Progressive Familial Heart Block — Two Types

A. J. BRINK,   M. TORRINGTON

SUMMARY

Two types of heart block which occur extensively in families in the Republic of South Africa are reported. A type I heart block tends to have the pattern of a right bundle-branch block and/or left anterior hemiblock occurring individually or together, and manifesting clinically when complete heart block supervenes, either with syncopal episodes, Stokes-Adams seizures or sudden death. The condition is inherited as an autosomal dominant gene and appears to be progressive in nature; the risk to life appears to be greatest at 3 particular periods: at or soon after birth, during puberty and the early 20s, and again towards middle age.

The type II condition also appears to be progressive and is inherited as an autosomal dominant gene. The pattern, however, tends to develop along the lines of a sinus bradycardia with a left posterior hemiblock, again presenting clinically as syncopal episodes, Stokes-Adams seizures or sudden death when complete heart block supervenes. Both conditions are likely to be widely prevalent throughout the Republic of South Africa. The pathogenesis is discussed in relation to the patterns of the conduction disturbances.

It is of considerable importance to know that in the White South African community we have at least two hereditary types of heart block which may prove to be at least as prevalent and more often fatal, particularly in young age groups, than other recognized hereditary forms of disease in this country, such as porphyria.

The appearance of complete heart block is always serious and often fatal. Implantation at an opportune time of one of the wide range of pacemaking devices available can not only be lifesaving but, in the setting of congenital heart block without other structural heart lesions, may also enable the patient to lead a normal and productive life.

Furthermore, the two familial types to be described in this article may be detected by means of the electrocardiogram at an earlier stage of the conduction disturbance, which can be progressive in nature. When fully developed, the condition can result in sudden death without warning, or it may present with premonitory episodes of syncope or full-blown Stokes-Adams attacks.

Since both types appear to have a dominant pattern

Cardiac Unit, Department of Internal Medicine, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP

A. J. BRINK, M.D., F.R.C.P., D.SC.

National Research Institute for Nutritional Diseases of the South African Medical Research Council, Parowvallei, CP

M. TORRINGTON, M.SOC.SCI.

of inheritance, it is vital that all known relatives should as far as possible be screened by means of an electrocardiogram at the earliest possible age; all affected members should be followed up regularly for evidence of progression and for timely intervention.

Although a conduction defect could be a frequent cause of sudden death in White South Africans, both young and old, another familial form of heart disease, dysrhythmic congestive cardiomyopathy, has also been recognized as a condition capable of causing sudden death in children and young people in certain families in this country.[1]

In the conditions to be discussed, the dominant type of genetic inheritance shown to be present has resulted in the condition being present in families with names well known throughout the country.

TYPE I (RBBB/LAHB/CHB — BROAD QRS)

The proband in this family (Fig. 1) was born by caesarean section because of supposed fetal distress on account of a fetal heart rate of approximately 80/min. After birth, electrocardiograms established the presence of a high-grade 3:1 heart block, trifascicular block and a ventricular rate of 55 (Fig. 2).

The infant was observed anxiously over the next 6 months and it was noted that the degree of heart block varied. At times a 4:1 block was recorded, or runs of ventricular escape with complete heart block, or back to a 3:1 or even a 2:1 heart block (Fig. 3). It was learnt that another infant previously under our care, who had had a pacemaker implanted at the age of 1 year because of a complete heart block with a slow heart rate of 20/min and a bifascicular bundle-branch block pattern, was closely related to the proband. To avoid the possibility of a potentially fatal situation developing in this only child of the parents, a pacemaker was implanted in the proband at the age of 6 months. She has thrived normally and the original mercury battery power supply has recently been replaced by a lithium power source, the first to be implanted in an infant. This new implantation promises a battery life of up to 10 years.

