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HEART-BLOCK AND NODAL RHYTHM IN THE ACUTE INFECTIONS

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Reprinted from THE LANCET, February 3, 1912.

HEART-BLOCK AND NODAL RHYTHM IN THE ACUTE INFECTIONS.

IT has been known for more than a century that acute rheumatism is peculiarly prone to affect the pericardium and the valves of the heart, and is, indeed, the most common cause of chronic valvular disease; but it is only within the last few years that its special action upon the cardiac muscle has been recognised, and even now our knowledge of its effects is by no means complete.

Acute rheumatism may produce gross lesions in the connective tissues. The occurrence of subcutaneous nodules was first described by Hillier[1] in 1863 in a case of chorea, and Meynet[2] (1875) and others subsequently recorded their association with acute rheumatism, but these early observers failed to appreciate the full significance of their appearance. In 1881, however, Sir T. Barlow and Warner[3] pointed out the close connexion between the eruption of nodules and the occurrence of acute endocarditis, the presence of large nodules being an almost invariable sign of serious valvular disease, and indicative of a grave prognosis.

It had already been recognised that in certain fatal cases of rheumatic endocarditis the latter seemed insufficient to account for the fatal issue. In some instances pericarditis co-existed and doubtless aided in the progress towards death. But in others it was absent, and the chief clinical phenomenon was a progressive weakness and dilatation of the heart. To these cases Sturges[4] (1894) drew attention in his Lumleian lectures, maintaining that the rheumatic affection of the heart was not merely endocarditis or pericarditis, but *carditis*, all the tissues of the organ being involved in greater or in less degree. It was already known that fatty and granular changes were not infrequently present in the cardiac muscle cells in the acute infections, but it was only in 1899 that Poynton[5] demonstrated the essential rheumatic lesion in the cardiac muscle, the microscopic submiliary nodule, which,

[1] Medical Times and Gazette, 1863, vol. ii., p. 142.
[2] Lyon Médical, 1875, p. 495.
[3] Transactions of the International Medical Congress, 1881, vol. iv., p. 116.
[4] THE LANCET, 1894, vol. i., pp. 583, 653, 723.
[5] THE LANCET, 1899, vol. ii., p. 1163; Medico-Chirurgical Transactions, London, vol. lxxxii., p. 355.

though usually smaller, is exactly comparable to the nodules which occur in the subcutaneous tissue.

Within the last few years many observers—Cowan[6] (1903), Geipel[7] (1905), Aschoff[8] (1906), Carey Coombs[9] (1907), and others—have extended the investigation and have emphasised the importance and the frequency of myocardial lesions in the acute infections. The muscle cells in these diseases are generally abnormal to some extent if the illness has lasted for more than a few days, and submiliary nodules may occur,[10] though they are most common in cases where endocarditis co-exists.

Submiliary nodules are rarely of great size and are generally invisible on naked eye examination. The smaller nodules interfere but little with the adjacent muscle cells, but the latter are always abnormal if the nodule is large.

Microscopic examination shows that the essential lesion is a round-celled infiltration of the interstitial tissue. These infiltrations occur most frequently in the ventricular muscle, especially on the left side. They are usually situated around an arteriole or in its immediate vicinity, and sometimes involve the vessel wall, which may be so swollen that the lumen is almost obliterated. The cells may be few in number and the adjacent muscle apparently normal; but they may be numerous and infiltrate between the muscle cells, which are then more or less degenerate. In most cases the cells are arranged in discrete foci or nodules (Fig. 7), separated from each other by normal tissue; but in others the infiltration is diffuse (Figs. 8 and 9), and much larger areas are involved.

The cells are mainly mononuclear; the majority are evidently lymphocytes, but a few larger cells with a fair amount of protoplasm, which are probably of connective tissue origin, are often present, and occasionally a few polymorphonuclear leucocytes may be seen. In very malignant cases dense aggregations of polymorphonuclear leucocytes, with disintegrated muscle fibres, may be found; in other words, an acute suppurative myocarditis.

The rheumatic submiliary nodule is said to be characteristic (Carey Coombs[11]). The foci are chiefly composed of mononuclear cells superimposed upon a groundwork of fibrin, but also show certain very large cells which are often multinuclear. These may be globular or fusiform in shape, and their protoplasm takes up both acid and basic dyes, so that they appear much darker than the surrounding tissue. We have observed these cells in several cases in the cardiac tissue at the base of inflamed valves, but we have only once

[6] Journal of Pathology and Bacteriology, 1903, vol. ix., p. 87.
[7] Deutsches Archiv für Klinische Medizin, 1905, vol. lxxxv., p. 75.
[8] Brit. Med. Jour., 1906, vol. ii., p. 1103.
[9] Brit. Med. Jour., 1907, vol. ii., p. 1513; Quarterly Journal of Medicine, 1908, vol. ii., p. 26; THE LANCET, 1909, vol. i., p. 1377.
[10] Pneumonia, pleurisy, chorea, sepsis, leukæmia, small-pox, enteric fever, diphtheria, scarlatina, blackwater fever.
[11] Journal of Pathology and Bacteriology, 1911, vol. xv., p. 489.

(Case 5) found them in interstitial nodules. The arteries, too, in these cases may be thrombosed (Romberg), most often in the vicinity of the auriculo-ventricular junction. We have found arterial thrombosis with arteritis and periarteritis in one case of acute myocarditis.

Cellular infiltrations are very commonly present in the tissues at the bases of inflamed valves, especially the mitral valve, a circumstance which is important on account of their proximity to the primitive tissue of the heart. Bacteria have not hitherto been found in the non-suppurative myocardial nodules, which thus seem to be the result of a local toxæmia. As regards their ultimate fate, the smaller nodules are probably completely absorbed, but it seems certain that the larger lesions may become the foundation of a subsequent fibrosis of the myocardium.

The cardiac muscle in cases of chronic valvular disease is frequently fibroid, patches of sclerosed connective tissue of varying size being scattered here and there throughout the wall. In the majority of cases the fibrosis is the result of arterial occlusion and consequent necrosis of the muscle cells. In mitral disease, however, other causes are often active, and the fibrosis of the tips of the musculi papillares is generally believed to be often the result of a spread of the inflammation from the valves to the papillæ, and not infrequently the connective tissue at the base of the valves is excessive in amount and infiltrates into the adjacent structures. It is evident, too, that some of the more distant fibrous tissue owns a similar origin, and is the result of the healing of the submiliary nodules which we have just described. The patches are peri-arterial in site, multiple and widespread, and individually are of little practical importance, but their multiplicity may interfere considerably with the cardiac action, and they may, accidentally, involve important structures.

It is now generally believed that the rhythm of the heart and the proper sequence of contraction of its various chambers are intimately associated with the integrity of the undifferentiated cells which are present in certain places, the sino-auricular node of Keith and Flack, the auriculo-ventricular node of Tawara, and the auriculo-ventricular bundle of Stanley Kent. It has been repeatedly shown that heart-block may be due to lesions in the auriculo-ventricular bundle, though in certain cases this has been found to be normal, and the block has been ascribed to vagal lesions.

James Mackenzie[12] has suggested that extra-systoles occur as the result of impulses which arise in the primitive tissue. It has been shown that the normal contractions originate in the immediate vicinity of the sino-auricular node, and presumably in it, and that the region of the auriculo-ventricular tissue is more irritable than the muscle elsewhere, stimulation of the former being followed by a *series* of contractions (Gaskell), while stimulation of the latter only produces an isolated beat.

