the liver; tuberculosis of the liver(?); chronic cyanotic induration of the kidney with slight chronic interstitial nephritis.

Histological findings: Only one ganglion was found. It was very small and showed only three cells. These were probably the most diseased of all the cells that we examined. They were so changed as to justify the designation "shadow cells" as nothing but the general cell-outline was preserved. The nuclei and the Nissl granules had disappeared. Isolated nerve cells were also found, and though some of them had nuclei the cytoplasm was vacuolated and the chromophilic substance seemed to be diffused.

P. G. H. Vol. XVII., p. 34. M. L. White female. Aged 13 days.

Autopsy findings: Spina bifida; cutaneous ulceration; spinal meningitis; congestion of the lungs; parenchymatous nephritis.

Histological findings: Only one ganglion was found and studied. Some of the cells appear normal though they give one the impression that they are distinctly smaller than the corresponding cells in the ganglia of the adult heart. About one-half of the cells are more or less puckered, and show more or less diffusion of the chromophilic substance.

P. G. H. Vol. XXVII., p. 38. A. N. White man. Aged 53 years.

Autopsy findings: Thrombosis of both femoral arteries; atheroma of both iliac arteries; decubitus; congestion and edema of the lungs; hydrothorax; infarcts of the spleen; anemic infarcts of both kidneys; slight cirrhosis of the liver; myocarditis.

In this case the heart is described as somewhat enlarged, milk patch



over the right ventricle near the beginning of the pulmonary artery, the size of a quarter of a dollar.

The right ventricle contains post-mortem clots; the left ventricle has a slightly thickened wall which is pale. The mitral and aortic valvular leaflets are slightly thickened.

Histological findings: Only one small ganglion was found. The cells it contained were quite normal in appearance.

P. G. H. Vol. XXVII., p. 39. J. S. Colored man. Aged 58 years.

Autopsy findings: Brown atrophy of the heart; chronic interstitial nephritis; atheroma of the aorta; sclerosis of the vessels at the base of the brain; pulmonary emphysema; pleuritic adhesions; chronic peritoneal adhesions; constriction of the ileum by the vermiform appendix.

Histological findings: Only a few ganglia were found. They all showed shadow cells with diffusion of the chromophilic substance.

P. G. H. Vol. XXVII., p. 40. H. S. White male. Aged 20 days. (This child was supposed to have died of congenital syphilis.)

Autopsy findings: No gross signs of syphilis were found in the body of the child. There were no gross signs of disease. There was no Wegner's sign.

Histological findings: One fair-sized ganglion was found and studied. As in the other infant the impression one obtained was that the cells were somewhat smaller than the corresponding cells in the ganglia in the adult heart. A few of the cells were quite normal in appearance, but others showed loss of the nuclei and more or less diffusion of the Nissl bodies and were approaching the stage of the "shadow cells."

P. G. H. Vol. XXVII., p. 45. R. K. White woman. Aged 20 years.

Autopsy findings: Hypostatic congestion of both lungs; bilateral chronic pleuritis; cloudy swelling of the liver; hypertrophy of the left side of the heart.

Histological findings: No ganglia were found. Several isolated nerve cells were found and studied, some of which were to all appearances normal, while others were puckered and stained diffusely.

P. G. H. Vol. XXVII., p. 46. J. H. White man. Aged 70 years.

Autopsy findings: Acute vegetative endocarditis; chronic sclerotic mitral and aortic endocarditis; fibrous mural endocarditis of the apex of the left ventricle; atheroma and calcification of the coronary arteries; edema and congestion of the right lung; arterio-sclerotic and congested kidneys; congestion of the liver; purulent lepto-meningitis. (The heart was enlarged, the ventricular wall thickened, the aortic and pulmonary valves normal.)

Histological findings: Four ganglia were found and studied. Of these, one showed six cells to the section. One cell was very large,

exceedingly pale, finely granular, and had frayed out edges. Three of the cells were puckered, showed dark granular cytoplasm, and sharply defined dark nuclei. Two cells were scarcely recognizable as such.

