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Aetiology of Chronic Heart Block

A Clinico-pathological Correlation in 65 Cases

ALAN HARRIS, MICHAEL DAVIES, DAVID REDWOOD, AUBREY LEATHAM, AND HAROLD SIDDONS

From the Cardiac Department, St. George's Hospital, London S.W.1

The cause of chronic heart block is often obscure on clinical grounds alone. Consequently there is considerable difficulty in deciding the prognosis of a patient with complete heart block even with successful artificial pacing. Coronary artery disease has been generally accepted in the past as the predominant cause of heart block, and Penton, Miller, and Levine (1956) estimated an incidence of 43 per cent, Wright *et al.* (1956) one of 69 per cent, and Friedberg, Donoso, and Stein (1964) one of 48 per cent. These estimates were based on clinical and electrocardiographic evidence. Other studies suggested that areas of fibrosis involving the conducting system, either alone or in association with scattered areas of fibrosis in the myocardium, were responsible for heart block (Lenègre and Moreau, 1963; Lev, 1964; Zoob and Smith, 1963). In one of our earlier patients, the only cardiac abnormality was fibrotic lesions confined to the conducting tissue, a surprising finding as severe coronary disease had been suspected, and this made us realize the importance of developing techniques for long-term artificial pacing (Portal *et al.*, 1962). With the continuing improvement of these techniques, the prognosis of a patient will become more dependent on the cause of the heart block. In an effort to improve the clinical diagnosis of the underlying cause of heart block, a retrospective survey was carried out in 65 consecutive patients with chronic heart block who had come to necropsy during the past 3 years.

Subjects and Methods

There were 65 patients, 25 female and 40 male, and their ages ranged from 10 to 82 years (mean 62·5 years). All the patients had been referred to the Pacing Unit at St. George's Hospital for consideration of long-term pacing for chronic heart block. Patients presenting with acute infarction complicated by block have been excluded.

Each patient had at the time of admission to hospital a full clinical assessment and chest *x*-rays together with electrocardiograms. In 61 patients medical treatment had failed, and long-term pacing was carried out by the endocardial technique (Furman and Robinson, 1958; Harris *et al.*, 1965a) in 50 patients, and by the epicardial technique (Siddons, 1963) in 10 patients. In the remaining 5 patients medical treatment alone was used.

The necropsy examination included a special study of the conducting tissue by serial sectioning at 6μ intervals, and multiple blocks were taken from all valves and chambers. The coronary arteries were studied by a simple injection technique and serial blocks which included the artery to the AV node. The same technique was used to examine 40 control subjects aged 50 to 104 years with normal electrocardiograms recorded during their last 3 months of life.

The clinical data have been analysed on the basis of the histological findings (Table I).

Results

Data relating to the investigations have been tabulated (Tables II–VI).

Group 1: Bilateral Bundle-branch Fibrosis. There were 26 patients in this group, 12 women and 14 men, and their ages ranged from 36 to 82 years (mean 70 years).

Recurrent syncope was the presenting symptom in 23 patients, left ventricular failure alone in 3 others. Five patients had a history of congestive cardiac failure in addition to syncopal attacks. The history of syncopal attacks ranged from 1 week to 10 years (mean 42 months) and the 3 patients with left ventricular failure had symptoms of up to 12 months' duration. In addition, 6 patients gave a history of angina of effort. Two patients had a history of diphtheria during childhood.

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TABLE I

HISTOLOGICAL FINDINGS, SEX, AND AGE ON REFERRAL IN 65 CONSECUTIVE PATIENTS WITH CHRONIC HEART BLOCK

	Men	Women	Age (yr.)	Total
Bilateral bundle-branch fibrosis	14	12	36–82 (mean 70)	26 (Group 1)
Cardiomyopathy	8	3	50–82 (mean 69)	11 (Group 2)
Coronary artery disease	7	3	56–80 (mean 69)	10 (Group 3)
Myocarditis	1	3	45–68 (mean 59)	4 (Group 4)
Calcification of valve or valve rings	2	2	68–76 (mean 71)	4 (Group 5)
Collagen disease	3	0	59–68 (mean 62)	3 (Group 6)
Amyloid deposits	2	0	68 and 84	2 (Group 7)
Transfusion siderosis	2	0	10 and 17	2 (Group 7)
Aneurysm of membranous septum	0	1	62	1 (Group 8)
Congenital heart block	0	1	54	1 (Group 8)
Syphilitic cardiovascular disease (gumma)	1	0	61	1 (Group 9)

The cardiothoracic ratio on the chest *x*-ray ranged from 48 to 80 per cent (mean 60%), and did not change with pacing. Six patients had pulmonary venous congestion.

All 26 patients had electrocardiograms showing abnormalities of conduction. The rhythm in 21 patients was complete heart block, with an atrial rate ranging from 70 to 100/min. (mean 83/min.) or atrial flutter (1 patient), and a ventricular rate ranging from 24 to 54/min. (mean 36/min.), and the QRS showed a right bundle-branch block pattern in the chest leads in 18, and left bundle-branch block in 5. In 2 patients the QRS periodically changed from right to left bundle-branch block. One patient with intermittent block and 2 with complete block showed a normal QRS. The dominant rhythm in 5 patients was sinus, 4 with periods of 2:1 block and the other with first degree block. The mean frontal axis was left in 13 patients, normal in 11, and right in 2 others. The rhythm underlying the syncopal attacks was asystole in all patients, and in one there were additional episodes of ventricular tachydysrhythmia.

Histological examination showed that all patients had normal AV nodes and main bundles. The fibrotic lesions involved the first part of the right and left bundles, and in some patients extended to the peripheral ramifications on each side (Fig. 1a and b). No patient had significant coronary disease or old myocardial infarct. Though the large and medium sized coronary arteries were normal, there was hyaline sclerosis of the smaller arterioles but to no greater extent than in the 40 elderly control subjects. The heart weights ranged from 360 to 600 g. (mean 480 g.).

Group 2: Cardiomyopathy. There were 11 patients in this group, 3 women and 8 men, and their ages ranged from 50 to 82 years (mean 69 years).

All patients had recurrent syncopal attacks and in addition 4 had cardiac failure. The history of syncopal attacks ranged from 1 day to 2 years (mean 6 months) and was less than 2 weeks in 5 of the 10 patients. Two patients had a history of angina of effort of 3 years' duration.