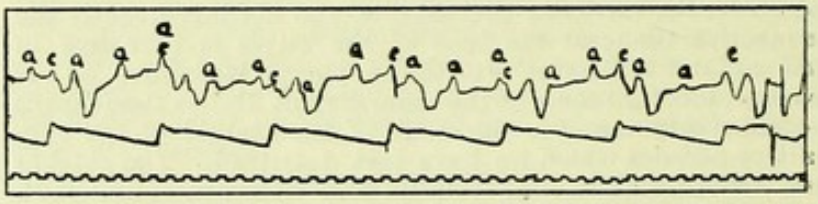
[12] Diseases of the Heart, London, 1908.

In chronic heart disease many lesions may be present in the heart—valvular defects, arterial disease, pericardial adhesions, myocardial fibrosis, &c.—and the lesions may be widespread. Variations in the cardiac rhythm are common events in these cases, but it is extremely difficult to disentangle the cause of the abnormal rhythm from the jumble of lesions which is found post mortem, and the maxim concerning *post* and *propter* must be kept in mind. Variations in the cardiac rhythm occur not infrequently in acute disease, and the cardiac lesions are generally more simple and less diffuse than those found in chronic affections; and the relations of cause and effect can, in consequence, be more accurately distinguished. During the last few years we have been engaged in the examination of the heart in such cases, and now report the results in five instances.

Heart-Block.

CASE 1.—The patient, a girl aged 10, was admitted into Ruchill Fever Hospital on Feb. 5th, 1910, suffering from diphtheria of five days' duration. Her previous health had not been good, but no details could be obtained. She had had attacks of measles, whooping-cough, and chicken-pox.

FIG. 1.



CASE 1.—Complete heart-block. Auricular rate about 110, ventricular rate about 46.

The girl's illness had commenced on Feb. 1st, the initial symptoms being headache, vomiting, and sore-throat. On admission she was found to be a poorly nourished and neglected child. The throat and pharynx were congested, the right tonsil was slightly ulcerated, and there was a considerable amount of loose membrane on the back of the throat. The toxæmia was severe, but the viscera seemed normal, and the urine did not contain albumin. Fever was slight, 99·2°F.

For the next two days the child's progress seemed satisfactory, and she was bright and cheery; but on the 9th she became dull and listless, and vomiting ensued; symptoms of palatal palsy made their appearance, and the heart dilated. On the 10th the vomiting persisted, and the child was restless and irritable. The weakness increased, and she died in the evening from cardiac failure.

The heart on admission seemed normal, but evidence of dilatation was manifest on Feb. 9th. There was widespread pulsation over the præcordium and very frequent and obvious pulsation in the neck above the clavicles. The first sound was somewhat short and muffled, and the second was occasionally reduplicated. No sounds corresponding to the auricular contractions could be heard. The pulse-rate during her residence was generally infrequent and varied greatly at different times. On admission it numbered 96; on the 6th 62; on the 7th it varied between 88 and 40; on the 8th between 80 and 52; on the 9th between 72 and 48; and on the day of death between 62 and 40.

Tracings were obtained on the three days immediately preceding death, and all showed complete heart-block, the auricular contractions numbering 100–110, and the ventricular 46–54 per minute. (Fig. 1.)

Necropsy.—The heart alone was examined post mortem. It was distinctly dilated and the muscle was rather pale. The cusps of the valves were healthy, but the auriculo-ventricular valves were slightly dilated.

Microscopic examination of the *a.-v.* node and bundle [13] showed that the node and the upper part of the bundle were involved in a well-marked acute inflammatory process (Figs. 7 and 8). The capillaries were notably congested and many cellular collections were present. The cells were chiefly mononuclear, and mainly lymphocytes, but a fair number of polymorphonuclear cells were also found. The bundle was diffusely infiltrated in many places, and its fibres distinctly separated from each other; and at one place about its middle considerably damaged by a larger nodule. The lower part of the bundle and its branches seemed normal.

The cardiac muscle generally showed evidence of interstitial inflammation, both focal and diffuse.

The vagus nerves were examined by Donnaggio's second method for early degenerative changes, but were found to be normal.

CASE 2.—The patient, a man aged 26 years, was admitted into hospital on June 5th, 1909, complaining of weakness and of breathlessness on exertion of some months' duration.

The patient's health had been good save for occasional "growing pains" and an attack of tonsillitis in boyhood, and gonorrhœa in the early part of 1903, until an attack of enteric fever later in the same ear, for which he was in hospital in Japan for about three months. He never regained his former health, and his feet were often swollen at night, but he was able to work until July 1908, when he was thrown out of employment by the failure of his firm. He stayed at home in fairly comfortable circumstances until he procured a new situation on Feb. 19th, 1909. In the early part of February he had caught cold and he was feeling "run down" when he commenced his new work. This entailed a daily walk of four miles, and he felt exhausted at night, and also during the day when walking uphill; but though he steadily became weaker he continued at his post until six weeks before admission, when he was compelled to go to bed. His cough, accompanied by a slight mucoid spit, persisted from February until May. He had frequent attacks of shivering at night after getting home; they were fairly severe, and lasted for 15 to 20 minutes, and he felt hot after he got into bed, and often sweated profusely in the early morning. About a fortnight before admission his right forearm and elbow became sore to the touch and on movement, and this continued for a few days Four days before admission the left hip and ankle became painful, and this still persisted.

On admission the patient was found to be a thin, pale, badly nourished man, with flabby muscles and little subcutaneous fat. The left hip and ankle were painful and tender, and there was a small tender area of induration on the back of the left forearm. The right calf was, he said, painful, but nothing abnormal could be detected. There were several minute ecchymoses on the conjunctival surface of the right lower eyelid, and a fairly large one on the conjunctiva of the left bulb, while ophthalmoscopic examination revealed a medium-sized flame-shaped hæmorrhage on the course of the left superior temporal vein. The lungs were normal, the tongue was clean, and digestion good; the liver and spleen were slightly enlarged; the urine contained a small amount of albumin. The heart was but little enlarged, though there was a well-marked mitral systolic murmur. The pulse was frequent, regular, small, and soft; and he was slightly fevered at night.

Progress after admission was slowly but continuously in the wrong direction. Many embolisms occurred, chiefly in the limbs, but once, at any rate, in the spleen and twice in the kidneys. He had several "faint turns" of a few minutes' duration without obvious cause. The weakness increased, and after the middle of July œdema was more or less continually present in the legs. There were occasional rigors and

[13] The *a.-v.* node and bundle in these cases were examined in serial sections, *every section* through which the *a.-v.* node and bundle passed being examined.

generally profuse sweats at night. On August 25th a left hemiplegia occurred, and he died on August 29th.

The pulse during the patient's residence in hospital was always regular until immediately before death; and the venous curves were normal, save that the *a.-c.* interval was invariably prolonged, measuring about 0·25 sec. and never touching 0·2 sec. or 0·3 sec.

Necropsy.—Post-mortem examination revealed an acute endocarditis of the mitral valve. Two emboli were present in the right middle cerebral arteries, and septic infarctions were present in the left kidney and the spleen; from the latter the pneumococcus and B. coli communis were isolated in culture. Blood cultures during life had proved sterile.

The mitral valve was dilated. Numerous vegetations were present on the cusps, some small and wart-like, others long and luxuriant. The endocardium of the left auricle was thick and opaque, and a few minute granulations were present on the contra-fossal wall immediately above the valve; the endocardium at this point was notably thickened. There was no evidence of mural implication elsewhere.