It was possible to gather information over 6 generations and to investigate members of the last 3 generations of this family, which has many branches throughout the country. Of the 261 known relatives (Fig. 4a) about whom information has so far been obtained over 6 generations, 55 members in the last 3 generations could, up to now, be subjected to electrocardiography (Fig. 4b). A total of 31 of these had conduction defects (Fig. 4c). The average age of the electrocardiographically affected individuals (Fig. 4d) diminished in the more recent generations. This observation in itself is not unexpected, since we are dealing with a younger age group in each successive generation.
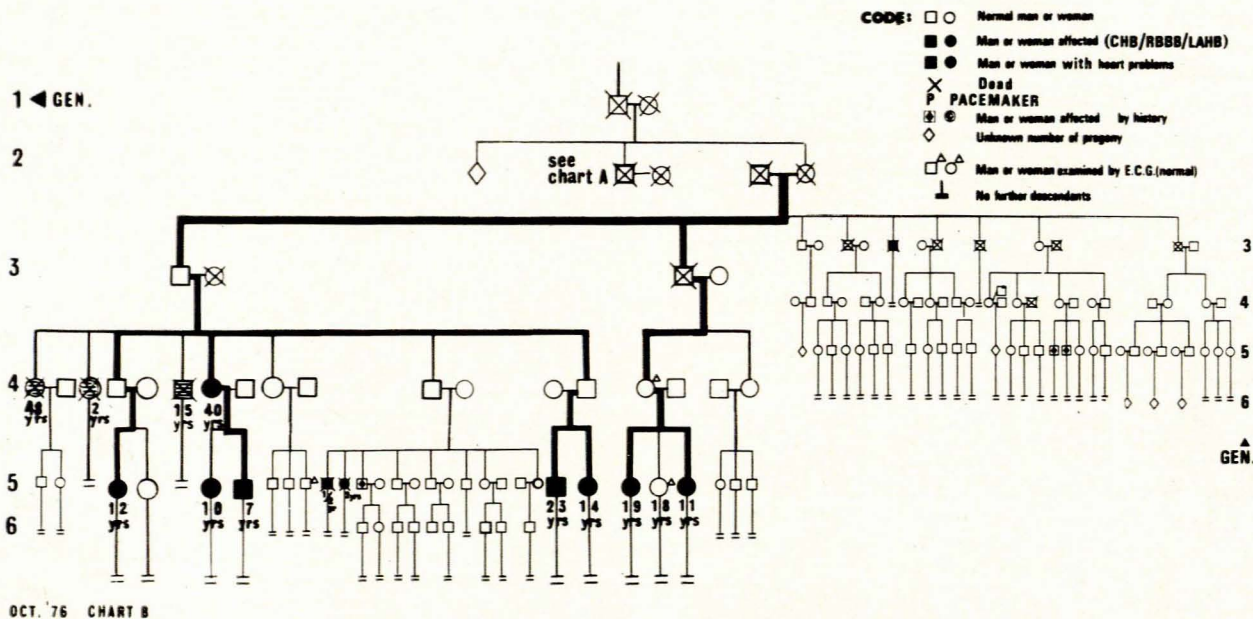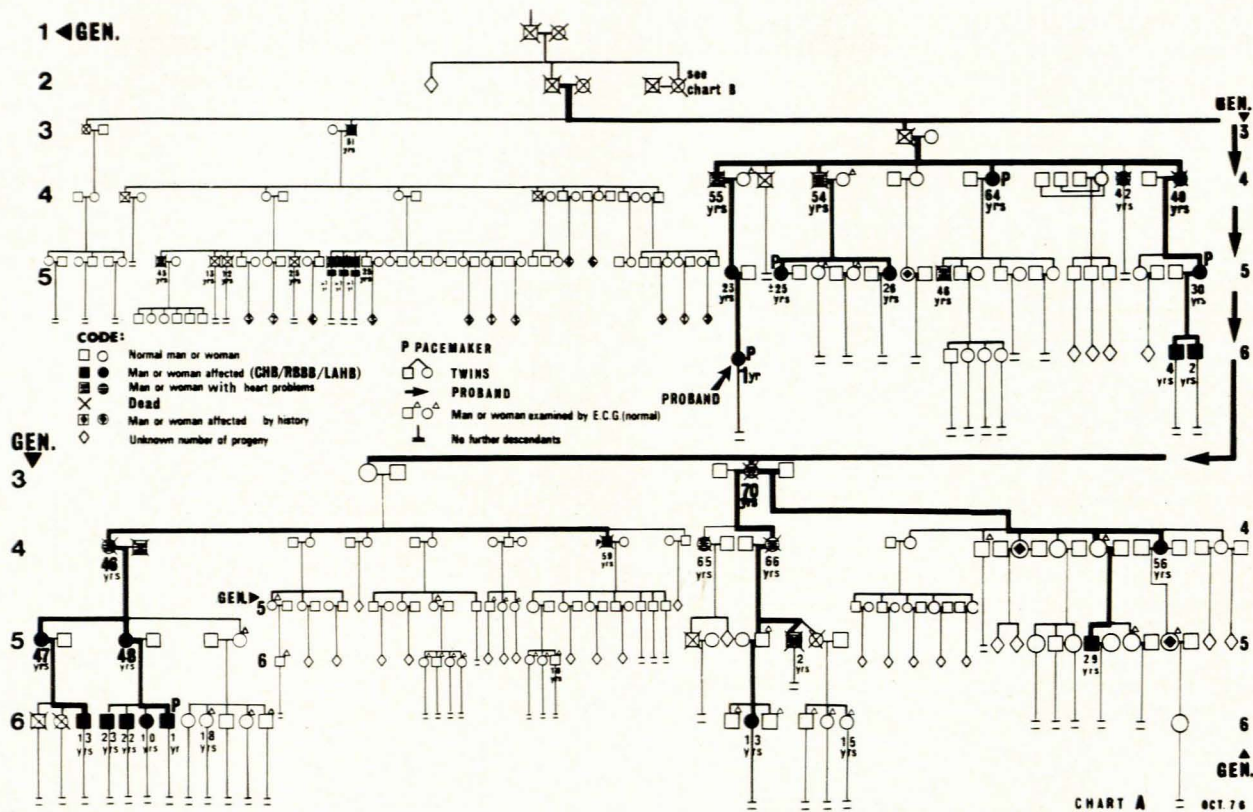
Fig. 1. The family tree of patients with type I (RBBB/LAHB/CHB — broad QRS) familial progressive heart block.