The cardiothoracic ratio on *x*-ray ranged from 47 to 63 per cent (mean 56%) and did not change with pacing. Three patients had pulmonary venous congestion and one patient developed pulmonary venous congestion after cardiac pacing was started.

The rhythm on the electrocardiogram in all patients was complete heart block with ventricular rates varying from 14 to 50/min. (mean 34/min.), and an atrial rate ranging from 66 to 110/min. (mean 92/min.) or atrial fibrillation (1 patient). The QRS showed right bundle-branch block pattern in the chest leads in 8 patients, left bundle-branch block in 2, and was normal in the other. Two of the 8 patients with right bundle-branch block, intermittently showed a left bundle-branch block pattern. The mean frontal axis was left in 9 patients and right in the other 2. The rhythm underlying the syncopal attacks was asystole in 6 patients and ventricular tachydysrhythmia in the other 5.

The pathological changes in all patients consisted of muscle degeneration, with scattered inflammatory cells and diffuse myocardial fibrosis. Similar changes were present throughout the conducting system and were maximal in the bundle-branches. The heart weights ranged from 340 to 1050 g. (mean 670 g.).

Group 3: Coronary Artery Disease. There were 10 patients in this group, 3 women and 7 men. Their ages ranged from 56 to 80 years (mean 69 years).

A history of recurrent syncope for periods of time ranging from 1 week to 4 years (mean 14 months) was the presenting symptom in 7 patients, and left ventricular failure for 6 months and 3 weeks in two others. One other patient presented with a 2-day history of crescendo angina with heart block. It was of interest that only 4 of the 10 patients had a

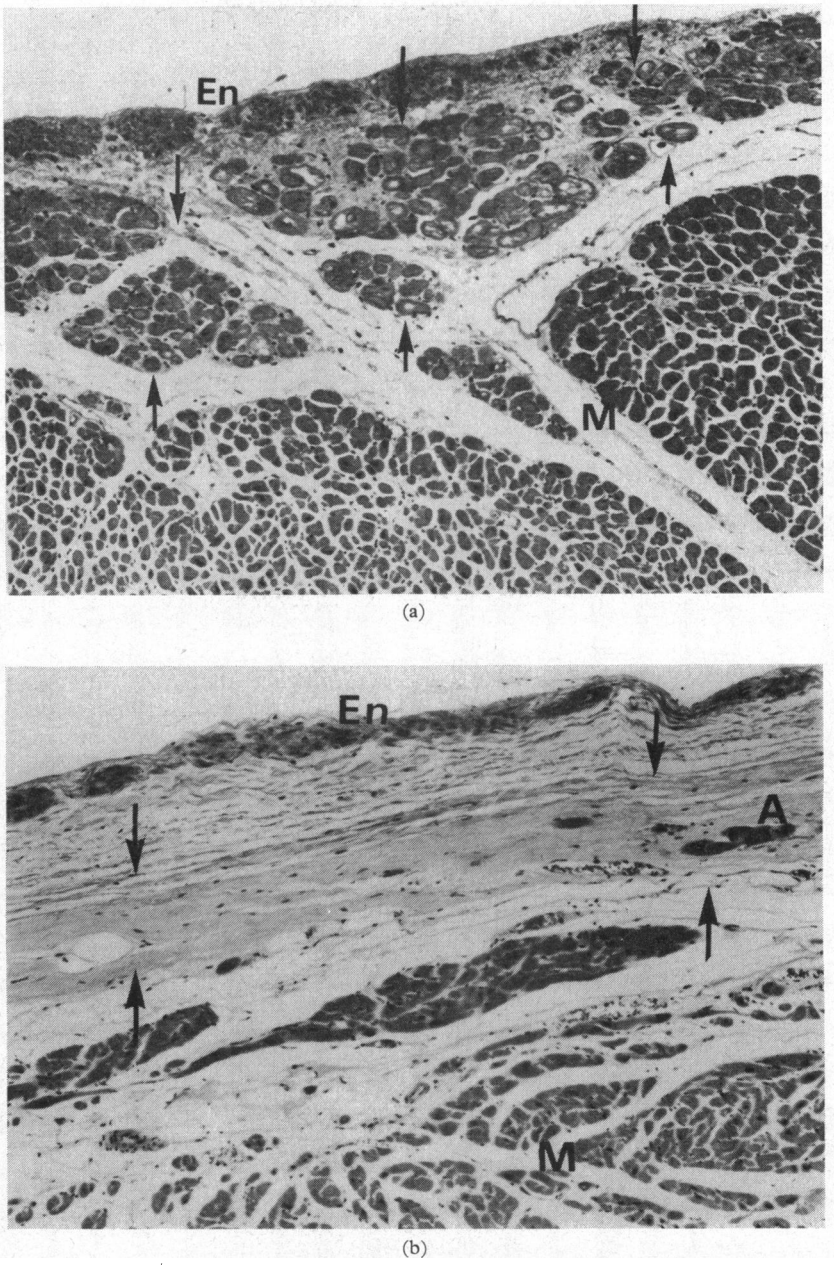

FIG. 1.—Distal left bundle-branch (a) from a normal subject, showing numerous large vacuolated conduction fibres; (b) from a patient with bundle-branch fibrosis (arrows); the bundle-branch is a fibrotic strand with only one or two residual conduction fibres (A). En, endocardium; M, myocardium. (H. and E. ×35.)

history of angina of effort or myocardial infarction. Following the development of complete heart block one patient became free from angina. One patient had a history of diphtheria during early childhood.

The cardiothoracic ratio on *x*-ray ranged from 58 to 63 per cent (mean 59%) and did not change with pacing. Four patients had pulmonary venous congestion.

The electrocardiogram in 9 patients showed complete heart block with a ventricular rate ranging from 25/min. to 50/min. (mean 43/min.) and an atrial rate ranging from 75/min. to 110/min. (mean 87/min.). The dominant rhythm in 1 patient was sinus with intermittent complete AV block. The QRS showed a right bundle-branch pattern in 5 patients, left bundle-branch block in 4, and a normal QRS in 1. The mean frontal axis was left in 8 patients and normal in 2. The rhythm underlying the syncope was asystole, and in addition 1 patient also had episodes of ventricular tachydysrhythmia.