Microscopic examination of the *a.-v.* node and bundle revealed well-marked congestion. The node was otherwise normal, though two small foci of round cells were found in the auricular muscle in its immediate vicinity. The bundle was involved in three separate places by foci of the same kind. The first was of small size and was situated immediately below the node; the second, which was considerably larger, was found a little lower down, between the auricular muscle and the bundle, and implicated both; the third, of fair size, occupied the central part of the bundle, and occurred immediately above the point where it passed through the central fibrous body. The cells were all mononuclear and chiefly lymphocytes. The fibres of the *a.-v.* bundle seemed normal, save in the immediate vicinity of the two larger foci, where they were evidently degenerate. The fibrous tissue of the bundle was not excessive in amount. The cardiac muscle generally showed evidence of interstitial myocarditis in an early stage, and the muscle fibres in some of the patches were degenerate.

The majority of the cases of heart-block which have been recorded have been associated with chronic lesions of the *a.-v.* bundle, the most common cause being fibrosis with or without calcification (Lewis[14]). In 1905, however, James Mackenzie[15] reported the transient occurrence of the milder grades of block in cases of acute rheumatism and influenza; and in 1908 several cases were reported in which full heart-block was found to be due to acute lesions. In one (Jellinek and Cooper[16]) where death resulted from acute gonorrhœal endocarditis, there was an acute necrosis of the interventricular septum; in a second case (James[17]), there were ulcerative endocarditis and an ulcer of the interventricular septum immediately beneath and posterior to the membranous septum; in a third (Gerhardt[18]) the patient suffered from rheumatic fever, followed quickly by enteric fever; inflammatory lesions were found in the *a.-v.* bundle. More recently Magnus Alsleben[19] has reported a case of diphtheria where full heart-block was due to a severe parenchymatous degeneration of the *a.-v.* bundle.

[14] The Mechanism of the Heart Beat, London, 1911.
[15] Brit. Med. Jour., 1905, vol. i.
[16] Ibid., 1908, vol. i., p. 796.
[17] American Journal of Medical Sciences, 1908, vol. cxxxvi., p. 469.
[18] Deutsches Archiv für Klinische Medizin, 1908, vol. xciii., p. 485.
[19] Zeitschrift für Klinische Medizin, 1910, vol. lxix., p. 82.

A partial or full heart-block is by no means of rare occurrence in acute disease. Rihl[20] has reported a case in which full heart-block seemed to have followed an attack of acute rheumatism. Griffith[21] has twice observed heart-block in gonococcic infections; Wenckebach[22] has seen it in influenza; Hay[23] has found it in diphtheria and in a gonococcic infection; and Magnus Alsleben[24] in pneumonia and enteric fever. Transient defects are not uncommon in acute rheumatic endocarditis, and we have now observed at least five examples. In one the defect persisted for nearly four weeks; in another it disappeared after six days, recurred three days later, and again lasted for six days. In none of these cases was there complete heart-block, but in one the ventricles only responded to every second auricular contraction. All the cases made good recoveries, and in one alone was the ultimate valvular lesion severe. We have observed three other cases in which a transient defect occurred. One was a case of enteric fever, another of diphtheria, the third of scarlatina. In none was there any evidence of endocarditis, and in all recovery was good.

Defects in conductivity can only be recognised by means of graphic methods, though they are, of course, suggested by extreme slowness or irregularity of the pulse. In one of our cases, however, the auscultatory phenomena were striking. A systolic murmur was audible at the apex. The ventricular contractions were infrequent and irregular, but occasionally two or three beats occurred in more rapid succession. With the isolated contractions the mitral murmur was long and loud, but when a series of frequent contractions obtained the murmur accompanying the second and third beats was much shorter and less distinct. The explanation was obvious on examination of the jugulo-carotid curves. (Fig. 2.) Conductivity was defective, but after the long pauses was sufficiently good to permit the completion of the ventricular contraction before the commencement of the succeeding auricular contraction; but, when the pause was short, became so defective and prolonged that the ventricular contraction coincided with the succeeding auricular contraction. The regurgitation into the auricle was in consequence minimal, and the murmur became shorter and less distinct.

The causes of heart-block are numerous and not necessarily associated with lesions of the *a.-v.* tissues, as it has been produced experimentally by the administration of various drugs (digitalis, aconitine, adrenalin, muscarin physostigmine), by the induction of asphyxia, and by vagus stimulation. It thus seems probable that nervous and toxic influences may produce heart-block in man without there

[20] Zeitschrift für Experimentelle Pathologie und Therapie, Berlin, 1905, vol. ii., p. 83.

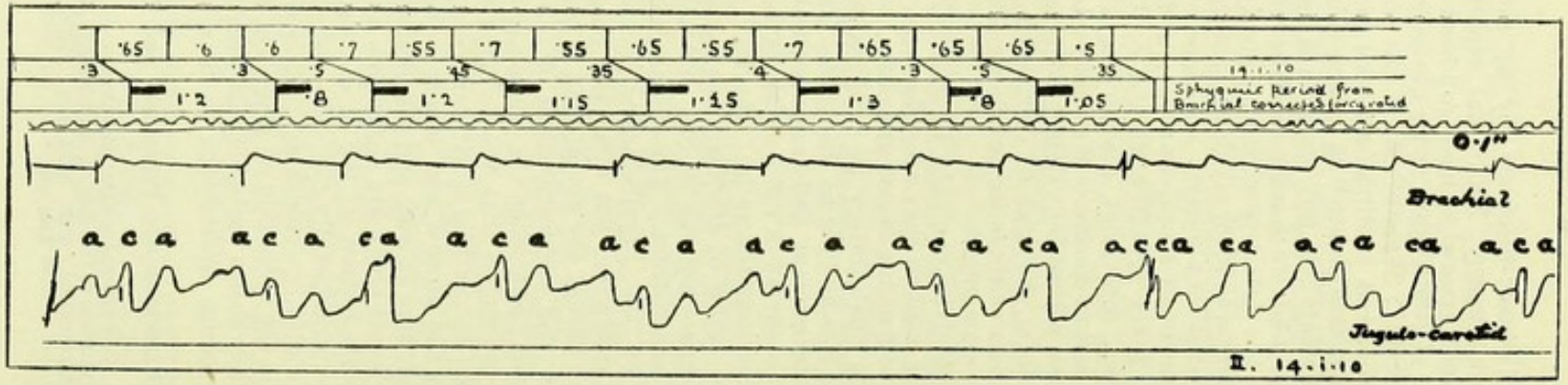
[21] Personal communication.

[22] Arrhythmia of the Heart, Edinburgh, 1904.

[23] Personal communication: Brit. Med. Jour., 1910, vol. i., p. 20.

[24] Loc. cit.

FIG. 2.



Partial heart block. The ventricular contractions (1–2) are completed before the succeeding auricular contractions (2–4) occur. Conduction is, however, so defective after the fourth auricular contraction that the third ventricular contraction is not completed before the fifth auricular contraction ensues.

being any lesion in the *a.-v.* tissues, but so far only one case has been recorded (Holst and Monrad-Krohn) with full post-mortem examination and graphic records in which the nervous origin seems definitely proved. In Case 1 of our series the presence of palatal palsy seems to point to a nervous origin of the block, but the post-mortem examination showed that the vagus nerves were normal. In our second diphtheritic case there was no evidence of any paralysis.

Nodal Rhythm.

Case 3.—The patient, a man, aged 24, was admitted into hospital on July 15th, 1909. His previous health had been good, save for attacks of measles and enteric fever in childhood; but he was often troubled with gumboils, and was frequently wetted at his work.