Types of Electrocardiographic Conduction Defects (Fig. 5)

A left anterior hemiblock (LAHB) pattern was present in 3 members (Fig. 5a) and in 2 of these the block was bifascicular, having an associated right bundle-branch block (RBBB) pattern. The commonest pattern was that of a monofascicular RBBB, which was present in 16 and, in association with the LAHB, in a further 2 (Fig. 5b).

Complete heart block (CHB) was present in 6 members, 2 in each of the 3 recent generations; all had had

pacemakers implanted (Fig. 5c). A total of 27 were therefore affected (Fig. 5d).
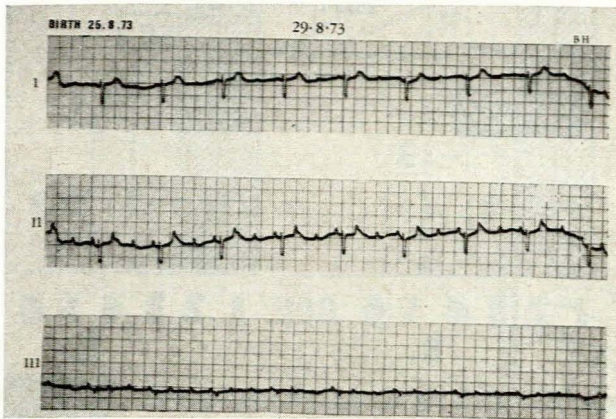