Pathological examination showed a normal AV node, with one exception, old thrombotic occlusions involving all three major coronary vessels, and ischaemic scarring involving both bundle-branches. Eight patients had old posterior infarcts and 2 patients had old large anterior infarcts. The patient with the normal QRS had an occlusion of the nodal artery with complete destruction of the main bundle and AV node. The heart weights ranged from 310 to 750 g. (mean 450 g.).

Group 4: Active Myocarditis. There were 4 patients in this group, 3 women and 1 man, and their ages ranged from 54 to 68 years (mean 59 years).

They presented with recurrent syncope, and in addition 2 had cardiac failure. The history of syncopal attacks ranged from 5 months to 2 years (mean 13 months). There was no history suggesting the occurrence of a significant systemic illness in the 2 years before admission to hospital, nor a previous attack of rheumatic fever or chorea.

The cardiothoracic ratio on *x*-ray ranged from 51 to 66 per cent (mean 58%) and did not change with pacing. Two patients had pulmonary venous congestion.

The electrocardiogram showed sinus rhythm in 2 patients with intermittent complete heart block and complete block in the 2 others. When in complete block the ventricular rates of the 4 patients ranged from 30 to 40/min. (mean 34/min.) and the atrial rates between 86 and 110/min. (mean 95/min.). Three patients had right bundle-branch block and the other left bundle-branch block. The mean frontal axis was normal in 3 patients and right in the other. The syncopal attacks were due to periods of ventricular tachydysrhythmia as well as periods of asystole.

The pathological findings gave evidence of active myocarditis with involvement of both bundle-branches, but intact AV nodes. Two patients showed the typical histological features of active rheumatic myocarditis with minimal mitral and tricuspid valve disease (clinically unsuspected), and in the other 2 the myocarditis was "non-specific". The heart weights ranged from 380 to 850 g. (mean 555 g.).

Group 5: Calcification of Valves or Valve Rings. There were 4 patients in this group, 2 women and 2 men, and their ages ranged from 68 to 76 years (mean 71 years).

Two presented with recurrent syncope for 1 year and for 6 months, respectively, and the 2 others with cardiac failure for 2 and 5 months. One patient had the clinical signs of aortic stenosis (Harris, Sleight, and Drew, 1965b) and 1 other the signs of mitral regurgitation. The 2 other patients did not present any clinical signs of significant valvular disease. The patient with aortic stenosis had, in addition to syncopal attacks, an 8-year history of angina of effort. No patient had a past history of rheumatic fever or chorea.

The cardiothoracic ratio on *x*-ray ranged from 50 to 57 per cent (mean 54%) and did not change with pacing. All patients had areas of calcification in the region of the mitral or aortic valve rings and also in the aortic valve in the patient with aortic stenosis. Two patients had pulmonary venous congestion.

The electrocardiogram in 2 patients showed sinus rhythm with intermittent complete heart block, and in 2 complete heart block. When in complete heart block the ventricular rates of the 4 patients ranged from 25 to 40/min. (mean 34/min.) and the atrial rates 65 to 100/min. (mean 80/min.). Three patients had left bundle-branch block and in the other the QRS was normal. The mean frontal axis was left in all patients. The syncopal attacks were always due to asystole.

At pathological examination the AV node was normal in all patients and there was no appreciable coronary disease. Massive mitral valve calcification was present in 2 patients and was secondary to old rheumatic valve disease. The deposits of calcium had destroyed the main and left bundle-branches. One patient had senile calcification of the aortic and mitral valve rings, but normal valve function (Fig. 2a and 2b). The deposits of calcium had destroyed the main and left bundle-branches. Another patient had severe calcific aortic stenosis. The calcium involved the aortic valve ring and cusps and had destroyed the main left bundle-branches. The heart weights ranged from 330 to 610 g. (mean 502 g.).

Group 6: Collagen Disease. There were 3 patients in this group, all men, 2 aged 59 and 1 aged 68 years.

Angina of effort was a dominant feature in the history of all 3 patients over a period of 1, 3, and 13 years, respectively. In addition, 2 patients had

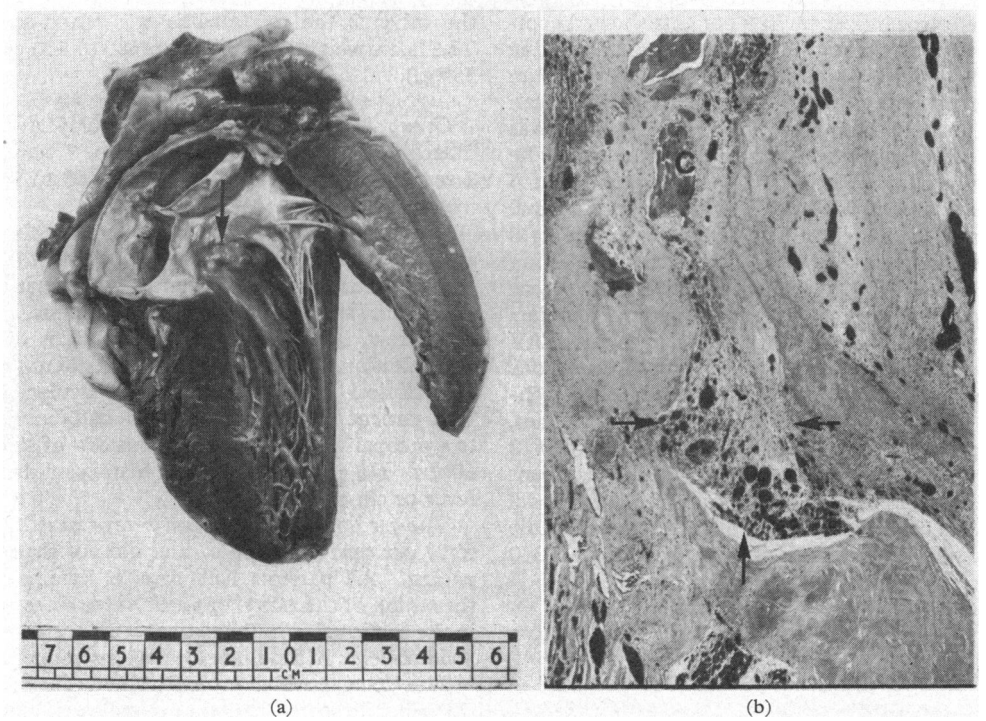

FIG. 2a.—Calcification of the mitral and aortic valve rings extending into the membranous interventricular septum (arrow) in the region of the main bundle. The calcification is an exaggerated age change and there was no aortic stenosis.