The patient's present illness dated from July 1st, when he had had one of his molars extracted on account of a gumboil from which he had suffered for a day or two. In the evening he felt sick and shivery, and probably was fevered. These symptoms continued, and on the afternoon of July 4th he had a definite rigor. On the 7th he felt better, and on the 8th he went to Ardrossan, walking from the station to the house at which he stayed (two miles). After this he improved until the 12th, though he had a slight cough after the 6th, with discomfort in the left chest. But on the 12th he had to go to bed as the pain in the side became worse and was much intensified on coughing. The left arm, too, was stiff, and he was very breathless and had to sit up in bed at night. On the evening of the 13th he was better, and able to sleep quietly lying down.

On July 14th the man felt so well that he dressed and went downstairs to breakfast, which he did without any difficulty or assistance; after breakfast he sat down on a chair, and on attempting to rise an hour later found that his legs were powerless and "had no feeling" in them. He had to be carried back to bed.

On admission the patient was found to be notably emaciated, with small muscles and scanty subcutaneous fat. His complexion was somewhat sallow and his expression anxious, while he had to be propped up in bed on account of breathlessness. The skin was hot and dry and there was a little œdema of the feet and slight pitting with the stethoscope on auscultation over the cardiac area. He was slightly fevered at night. The patient, though weak, was quite clear mentally, spoke correctly, and answered questions accurately and sharply. He had little power in his legs, but was able to pull up both knees, though he was unable to move the toes of the right foot. The movements were more free on the left side. There was considerable anæsthesia in both legs. Power was perhaps deficient to some slight extent in the left arm, but in the right was good; and sensation seemed normal. The right pupil was slightly smaller than the left; both reacted to light and on accommodation.

The tongue was dry and coated, many of the teeth were absent, and most of the remainder were carious, and the mouth generally was very foul. The pulse was soft, regular, and infrequent. Palpation of the apex beat, which was full and widespread, showed that every other beat was missed at the radial, the cardiac action being regularly coupled. A systolic murmur was audible all over the cardiac area. It was heard best at the apex, where it was long and soft, replacing and running out of the first sound; the second sound was not audible here. The respirations were difficult and cyclic, but without any full apnœa. A consolidation was found in the upper part of the right chest and in the left lower axilla friction sounds were audible. The urine contained a trace of albumin.

For a few days the patient's general condition improved slightly. The coupled rhythm ceased on the 16th, and he rested fairly well at night. On the 17th movement was more free in the left leg, but the palsy below the right knee persisted. About midnight on the 18th he was

noticed to be restless and was found to be semi-conscious and unable to say more than "yes," and there was a well-marked full right hemiplegia. He gradually became weaker and more comatose, and he died with cardiac failure on July 27th, 1909.

The pulse remained "single" until the day of death, when it was noticed to be "coupled" again for a short time. The tracings, which were obtained in this case during the coupled rhythm showed that there was a slight increase of the *a.-c.* interval (0·25 sec.) with the first or larger beat of the couple, and that the second or smaller beat was a ventricular extra-systole which did not interfere with the auricular rhythm. Tracings of the "single" pulse obtained on July 23rd showed a regular pulse and a very short *a.-c.* interval measuring little more than 0·05 sec.

Necropsy.—Post-mortem examination revealed an acute ulcerative endocarditis of the mitral valve, engrafted on a lesion of older standing. The upper and middle lobes of the right lung were solid from a somewhat chronic pneumonia, and there were numerous infarcts in the spleen and kidneys. The left middle cerebral artery was occluded by a large pale embolus which resembled the vegetations on the mitral valve, and was associated with a very extensive softening. Streptococci were isolated on culture from the spleen. No blood cultures were made during life.

The mitral valve was stenosed, the cusps being notably shortened, the chordæ tendineæ short and thick, and the tips of the papillary muscles fibrous. There was well-marked evidence of fibrosis spreading upwards from the bases of the cusps in the direction of the central fibrous body of the heart. Enormous soft recent vegetations almost occluded the valve, and there were in addition extensive ulceration and perforation of the anterior mitral cusp. There was no evidence of any acute mural endocarditis; but the endocardium of the left auricle was thick and opaque, with a special area of thickening about as large as a shilling on the contra-fossal wall just above the valve.

Microscopic examination of the *a.-v.* tissues revealed considerable congestion of the tissues generally. The node was the site of a profound inflammatory disturbance, many focal collections of round cells being present, as well as, in places, a diffuse infiltration. (Fig. 9.) The fibres of the *a.-v.* node were probably normal, and there was no evidence of old-standing fibrosis. The walls of a microscopic artery were infiltrated with round cells, though the lumen was patent; the other vessels seemed normal. The intensity of the lesions varied at different levels, but the whole of the node was more or less affected. The bundle, on the other hand, was not implicated, save at one place immediately below the node, where one or two small foci in the auricular muscle immediately adjoining it passed in for a short distance between a few of its fibres.

There was a well-marked myocarditis, involving both ventricle and auricle, but it was only extreme at the base of the mitral valve, and in the auricular sections immediately above the node itself.

Case 4.—The patient, a man, aged 42, was admitted to hospital on Jan. 31st, 1911, complaining of breathlessness and of swelling of the feet and legs of two or three months' duration.

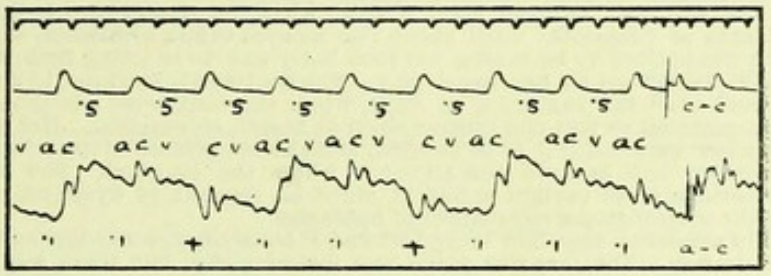
He had always enjoyed good health prior to the onset of his present illness, save for pneumonia at the age of 30, and attacks of measles in childhood and at the age of 32. He had habitually used tobacco and alcohol to excess.

In the preceding April he had caught cold and had never been well since. The cough and spit persisted and he lost appetite and felt weak and unable to do his work. In July he noticed that his feet were sometimes swollen at night, and he began to be very breathless on exertion. In August the œdema became permanent and, steadily increasing in amount, soon compelled him to remain in bed In December he one day suddenly felt severe pain in his right side and spat blood in considerable quantities for some weeks. He had to be propped up in bed on account of breathlessness, the spit and the œdema steadily increased in amount, and his general strength rapidly failed. In January he attempted a short walk, but fell down in a faint on the pavement.

On admission the patient was extremely ill. He sat bolt upright in bed, coughing continually and spitting up large quantities of watery mucoid material. Œdema was universal and very marked in the legs and scrotum. Detailed examination was impossible, but evidence was found of a consolidation of the middle lobe of the right lung and of pleurisy on the same side. The heart was enlarged and double aortic murmurs were audible down the sternum. Progress was continually in the wrong direction. The hæmoptysis recurred, the dyspnœa and œdema increased, exhaustion became more and more extreme, and he died suddenly on Feb. 5th.

The respiratory difficulty prevented continuous observation of the cardiac irregularities. The pulse on admission was notably irregular in rhythm from the frequent occurrence of extra-systoles, but a series of 20 or 30 fairly regular beats of slow rate occasionally obtained. The extra-systoles were sometimes isolated and sometimes in salvoes of 2, 3, or 4. On Feb. 1st the same state continued. On the 2nd the pulse was very irregular and very mobile, a bout of coughing quickening the rate from about 90 to about 120–130, the frequent rate persisting for a minute or two after the cough ceased. On the 3rd the irregularity was more marked, but on the 4th had disappeared, the pulse being quite regular with a rate of 110–120; alternation was distinct. It remained regular until death.