One ganglion showed four cells to the section. One cell was quite normal, one had the nucleus at the extreme edge of the cell, and the Nissl bodies distributed, two cells were puckered, had no nuclei, and seemed to be going to pieces.

One ganglion showed three cells to the section. All are without nuclei, are more or less puckered, and in all the cytoplasm is darkened and finely granular from dissolution of the bodies of Nissl.

One ganglion shows five cells to the section. One of these is almost unrecognizable as a cell, three are disintegrating, one is puckered along the edges, though otherwise in fairly good shape.

Five isolated and scattered nerve cells, mostly along the course of a medullated nerve fiber, are all somewhat puckered at the edges and stain more or less diffusely because of the presence of fine granules.

One ganglion cell of the multipolar or motor type was found in this specimen.

P. G. H. Vol. XXVII., p. 47. P. M. White man. Aged 60 years.

Autopsy findings: Brown atrophy of the heart; edema of the lungs; broncho-pneumonia; congestion of the liver and kidneys.

Histological findings: Only isolated nerve cells — no ganglia — were found. One cell was to all appearances perfectly normal. Another had the nucleus at the extreme edge, and was slightly puckered at the edge. A third cell was apparently going to pieces.

P. G. H. Vol. XXVII., p. 49. C. S. White man. Aged 52 years.

Autopsy findings: Tumor of the mediastinal lymphatic nodes; secondaries in the left lung, both pleuræ, pericardium, diaphragm, tail of the pancreas, mesenteric lymphatic nodes, pelvic lymphatic nodes on the right side, and of the liver; hydrothorax on the left side; atelectasis and congestion of the lungs; parenchymatous nephritis; arterio-sclerosis with atheroma, sclerosis and calcification of the thoracic aorta; chronic pleuritis of the right side.

Histological findings: Only isolated nerve cells — no ganglia — were found. These cells were all more or less puckered, stained diffusely, and had indistinct nuclei.

P. G. H. Vol. XXVII., p. 54. A. B. Colored woman. Aged 50 years.

Autopsy findings: Chronic interstitial and parenchymatous nephritis; ulcerative colitis; atheroma of the aorta; chronic peritoneal adhesions; pleuritic adhesions on the left side.

Histological findings: Two ganglia were found and studied. One ganglion showed six cells to the section, only one of which was normal.

In the other five cells the staining was diffuse, the bodies of Nissl being broken up and their granular products distributed throughout the cytoplasm. The nuclei are situated at the very edges of the cytoplasm of the cells. Where nucleoli can be seen, they are situated at the edges of the nuclei.

One ganglion shows three cells in the section, all of which appear to be quite normal.

P. G. H. Vol. XXVII., p. 55. J. J. White man. Aged 36 years.

Autopsy findings: Lobar pneumonia, early gray hepatization of the entire right lung; chronic pleuritis of both sides; congestion and edema of the left lung; chronic double pleuritis; acute parenchymatous nephritis; chronic perihepatitis; tuberculosis of the right pulmonary apex; fibrous-mural endocarditis of the left ventricle of the heart. (In this case the mural endocardium was thickened and white over the posterior wall of the left ventricle. The valves were normal.)

Histological findings: Only one tiny ganglion was found. It contained only two cells in the section. One cell appeared to be quite normal, the other showed diffusion of the finely granular chromophilic substance.

M. C. C. 346. A. E. V. S. White man. Aged 41 years.

Autopsy findings: Surgical wound of the head following a decompression operation; sub-dural hemorrhage; chronic adhesive pleuritis and peritonitis; edema of the lungs; chronic interstitial nephritis; arteriosclerosis of the coronary arteries, aorta, and vessels of the base of the brain.

Histological findings: Only one ganglion was found for study. One cell was quite normal in appearance, but all of the others were more or less puckered and stained diffusely. The nuclei were all at the edges of the cells.