FIG. 2b.—The main bundle (arrows), showing loss of conduction fibres with calcific masses (C) lying in close proximity; immediately anterior to this section no trace of the main bundle could be found, the whole area being occupied by calcific debris. (H. and E. ×30.)

multiple syncopal attacks over a period of 1 and 13 years, respectively. There was no clinical evidence of a chronic collagen disorder.

The cardiothoracic ratio on *x*-ray was 42, 45, and 54 per cent, respectively, and did not change with pacing. One patient had pulmonary venous congestion.

The electrocardiogram in all 3 patients showed complete heart block, with ventricular rates ranging from 45 to 85/min. (mean 50/min.) and atrial rates between 80 and 90/min. (mean 82/min.). The QRS was initially normal in all patients, as was the mean frontal axis. Shortly after admission to hospital 1 patient developed right bundle-branch block with a mean left frontal axis. The syncopal attacks in 2 patients were caused by both periods of asystole and ventricular tachydysrhythmia.

The pathological examination showed in all patients destruction of the AV node and main bundle by proliferating fibrous tissue and chronic inflammatory cells. In addition, the fibrous tissue extended into the bundle-branches, and there was diffuse myocardial fibrosis. The small branches of the coronary arteries, including the nodal artery, were involved in the chronic inflammatory process. Though there was no clinical evidence of collagen disease the pathological changes in the heart were similar to those described in scleroderma and ankylosing spondylitis (Bernstein, 1951; Sobin and Hagstrom, 1962; Lev *et al.*, 1966; Weed *et al.*, 1966). One patient, in addition, had an old occlusion of the right coronary artery and an old posterior wall infarct not involving the septum or the artery to the AV node. The heart weights were 410 g., 550 g., and 730 g., respectively.

Group 7. Amyloidosis and Transfusion Siderosis. There were 4 patients in this group, all male, and the 2 with amyloidosis were aged 68 and 84 years, and the 2 with transfusion siderosis were aged 10 and 17 years.

The 2 patients with amyloidosis presented with recurrent syncopal attacks of 3 and 6 years' duration, and in addition 1 patient was in congestive cardiac

failure at the time of admission to hospital. There were no clinical features of chronic disease in either patient apart from complete heart block. The 2 patients with transfusion siderosis had been treated for hypoplastic anaemia by repeated transfusion over a 7- and 10-year period, respectively, and complete heart block developed during the last year of life.

The cardiothoracic ratios on *x*-ray were 47, 47, 48, and 54 per cent, and the 2 latter were associated with pulmonary venous congestion; there was no change in the cardiothoracic ratio in those patients who were paced.

The electrocardiograms of the patients with amyloid deposits showed complete heart block with ventricular rates of 28 and 45/min. (mean 37/min.) and atrial rates of 80 and 100/min. (mean 90 min.). The 2 patients with amyloidosis had bundle-branch block, one right and the other left, with right and left axis deviation, respectively. The rhythm underlying the syncopal attacks was asystole in both patients and in addition one patient had ventricular tachydysrhythmia.

The electrocardiograms of the patients with transfusion siderosis showed complete heart block with ventricular rates of 40 and 50/min., and atrial rates of 80 and 120/min. The mean frontal axis and QRS were normal in both the patients with transfusion siderosis and neither patient had syncopal attacks.

Pathological examination showed massive deposits of amyloid in 2 patients in the atrial and ventricular muscle and AV node, but not in the bundle-branches, and in the medium-sized coronary arterioles; the heart weights were 360 and 500 g. The other 2 patients had massive deposits of iron in the atria and ventricles; the AV nodes were destroyed, but the main bundle and branches were little affected: the heart weights were 155 and 305 g.

Group 8: Congenital Heart Disease. There were 2 patients in this group, both women, aged 54 and 62 years, and they presented with a history of recurrent syncope for 13 and 4 years. In addition, 1 patient was in congestive cardiac failure at the time of admission to hospital.

The cardiothoracic ratio on *x*-ray was 54 and 55 per cent, respectively, and there was no change after pacing. One patient had pulmonary venous congestion.

The electrocardiogram showed complete heart block with ventricular rates of 25 and 40/min. and atrial rates of 70 and 100/min., respectively. There was right bundle-branch block with a normal mean frontal axis in 1 patient, and left bundle-branch block with left axis deviation in the other. The syncopal attacks were caused by asystole in both patients, but in addition 1 patient had episodes of ventricular fibrillation.

On pathological examination 1 patient had an aneurysm of the membranous portion of the interventricular septum, which had destroyed the bifurcation of the main bundle; the AV node was normal and the heart weighed 380 g. The other patient had a normal AV node but complete absence of the main bundle. The peripheral bundle-branches were normal. These appearances are similar to those found in congenital heart block (Lev, 1964), but extended much further into the origin of the bundle-branches than usual. The heart weighed 320 g.

Group 9: Syphilitic Cardiovascular Disease. The one patient was a man aged 61 years who presented with a 1-month history of angina and dyspnoea on exertion and the physical signs of mild aortic regurgitation.

The cardiothoracic ratio on *x*-ray was 50 per cent and did not change with pacing. The electrocardiogram showed complete block with a ventricular rate of 41/min. and an atrial rate of 96/min. The QRS showed left bundle-branch block with a normal mean frontal axis.

On pathological examination there was a gumma of the interventricular septum involving the main bundle and origin of both bundle-branches, and syphilitic aortitis but normal coronary ostia.

Duration of Pacing. Sixty of the 65 patients were paced on a long-term basis. The duration of pacing is summarized in Table II.

TABLE II

DURATION OF PACING IN THE 60 PACED PATIENTS

Histology	No. of patients	Period paced (range)	Mean (mth.)
Bilateral bundle-branch fibrosis	26	4 dy.–53 mth.	17
Cardiomyopathy	9	1 dy.–36 mth.	12
Coronary artery disease	10	1 dy.–58 mth.	16
Myocarditis	4	11–36 mth.	21
Calcification of valves or valve rings	4	1 dy.–16 mth.	6
Collagen disease	3	6–33 mth.	17
Amyloid deposits	1	53 mth.	
Aneurysm of membranous septum	1	6 mth.	
Congenital heart block	1	28 mth.	
Syphilitic cardiovascular disease (gumma)	1	13 mth.	