FIG. 3.



CASE 4.—The pulse is regular and the *a.-c.* interval regularly measures 0·10 sec. Respiratory movements deform the jugulo-carotid curve in places (+ +). T.= 0·2 sec.

Jugulo-carotid curves were only obtained on Feb. 2nd and 4th, and are somewhat deformed by the respiratory movements Tracings on the 2nd show the irregularity of the pulse, and the jugulo-carotid curve demonstrates that while the *a.-c.* interval in the case of the large beats is of normal length, it is much shorter with the extra-systoles, varying between 0·10 sec. and 0·15 sec. On the 4th, when the rhythm was regular but more frequent, the *a.-c.* interval is always short, and measures 0·10 sec. (Fig. 3). The tracings thus seem to show that on the 2nd extra-systoles were arising frequently in the vicinity of the node, the sinus rhythm, however, on the whole predominating; while on the 4th the pacemaker had changed, the sinus influence had been lost, and *every* contraction originated in the auriculo-ventricular node.

Necropsy.—On post-mortem examination the heart was found to be greatly enlarged, weighing 25½ ounces. The aortic valve was incompetent, the septal cusp having a fairly large perforation with well-defined margins a little below its free border. All the cusps showed some small recent warty vegetations, but were not thickened. The other valves were not affected, but the auriculo-ventricular valves were dilated. Two patches of superficial mural fibrosis were present in the left ventricle. One, which was small, was situated near the apex. The other, which measured about ½ in. in diameter, was situated on the interventricular septum underneath the anterior mitral cusp, its

anterior border being fully ½ in. behind the posterior border of the pars membranacea. The coronary arteries and the aorta were but little abnormal.

A small abscess was found in the lower lobe of the right lung as well as a large infarction; both pleuræ were adherent. The liver was adherent to the diaphragm, and there was a well-marked perisplenitis. The kidneys showed slight evidences of arterio-sclerotic fibrosis and one or two small infarcts.

Microscopic examination showed that the *a.-v.* node was involved in an acute inflammatory process. Many focal cellular collections were present and some small diffuse infiltrations, the fibres in their vicinity showing granular degeneration. The reaction was best marked in the upper portion of the node and in the part which was nearest to the base of the mitral valve. The cells were chiefly mononuclear and mainly lymphocytes, with only an occasional polymorphonuclear leucocyte. The *a.-v.* bundle was not definitely affected, but was slightly implicated by a nodule in the cardiac muscle immediately beneath and posterior to it. The fibrous tissue around the bundle appeared excessive in amount and showed traces of calcification.

The cardiac muscle generally showed evidences of cloudy swelling and a few nodules, which were most numerous at the base of the mitral valve and in the auricular muscle just above the node.

CASE 5.—The patient, a girl, aged 10, was admitted to hospital on June 10th, 1911, complaining of shortness of breath and of swelling of the feet of a week's duration.

The girl had enjoyed good health, with the exception of three attacks of "measles," until about two months before admission, when she was noticed to be taking her food badly and to be losing flesh, and to be disinclined for her usual play. She continued, however, to go to school until the beginning of June, when she contracted a cough unaccompanied by spit and became short of breath on exertion. Her face and feet were noticed to be swollen, and she complained of pain in the abdomen and beneath the sternum when she coughed. She had sometimes to sit upright in bed at night on account of dyspnœa, and in the mornings she complained of headache.

On admission the child looked ill and exhausted, and was inclined to be drowsy. The face was pallid and looked puffy, but there was no œdema. The tongue was thickly coated and the tonsils were slightly enlarged. Both hearts were enlarged, and there was pulsation in the second, third, fourth, fifth, and sixth interspaces, the apical impulse in the fifth space being diffuse. A long soft blowing murmur was audible at the apex, partly replacing and following the first sound, while the second sound was "doubled." Over the xiphoid the systolic murmur was loud and harsh and resembled a friction sound.

During the next fortnight the patient's general condition improved slightly, but she still looked ill and exhausted, and complained at times of substernal pain. An urticarial rash appeared upon the 24th and persisted for a few days. On the 29th pericardial friction was well marked and a small pleural effusion was discovered at the base of the left lung. In the beginning of July the symptoms became more serious, and she grew steadily weaker and sometimes sweated profusely at night. A crop of minute subcutaneous nodules developed on the backs of the hands and persisted for a few days. On the 14th vomiting set in and continued severely for the next three days. Exhaustion became more extreme, and she died on July 22nd.

The nature of the infection was obscure. There was no history of arthritis, and the joints were never swollen or painful during her residence, and the tonsils, though large, were not acutely inflamed. She was habitually slightly fevered at night, but the temperature only once rose above 101° F., and was more usually under 100°. The leucocyte counts varied between 8000 and 23,000. No other foci of infection were discovered, and the symptoms seemed to point to a rheumatic infection of the heart without arthritis.

The pulse on admission was regular, small, and extremely soft. At first the rate was 100–110, but it steadily increased, and for the last two weeks of her illness never ran below 120, though it only numbered 140 on two occasions. Tracings were obtained on several occasions and were regular and normal until July 3rd, when a ventricular extra-systole was

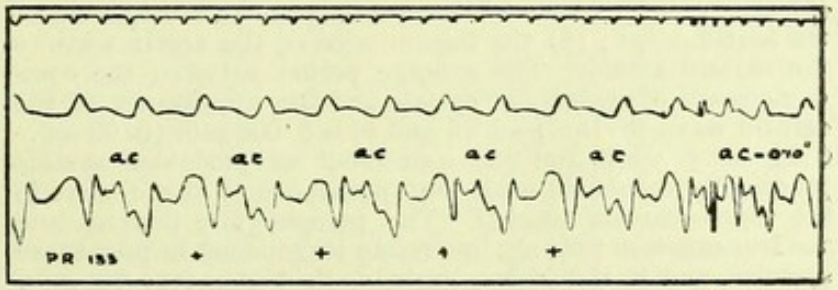
recorded. During the succeeding days the pulse was often slightly irregular from extra-systoles, but no satisfactory curves were obtained until July 17th (Fig. 4). The respiratory movements were frequent and deformed (+) every alternate pulse beat, but *a.-c.-v.* are distinct in the intervening contractions, and the *a.-c.* interval regularly measures 0·10 sec. A tracing on July 22nd again shows a regular pulse with an *a.-c.* interval of the same length.

Necropsy.—Post-mortem examination revealed a well-marked subacute pericarditis, the two layers of the pericardium being closely adherent to each other by fibrinous adhesions over the front of the heart, but only slightly over the posterior surface. The parietal pericardium was adherent in several places to the chest wall. The heart generally was enlarged. The mitral and tricuspid valves were both dilated and showed rows of recent pearly vegetations upon their auricular surfaces.

One or two caseous glands were found at the root of the right lung. Both pleuræ showed evidences of subacute pleurisy.

Microscopic examination showed a well-marked interstitial myocarditis. The nodules varied somewhat in their character. The majority were composed of mononuclear cells with a few polymorphonuclear leucocytes; others were of the "rheumatic" type, consisting chiefly of multinucleated giant cells with only an occasional lymphocyte; and a few were "mixed" with a few giant cells, many lymphocytes and an occasional polymorphonuclear leucocyte. The muscle cells in the vicinity were evidently degenerate.

FIG. 4.



CASE 5.—The pulse is regular and the *a.-c.* interval regularly measures 0·10 sec. Respiratory movements deform the jugulo-carotid curve in places (+ +). T. = 0·2 sec.