Review of Causes of Chronic Heart Block

The commonest cause of atrioventricular block, comprising 26 patients in the necropsy series of 65 patients, was bilateral bundle-branch fibrosis of

TABLE III

PRESENTING SYMPTOMS AND PAST MEDICAL HISTORY

Histology	No. of patients	Adams-Stokes attacks	Duration of Adams-Stokes attacks	Angina of effort	Congestive cardiac failure	Past medical history		
						Diphtheria	Rheumatic fever	Myocardial infarction
Bilateral bundle-branch fibrosis	26	23	1 wk.–10 yr. (mean 42 mth.)	6	3	2	0	0
Cardiomyopathy	11	11	1 dy.–2 yr. (mean 6 mth.)	2	4	0	0	0
Coronary artery disease	10	7	1 wk.–4 yr. (mean 4 mth.)	4	2	1	0	1
Myocarditis	4	4	5 mth.–2 yr. (mean 13 mth.)	0	2	0	0	0
Calcification of valves or valve rings	4	2	6 mth. and 12 mth.	1	2	0	0	0
Collagen disease	3	2	1 yr. and 13 yr.	3	0	0	0	0
Amyloid deposits	2	2	3 mth. and 6 yr.	0	1	0	0	0
Iron deposits (multiple blood transfusion)	2	0	0	0	1	0	0	0
Congenital heart block	1	1	13 yr.	0	0	0	0	0
Aneurysm of septum	1	1	4 yr.	0	1	0	0	0
Syphilitic cardiovascular disease (gumma)	1	0	1 mth.	1	0	0	0	0

unknown aetiology without apparent myocardial disease (Group 1, Table I). That coronary disease was not the cause was shown by the absence of occlusive changes in the coronary arteries at post-mortem injection and dissection, and the degree of coronary atheroma was the same as in the control group of the same age dying of other causes. Nor was there small vessel disease in this relatively common group. The patients, with one exception in this series, were elderly, and Lev (1964) suggested that the sclerotic and calcified degeneration of the upper part of the septum, commonly found in old age, spread into the conducting tissue. This seems unlikely, since these changes are not seen in the middle and lower parts of the septum adjoining the conducting tissue, and in any case, were found to be just as common in 40 patients of similar age without heart block on an electrocardiagram recorded shortly before death (Davies, Redwood, and Harris, 1967). It has been suggested that diphtheria plays a part in the development of chronic heart block (Butler and Levine, 1930; Leys, 1945; Penton *et al.*, 1956), but this also seems unlikely since in the 65 patients only 3 had diphtheria (Table III), 2 of the 3 patients having bilateral bundle-branch fibrosis and the other coronary arterial disease. In our first 100 patients with heart block (Harris *et al.*, 1965a) the incidence of diphtheria was 18 per cent, and was probably a reflection of the relatively high incidence of diphtheria during the childhood of these patients. That diphtheria probably has little to do with the development of chronic heart block was suggested by the study of Jones and White (1927) who re-examined 100 patients 5 or more years after severe or moderately severe diphtheria but found no case of complete heart block, though the study may be criticized on the grounds that the interval between the infection and re-examination was too short.

The evidence for obstructive coronary disease of the usual sort in large and medium vessels as the cause of the block in 10 patients (15%) was based on post-mortem injection, dissection, and histological examination. The estimations in the past of a much higher incidence such as 73 per cent (Rowe and White, 1958) and 48 per cent (Friedberg *et al.*, 1964) were based on the clinical evidence which can be misleading. For example, 6 patients with isolated disease of the conducting tissue had angina of effort and all 3 patients with collagen disease had angina of effort and electrocardiograms suggesting diaphragmatic infarction. It is possible that exercise can cause angina by a change of rhythm, and it precipitates block in some patients (Fowler, 1962). It is more likely, however, that there is some other unrecognized cause for the angina. Even when coronary disease is the cause of chronic heart block a history of angina or infarction may be absent (6 of 10 cases in this series) and the typical electrocardiogram is disguised by the bundle-branch block. In the series of 150 patients with myocardial infarction reported by Papp in 1952, 4 patients with complete heart block gave no history of pain, and it was suggested that either slow or fast heart rates abolished the pain of infarction. Possibly the only occasion when the clinical diagnosis of an ischaemic basis for chronic complete heart block can confidently be made is upon selective coronary arteriography or when, after an acute myocardial infarction, the progressive development of heart block can be observed electrocardiographically. Permanent block after acute infarction is a rare event occurring only once in our experience of 55 patients paced for

heart block after an acute cardiac infarction, again emphasizing the infrequency of coronary disease as the common cause of chronic Adams-Stokes disease.

Cardiomyopathy was a not uncommon cause of heart block and the low incidence in other series is probably related to the difficulty in clinical diagnosis, causing inclusion in the group of unknown aetiology (Johansson, 1966; Landegren and Biörck, 1963; Moreau, Gerbaux, and Lenègre, 1963).

During the acute phase of rheumatic heart disease heart block may develop, but almost invariably in association with valvular disease (Penton *et al.*, 1956; Rowe and White, 1958). In this series no patient had a history of previous episodes of rheumatic fever (Table III), but at necropsy 2 patients (Group 4) had active rheumatic myocarditis and valvulitis which was minimal and clinically unrecognized, and 2 others had chronic calcific rheumatic mitral valve disease (Group 5). One patient had severe calcific aortic stenosis. Disease of the aortic valve has long been recognized as a cause of heart block, particularly when the aortic valve is calcified. Five of the 7 patients originally described by Stokes (1846) had aortic valve disease. The onset of heart block may be very late in the course of aortic stenosis (Gilchrist, 1958), and the cause is involvement of the conducting tissue by downward spread of the calcium (Rytand and Lipsitch, 1946). One patient had senile calcification of the aortic and mitral valve rings extending into the main bundle without involving the valve cusps (Fig. 2). The incidence of aortic valve disease in this series was 2 per cent but has been recorded as high as 22 per cent (Ellis, Manning, and Connolly, 1964). In our first 100 patients the clinical evidence was 3 per cent, and it is probable that the lower incidence may be related to stricter criteria for the clinical diagnosis of heart block complicated by aortic stenosis (Harris *et al.*, 1965b). A routine overpenetrated chest *x*-ray was of considerable help in picking up calcified valve rings when there was no valve disease to attract attention.

Diffuse fibrosis of the myocardium was found in 3 patients. The histological features were those described as occurring in collagen disease, particularly rheumatoid arthritis (Brooks *et al.*, 1955; Olhagen, 1960) and scleroderma (Lev *et al.*, 1966; Weed *et al.*, 1966), though none of the patients in this series showed clinical evidence of a collagen disorder. Rheumatoid arthritis, however, was present in 4 per cent of a larger series of patients with chronic heart block (Harris *et al.*, 1965a). The 3 patients in the present series had been thought to have coronary disease because of a history of angina and an electrocardiogram resembling diaphragmatic infarction. Fibrous tissue proliferating from the septal area had narrowed the small coronary arteries and was thought to be the cause of the angina, and the diaphragmatic surface of the left ventricle showed fibrosis fitting with the electrocardiogram. The dominance of fibrosis in the septal area involving the main bundle with sparing of the bundle-branches probably accounted for the narrow QRS complex of the idioventricular rhythm. A narrow QRS is also found with congenital block, and also of course with transient block associated with acute infarction when the ischaemia most commonly affects the AV node alone.

Amyloidosis has been reported as a cause of heart block by James in 1966 and Rossi in 1961 and was present in 3 per cent of this series.

One patient had histological evidence of congenital heart block with a fault in the main bundle, and one other had a congenital aneurysm of the membranous septum destroying the bifurcation of the main bundle. It is extremely difficult to assess, on clinical grounds, the incidence of congenital heart block in a group of patients presenting for the first time in their 6th decade of life, but Campbell and Suzman (1934) stated that congenital heart block was probably more common than was thought. Congenital heart block is compatible with a normal development and survival (Yater, 1929; Campbell and Thorne, 1956; Nakamara and Nadas, 1964), but there is no doubt that Adams-Stokes attacks, though rare, can occur and probably reflect a poor prognosis (Smithells and Outon, 1959; Molthan *et al.*, 1962; Nakamura and Nadas, 1964). It is of interest that the patient with congenital heart block in this series was quite well until she was 41 years old and then had recurrent syncopal attacks for 13 years.

There are many other recorded causes of chronic heart block, such as myxoedema (Lee and Lewis, 1962), tumours, both primary and secondary (Mahaim, 1945; Reuling and Razinsky, 1941; Rowe and White, 1958), Paget's disease (Harrison and Lennox, 1946), Chagas' disease (Laranja *et al.*, 1956), non-specific myocarditis (Lev, 1964), and systemic lupus erythematosis (Schaub and Senning, 1963). Therefore, any careful histological study of a large series of patients with chronic heart block is likely to produce the odd rare cause, and the patients with transfusion siderosis and luetic disease fall into this category.

Conclusions

In the biggest group (26 patients) with almost isolated disease of the conducting tissue (bilateral bundle-branch fibrosis), in comparison with the groups where the myocardial disease involves the conducting tissue, symptoms would be expected to

TABLE IV

ELECTROCARDIOGRAPHIC FEATURES OF 65 PATIENTS BEFORE TREATMENT

Histology	No. of patients	Intermittent block	Complete heart block	Atrial rate*	Ventricular rate*	Mean frontal axis			Normal QRS	Bundle-branch block		Mechanism of Adams-Stokes attack	
						Normal	Right	Left		Right	Left	Asystole	Ventric. tachydysrhythmia
Bilateral bundle-branch fibrosis	26	5	21	70–100 (83)	24–54 (36)	11	2	13	3	18	5	22	1
Cardiomyopathy	11	0	11	66–110 (92)	14–50 (34)	0	2	9	1	8	2	6	5
Coronary artery disease	10	1	9	75–110 (87)	25–50 (43)	2	0	8	1	5	4	7	1
Myocarditis	4	2	2	86–110 (95)	30–40 (34)	3	1	0	0	3	1	4	4
Calcification of valves or valve rings	4	2	2	65–100 (80)	25–40 (32)	0	0	4	1	0	3	2	0
Collagen disease	3	0	3	80–90 (82)	45–58 (50)	3	0	0	3	0	0	2	2
Amyloid deposits	2	0	2	80, 100	28, 45	0	1	1	0	1	1	2	1
Iron deposits	2	0	2	80, 120	40, 50	2	0	0	2	0	0	0	0
Congenital heart block	1	0	1	70	25	1	0	0	0	1	0	1	0
Aneurysm of septum	1	0	1	100	40	0	0	1	0	0	1	1	1
Syphilitic cardiovascular disease (gumma)	1	0	1	96	41	1	0	0	0	0	1	0	0

* Means are given in parentheses.

be confined to Adam-Stokes attacks, less commonly to low cardiac output; ischaemic pain should not occur, nor such great cardiac enlargement, and the course should be long and benign with satisfactory pacing. In fact, none of these criteria for isolated disease of the conducting tissue proved to be correct (Tables III–VI). Angina was admittedly uncommon, but so it was also in the coronary group (4 of 10 patients). Cardiac enlargement on *x*-ray and weight at necropsy (Tables V and VI), with the exception of the cardiomyopathy group, were little different in the isolated disease of the conducting tissue group compared with the myocardial groups; nor was the duration of life different with pacing (Table II). There was, however, a shorter history of symptoms and a higher incidence of heart failure and of ventricular tachydysrhythmia in the myocardial group (Table III). Furthermore, a previous study of causes of death in paced patients (Harris *et al.*, 1968) has shown a much higher incidence of ectopic beats and fatal ventricular fibrillation, despite satisfactory pacing, in the myocardial group, again focusing attention on the tendency to ventricular irritability in this group, with important repercussions on therapy, e.g. the need for a demand pacemaker and suppressant drugs. With isolated disease

TABLE V

RESULTS OF CHEST *X*-RAY EXAMINATIONS

Histology	No. of patients	Cardiothoracic ratio* (%)	Pulmonary venous congestion
Bilateral bundle-branch fibrosis	26	48–80 (60)	6
Cardiomyopathy	11	47–63 (56)	4
Coronary artery disease	10	58–63 (59)	4
Myocarditis	4	51–66 (58)	2
Calcification of valves or valve rings	4	56–57 (54)	2
Collagen disease	3	42–54 (47)	1
Amyloid deposits	2	47, 54	1
Iron deposits	2	47, 48	1
Congenital heart block	1	54	0
Aneurysm of septum	1	55	1
Syphilitic cardiovascular disease (gumma)	1	50	0

* Means are given in parentheses.