The lesions were most extreme in the neighbourhood of the mitral and tricuspid valves. The *a.-v.* bundle was involved in a large focus which, occurring near the tricuspid valve, infiltrated the bundle for a short distance. The *a.-v.* node was notably affected; none of the infiltrating cells, however, were multinucleated. The capillaries were extremely congested, and the lymphatic vessels could be seen plugged with solid masses of lymphocytes. (Fig. 10.) The principal vein of the node showed an acute phlebitis and periphlebitis. (Fig. 11.) The majority of the cells in the wall of the vein were lymphocytes, but a considerable number of polymorphonuclear cells were also present, and at one place a group of giant cells. Around the vein the polymorphonuclear cells were almost as numerous as the lymphocytes, and infiltrated the auricular muscle immediately above it. The greater part of the phlebitis was above the node. Just before the vein left the node it was joined by a moderately large branch, and the vein above the junction was thrombosed, the thrombus consisting of a fibrinous matrix with numerous red cells and abundant polymorphonuclear leucocytes. (Fig. 12.) The thrombus was attached to the side of the vein, but did not completely occlude it, and could be traced through several sections.

In 1907 James Mackenzie[25] suggested that extra-systoles might arise in the *a.-v.* node (nodal extra-systoles). In certain extra-systoles the tracings show that the auricle contracts at a time when the ventricle is already in contraction and the auriculo-ventricular valves are shut. In the majority of these cases careful measurement demonstrates that the auricular rhythm is unchanged and that the coincident contraction of auricle and ventricle is due to a ventricular extra-systole occurring immediately before the regular sinus contraction of the auricle. In some cases, however, both the auricular and ventricular contractions are premature (Fig. 5), and, as in auricular extra-systoles, the prematurity of the contraction entails defective conduction, the extra-systole cannot originate in the auricle, and both auricle and ventricle must respond to a common stimulus arising between them. It seems probable that Mackenzie's theory should be slightly amplified.

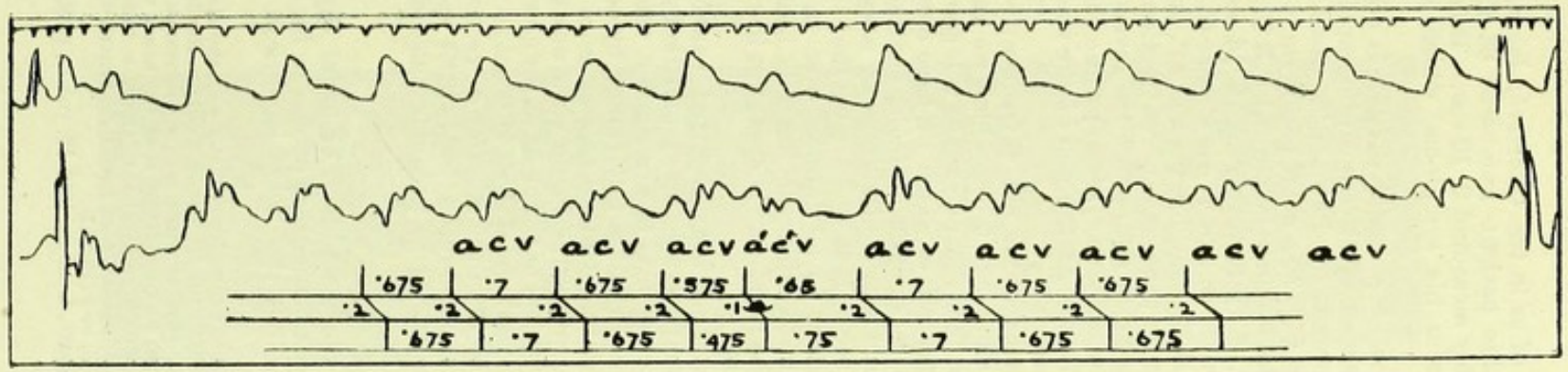
The *a.-c.* interval in jugulo-carotid tracings measures in the normal individual about 0·20 sec., being slightly shorter if the pulse-rate is frequent. During the *a.-c.* interval five events occur: (1) the auricular systole which lasts for about 0·10 sec.; (2) the passage of the stimulus from auricle to ventricle; (3) the latent period of ventricular contraction; (4) the period of ventricular systole prior to the opening of the aortic cusps; (5) the transmission of the aortic wave to the carotid artery. The average period between the commencement of ventricular systole and the appearance of the carotid wave in the neck (4 and 5) is 0·066 sec. (0·03 sec.–0.11 sec.), while the commencement of auricular systole practically coincides with the appearance of the *a* wave in the jugulo-carotid tracing. The presphygmic interval and the transmission time are invariably lengthened in premature systoles, and it thus seems probable that whenever the *a.-c.* interval in the jugulo-carotid curve measures less than 0·10 sec. the auricle and ventricle respond to a common stimulus which arises between them.

In Cases 3, 4, and 5 the *a.-c.* interval is short. In Case 3 it measures 0·06 sec.; in Case 4, 0·10 sec.; in Case 5, 0·10 sec. The rhythm of the heart in these cases is almost absolutely regular, and regular action of the heart probably denotes a common site of origin for all the contractions; so the conclusion is reached that the heart in these cases was responding to stimuli which arose regularly in an abnormal site, between the auricle and the ventricle (nodal rhythm). In Case 4 the earlier tracings make the conclusion even more certain, for they show that at one time extra-systoles were arising in the vicinity of the node, though the majority of the beats were in response to sinus stimuli.

We have been unable to find any tracings of a similar kind in the literature, with the exception of a case (Case 10)

[25] Quarterly Journal of Medicine, 1907, vol. i., p, 131.

FIG. 5.



Nodal extra-systole. a′ and c are both premature and the a'-c' interval is short. The succeeding auricular contraction is also slightly premature.

recorded by one of us in the *Quarterly Journal of Medicine*.[26] The pulse in this patient numbered 66-80, and the *a.-c.* interval invariably measured 0·10 sec. This patient made a fair recovery from his symptoms, which were chronic in character.

This conception of a nodal rhythm is confirmed, if not proved, by the series of electro-cardiographic curves which have been recorded by Lewis[27] in cases of paroxysmal tachycardia. In Fig. 26 a short paroxysm is shown. In the earlier part of the tracing the normal P.R.T. waves are well marked, the P.-R. interval being 0·14 sec. During the paroxysm the waves R. and T. are similar to those occurring during the normal rhythm, but the wave P. is *inverted*, which strongly suggests that the wave of contraction in the auricular muscle has travelled in a direction the reverse of the normal —i.e , from below upwards (Lewis) ; while the P.-R. interval is now only 0·08 sec. At the end of the tracing the normal rhythm is resumed.

Paroxysmal tachycardia not infrequently shows jugulo-carotid tracings similar to those which we have described in Cases 3, 4, and 5, but the pulse-rate is much more frequent, numbering in three curves which we have obtained, 160, 182, and 214. In all these cases auricular contractions regularly preceded the ventricular contractions by a period which did not exceed 0·10 sec. It is well known that the *a.-c.* interval varies to some extent in its duration even in the same individual, and is shorter when the heart is beating frequently than it is when the pulse-rate is slow, but in normal rhythms P. is never inverted.

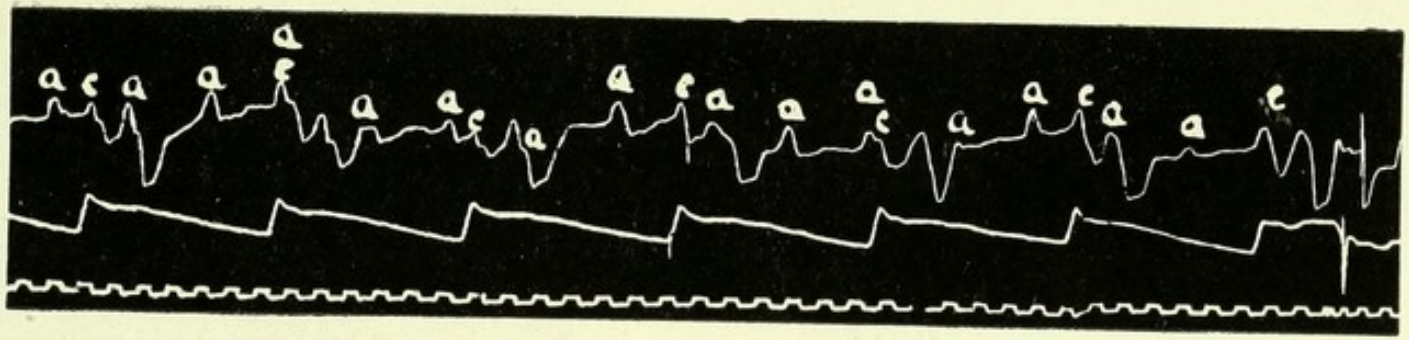
The cases which we have reported cannot, however, be regarded as examples of paroxysmal tachycardia. In all three the sequence of events was similar, the tracings showing at first a normal rhythm interrupted by occasional extra-systoles, and preceding death a *regular* more frequent action with a short *a.-c.* interval. In no case was the tachycardia excessive or paroxysmal or the onset of the new rhythm abrupt. It seems probable that nodal rhythm is not so uncommon as it would appear to be from the scarcity of records, for an ante-mortem rise in the pulse-rate attracts little special attention, though an infrequent or an irregular pulse does not escape investigation.

The inception of heart-block or nodal rhythm may conceivably be the proximate cause of death, for the mechanical difficulty under which the heart labours in these rhythms

[26] Cowan and Ritchie : Coupled Rhythms of the Heart, 1910, vol. iv., p. 55. Belski (Zeitschrift für Klinische Medizin, Berlin, 1909, vol. lxvii., p. 515) has reported several cases (acute rheumatism, scarlet fever, enteric fever) in which he considered that the heart was contracting in response to stimuli which originated in the *a.-v.* tissues. His tracings show a rhythmical appearance of nodal or ventricular extra-systoles, often in groups of 2, 3, or 4 (Belski).

[27] Heart, London, 1909-10, vol. i., p. 306

FIG. 6.

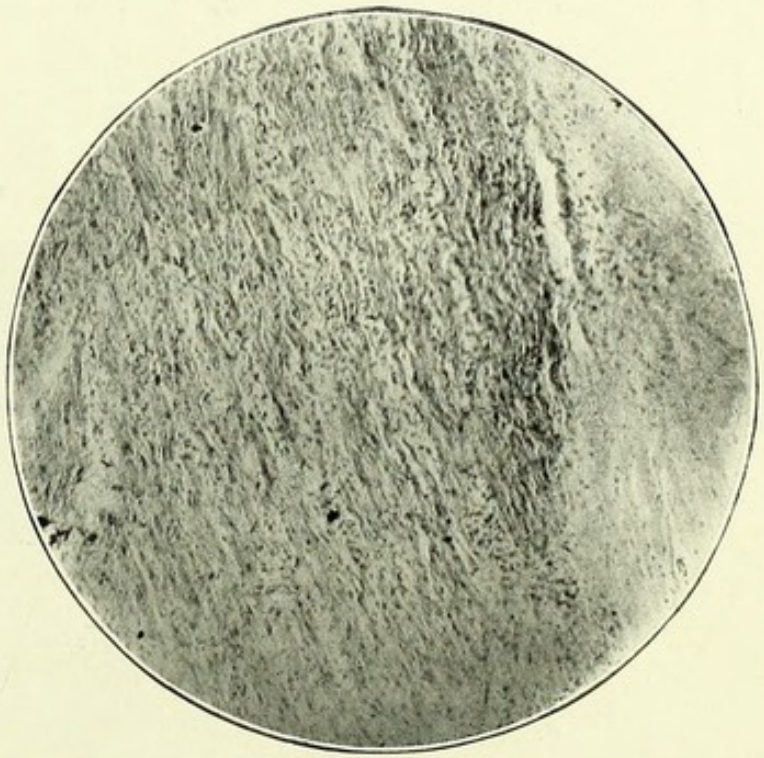


(Reproduced from *Heart*, a facsimile of the drum tracing shown in Fig. 1 on a small scale.)

FIG. 7.

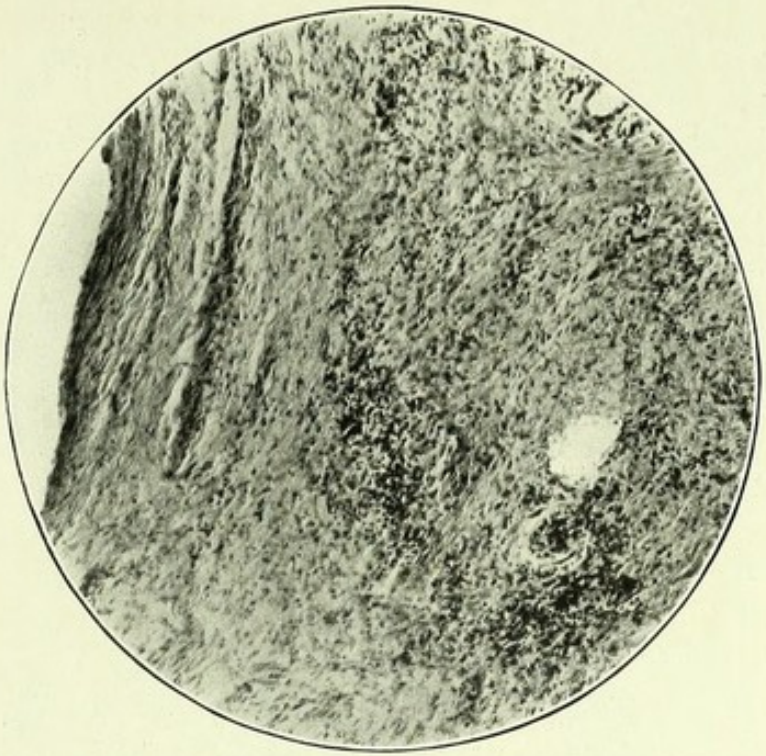
Showing a focal inflammatory lesion in the *a.-v.* bundle. (From Case 1.) (N.B.—Figs. 7 to 12 are × 90.)

FIG. 8.