TABLE VI

HEART WEIGHTS

Histology	No. of patients	Weight (g.)	
		Range	Mean
Bilateral bundle-branch block	26	360–600	480
Cardiomyopathy	11	340–1050	670
Coronary artery disease	10	310–750	450
Myocarditis	4	380–850	555
Calcification of valves or valve rings	4	330–610	502
Collagen disease	3	490–730	590
Amyloid deposits	2	360, 500	
Iron deposits	2	305, 155 (child)	
Congenital heart block	1	320	
Aneurysm of membranous septum	1	380	
Syphilitic cardiovascular disease (gumma)	1	500	

of the conducting tissue, however, there was a longer history of symptoms suggesting a more benign course, heart failure was uncommon, and ventricular tachydysrhythmia and ectopic beats with satisfactory pacing were rare. It was surprising that with isolated disease of the conducting tissue the duration of life was not longer than in the myocardial groups, but this is probably the result of technical problems in pacing which were frequent when most of this series was collected. The differences between the two groups are probably much more striking when considering living patients with heart block, and indeed the proportion with isolated disease of the conducting tissue will probably prove to be much higher.

The electrocardiogram was helpful in the diagnosis of Adams-Stokes disease, since there was evidence of a conduction defect in all patients, even when first seen, in this series, and there were no exceptions to this rule in a previous series of 100 living patients (Harris *et al.*, 1965a), though exceptions have been reported (Cookson, 1952; Johansson, 1961) and we have now seen 3 such patients. Those who were in sinus rhythm when first seen for symptoms invariably had a long P–R interval, or right bundle-branch block which has been stressed in the past as a precursor of complete block (Stokes, 1947; Portal *et al.*, 1962). Right bundle-branch block was more frequent than left, both with conducted and idioventricular or nodal rhythm, and represents the vulnerability of the narrow right bundle compared with the broad early decussating left, rather than any particular disease process, but was relatively more frequent with isolated disease of the conducting tissue. T inversion, other than secondary to bundle-branch block, might have been expected to indicate myocardial disease or ischaemia, but seemed to be related to the effect of artificial pacing and was transient (K. Chatterjee, 1968, personal communication), or was related to slow rate (Jacobson and Schrire, 1966). Thus the electrocardiogram, though valuable in diagnosis, was of little help in deciding the aetiology of heart block, but preliminary studies suggest that an abnormal ventricular gradient may be a pointer to a process affecting the myocardium as well as the conducting tissue.

Summary

The clinical findings in 65 patients with chronic heart block who came to necropsy have been analysed according to the myocardial histology. There were 25 female and 40 male patients, and their ages ranged from 10 to 82 years (mean 62·5 years).

Bilateral bundle-branch fibrosis was the commonest finding in 26 patients (40%); other causes were cardiomyopathy in 11, coronary artery disease in 10, myocarditis in 4, calcification of valves or valve rings in 4, collagen disease in 4, amyloidosis in 2, congenital heart disease in 2, haemosiderosis in 2, and luetic disease in 1 patient.

A history of angina or myocardial infarction did not necessarily indicate that coronary artery disease was the cause of the heart block, and frequently a history of ischaemic pain was absent in those patients with coronary disease. Only 2 of the 26 patients with bilateral bundle-branch fibrosis had a past history of diphtheria, suggesting that diphtheria has little to do with the development of chronic heart block. The chest *x*-ray was only helpful in the diagnosis of the underlying cause of heart block in those patients with calcification of the valves or valve rings.

The incidence of ectopic beats and fatal ventricular fibrillation, despite satisfactory pacing, was higher in those patients with significant myocardial disease. The history of symptoms was longer in those with bilateral bundle-branch fibrosis only.

There was evidence of a conduction defect in the electrocardiogram in all patients, even when first seen for symptoms.

The life expectancy of patients with artificial pacemakers was not materially affected by the underlying cause of the heart block, and only when pacing techniques are improved will the prognosis depend more on the underlying disease.

Examples of Cases

Bilateral Bundle-branch Fibrosis. Man, died at 66 years. After a syncopal episode at 62, he developed dyspnoea and central chest pain radiating into the arms on walking approximately 400 yards. A few months later a slow heart rate was noticed and treated with ephedrine. When he was 66 he was admitted to hospital after an episode of severe constricting chest pain lasting 12 hours, diagnosed as myocardial infarction. Subsequently exercise tolerance decreased and angina of effort was more easily provoked. Final admission precipitated by the acute onset of melaena due to gastric ulcer.

Past medical history included diphtheria when aged 7 years.

On examination in November 1965, heart rate 44 a minute, blood pressure 190/55 mm.Hg., apex beat normal, carotid pulse normal, jugular venous pressure, occasional cannon waves; on auscultation S1 varied in intensity, S2 widely split in expiration, grade 2/6 ejection systolic murmur present in the aortic area.

On *x*-ray, cardiac shadow within normal limits, and lungs normal.

Electrocardiogram showed complete heart block,

normal mean frontal axis, QRS 0·16 sec., right bundle-branch block, atrial rate 100/minute, ventricular rate 43/minute.

Barium meal confirmed the presence of a penetrating gastric ulcer, and in view of persistence of bleeding, a Bilroth I partial gastrectomy was carried out. The operation and immediate post-operative period was covered by continuous endocardial pacing. Post-operative course was complicated by bronchopneumonia and dehiscence of the abdominal wound. His general condition gradually deteriorated and he died 6 weeks after his gastrectomy.

At necropsy the heart weighed 570 g., with left ventricular hypertrophy. No stenosing atherosclerosis of coronary arteries was demonstrated by injection or dissection. Histological examination showed diffuse loss of conduction fibres in the upper two-thirds of the right branch and origin of the left bundle-branch. The myocardium appeared normal apart from an increased degree of interstitial scarring, as compared with control hearts of the same age. The myocardium immediately adjacent to the bundle-branches was normal.

Death was due to widespread metastases from a small carcinoma of the bronchus.