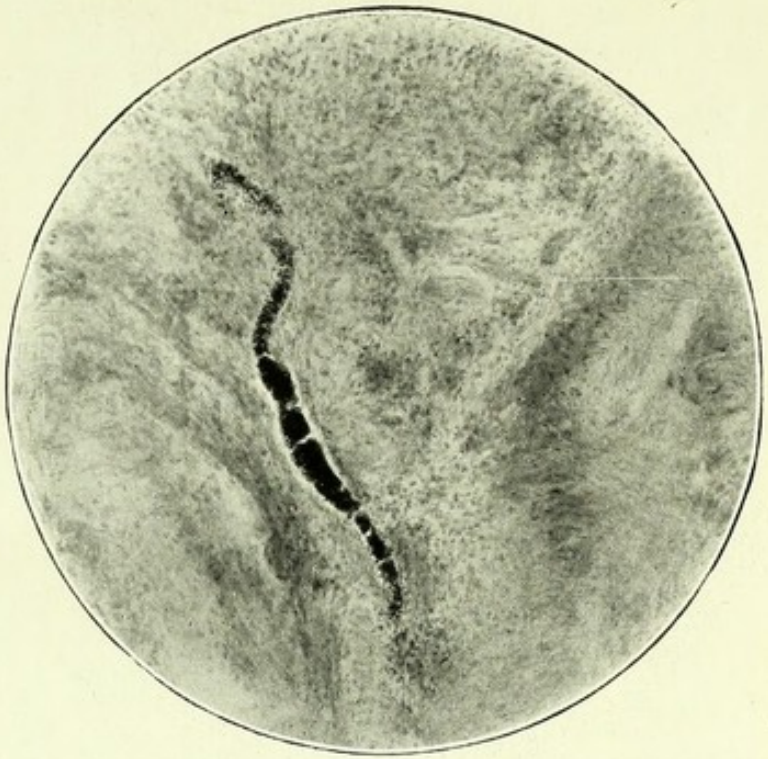
Showing a diffuse inflammatory infiltration in the *a.-v.* bundle. The fibres of the bundle are widely separated by cells infiltrating between them. (From Case 1.)

FIG. 9.



Showing diffuse inflammatory lesions in the *a.-v.* node. A small arteriole is seen cut obliquely and its walls are infiltrated with cells. (From Case 3.)

FIG. 10.



Showing a lymphatic vessel filled with a solid plug of lymphocytes, situated in the upper part of the *a.-v.* node. (From Case 5.)

Fig. 11.

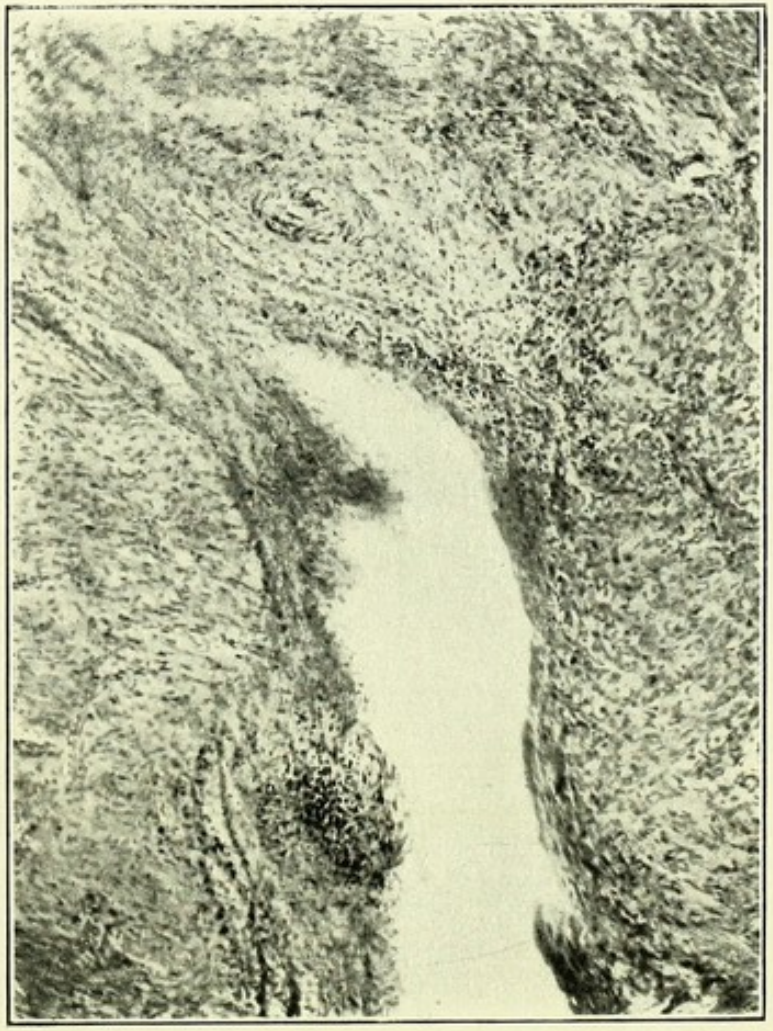
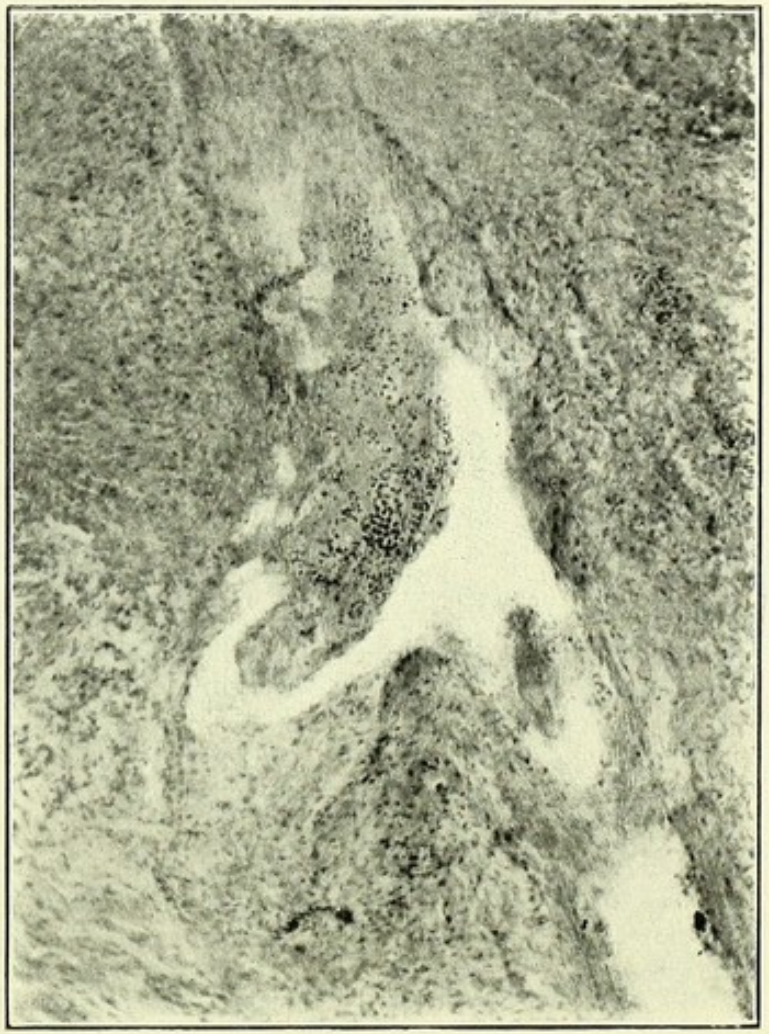


Fig. 12.



must be very considerable, the synchronous contraction of auricles and ventricles throwing the auricular blood backwards into the veins, and lessening in considerable degree the ventricular content and output. The blood pressure in these cases is in consequence always low and the pulse is always small. The serious import of paroxysmal tachycardia is now thoroughly recognised, for the continuance of a paroxysm for more than a few hours is known to lead rapidly to dilatation of the heart, a result which will ensue the more readily in cases where the valves are acutely inflamed and the cardiac muscle degenerate and weak.

Summary.—In a case of diphtheria, with full heart-block, the *a.-v.* bundle and node were found to be involved in an acute inflammatory process, and similar lesions were present in the *a.-v.* bundle in a case of malignant endocarditis in which conductivity was defective. In three cases of acute endocarditis, with nodal rhythm, the *a.-v.* node was acutely inflamed, the bundle being only and but slightly affected in one instance.

Glasgow.