Cardiomyopathy. Man, died at 81 years. First seen at the age of 81 in July 1965, with a 3-year history of angina of effort which was on occasions associated with syncope. Three weeks before admission he had developed progressive oedema of the legs and severe prolonged attack of retrosternal pain and dyspnoea at rest; a diagnosis of acute myocardial infarct was made.

On examination in September 1965, heart rate 20 a minute, blood pressure 160/60 mm. Hg, apex beat impalpable, carotid pulses normal, jugular venous pressure raised to 10 cm. On auscultation the heart sounds were soft, S2 widely split in expiration, grade 2/6 ejection systolic murmur in the aortic area. Oedema extended to the mid-thorax.

On *x*-ray cardiac shadow markedly enlarged, cardiothoracic ratio 60 per cent, bilateral pleural effusions with pulmonary venous congestion and septal lines present.

Electrocardiogram showed complete heart block, mean frontal axis −65°, QRS 0·12 sec., right bundle-branch block, atrial fibrillation, ventricular rate 42 a minute. Wide QRS T angle.

He was treated with diuretics and had a very good response, soon becoming free of oedema. However, he had repeated syncopal attacks which were controlled for a time with maximal doses of long-acting isoprenaline, but 2 months after first being seen he had an uncontrollable series of syncopal attacks requiring periods of external cardiac massage to maintain life. He was transferred to St. George's Hospital, and at the time of insertion of a transverse wire ventricular tachycardia was precipitated and eventually irreversible ventricular fibrillation occurred.

At necropsy heart weight was 750 g. No stenosing atherosclerosis of coronary arteries shown by injection or dissection. Histological examination showed widespread myocardial scarring with degenerative changes in myocardial fibres. The majority of the conduction fibres in the peripheral Purkinje network and in both bundle-branches were lost.

Coronary Artery Disease. Man, died at 72 years. Angina of effort occurred at 59 years, with considerable limitation of exercise tolerance which continued for the next 12 years. In 1966, when aged 72 years, he developed complete heart block with loss of angina of effort but with limitation of exercise tolerance by dyspnoea. In addition, many brief dizzy spells but with no syncope. For a short period, 3 months after the onset of complete heart block, he returned to sinus rhythm, with recurrence of angina of effort and loss of effort dyspnoea.

Past medical history included rheumatic fever in 1907, 1913, and 1942.

On examination in August 1966, heart rate 40 a minute, blood pressure 180/80 mm. Hg, apex beat left ventricular hypertrophy, carotid pulses felt a little slow rising, jugular venous pressure raised 5 cm. above the sternal angle with frequent cannon waves: on auscultation S1 normal, S2 widely split in expiration, a grade 3/6 ejection systolic murmur and a 2/4 early diastolic murmur at the left sternal border.

On *x*-ray cardiac shadow much enlarged, cardiothoracic ratio 63 per cent, and the aorta unfolded with areas of calcification. Bilateral pleural effusions present, more marked on the right.

Electrocardiogram showed complete heart block, mean frontal axis −95°, QRS 0·14 sec., right bundle-branch block, atrial rate 82/minute, ventricular rate 50/minute. Wide QRS T angle.

Initially treated with digitalis and diuretics, but during the diuresis developed acute retention of urine due to carcinoma of the prostate. His dizzy spells were controlled with oral long-acting isoprenaline until November 1966 and the carcinoma of the prostate was controlled with stilboestrol. He was readmitted to hospital 3 months later after a series of syncopal attacks, and transvenous endocardial pacing was attempted, but no area of right ventricle could be located with a low threshold for pacing. This was subsequently found to be due to the presence of an infarct in the area where the electrode tip had made contact. The heart was stimulated with high voltages, but terminally there was no mechanical response.

At necropsy heart weight was 650 g. Severe stenosing atherosclerosis in all 3 major coronary arteries. Histological examination suggested at least 2 occlusive episodes of the right coronary artery. There was a large old postero-septal infarct destroying the origins of both bundle-branches. A pacing wire in the right ventricle was impacted into the area of infarction.

Collagen Disease (diffuse myocardial fibrosis). Man, died at 75 years. Onset of syncopal attacks and dyspnoea on exertion in 1948 aged 59. He continued to have frequent attacks of syncope until 1952 when he developed typical angina of effort. He was admitted to hospital in 1952 after 2 episodes of severe prolonged retrosternal constricting pain diagnosed as myocardial

infarction. By 1958 the syncopal attacks were only occurring 2 or 3 times a year, but his dyspnoea on exertion and angina of effort increased. By June 1962 he was unable to continue his work and he was referred to St. George's Hospital for pacing.

On examination in September 1962, heart rate was 45 a min., blood pressure 180/60 mm. Hg, apex beat left ventricular hypertrophy, carotid pulse sharp, jugular venous pressure, frequent cannon waves: on auscultation S1 varied in intensity, S2 was normal, grade 2/6 ejection systolic murmur present in the mitral area.

On chest *x*-ray cardiac shadow enlarged, cardiothoracic ratio 54 per cent and lungs normal.

Electrocardiogram showed complete heart block, normal mean frontal axis, QRS 0·08 sec., atrial rate 90/minute, ventricular rate 45/minute; wide QRS T angle.

Initially paced with a transvenous wire but later changed to an epicardial system. While pacing, he continued to have frequent episodes of ventricular tachydysrhythmia which were suppressed by quinidine. In October 1963, during a routine pacemaker change, his unpaced electrocardiogram showed left bundle-branch block. Despite satisfactory pacing, in 1964 he developed symptoms and signs of left ventricular failure which responded to digitalis and diuretic therapy. The patient was found dead in bed on having omitted his quinidine therapy for 36 hours. The pacemaker was found to be functioning normally and the epicardial wires were intact.

At necropsy heart weight was 730 g., with hypertrophy and diffuse scarring of both right and left ventricles. The aortic valve cusps were thickened and fibrosis was present in great excess around the aortic root. The major coronary arteries showed no stenosing atheroma. Histological examination showed that the atrioventricular node, main bundle and origin of both bundle-branches were destroyed by proliferating connective tissue densely infiltrated with chronic inflammatory cells. Small arteries both within the conduction system and in the myocardium were similarly involved by actively proliferating fibrous tissue. These myocardial changes are identical to those described in scleroderma (Lev *et al.*, 1966) and rheumatoid arthritis (Olhagen, 1960).

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