Fig. 2. Three standard leads from the ECG of proband in type I condition, 4 days after birth, showing 3:1 trifascicular heart block.
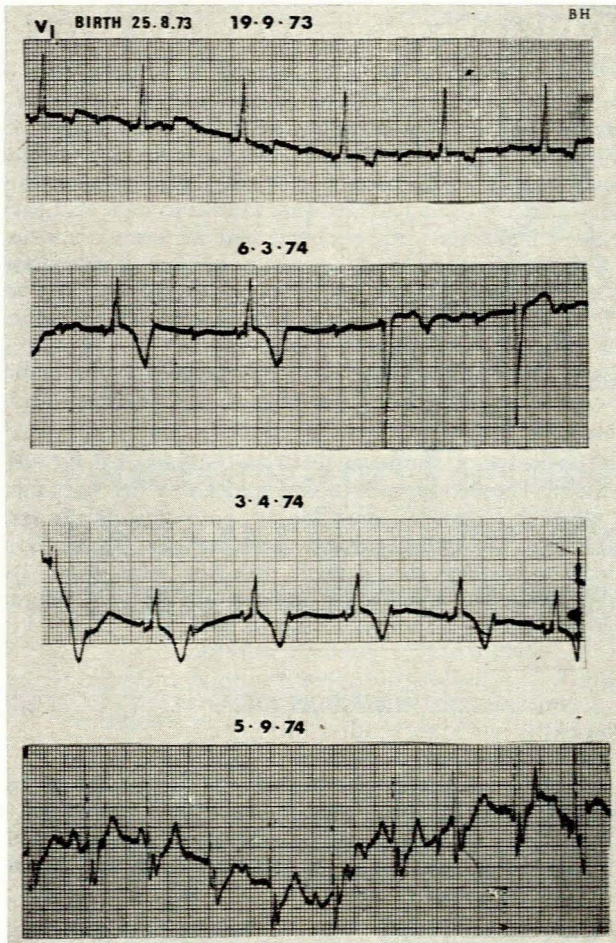

Fig. 3. Lead V1 from the ECG of proband at different dates showing the variable degree of heart block.
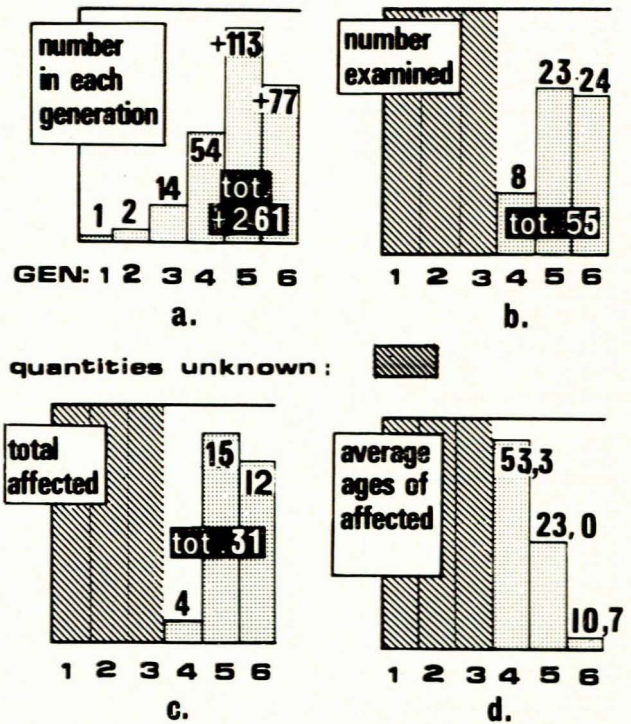

Fig. 4. Numbers of people involved in the investigation of type I conduction defect.

Other electrocardiographic anomalies were observed in a further 6 patients, and consisted of a short P-R interval without a Wolff-Parkinson-White pattern or a QT_c interval suggestively but not prominently prolonged.

The average age at which a pacemaker had been implanted in the 3 successive generations decreased from 54,5 years in the fourth to 25 years in the fifth to 1 year of age in the sixth generation (Fig. 6a and 6b).

Deaths in the family which could be attributed to a cardiac cause, and which in most instances appeared to have occurred suddenly and unexpectedly, totalled 22 in the last 3 generations (Fig. 7a); again the increasingly younger age at which death occurred in the successive 3 generations is apparent. This dropped from an average of 50,7 years to 44,7 years to 12,3 years in the sixth generation (Fig. 7b).

TYPE II (SB/LPHB/CHB — NARROW QRS)

The proband in this family (Fig. 8) received a pacemaker at the age of 42 because of Stokes-Adams episodes and electrocardiographic evidence of CHB with a ventricular rate of 33/min (Fig. 9).

It was learnt that there was a strong history of sudden death in the family and that other members of the family had had pacemakers implanted. Information could be obtained about 140 members of the family through 4 generations; to date, 24 have been subjected to electrocardiography. Ten of these were affected, and in this family, too, the average age of the affected members was lower in the more recent generations (Fig. 10).
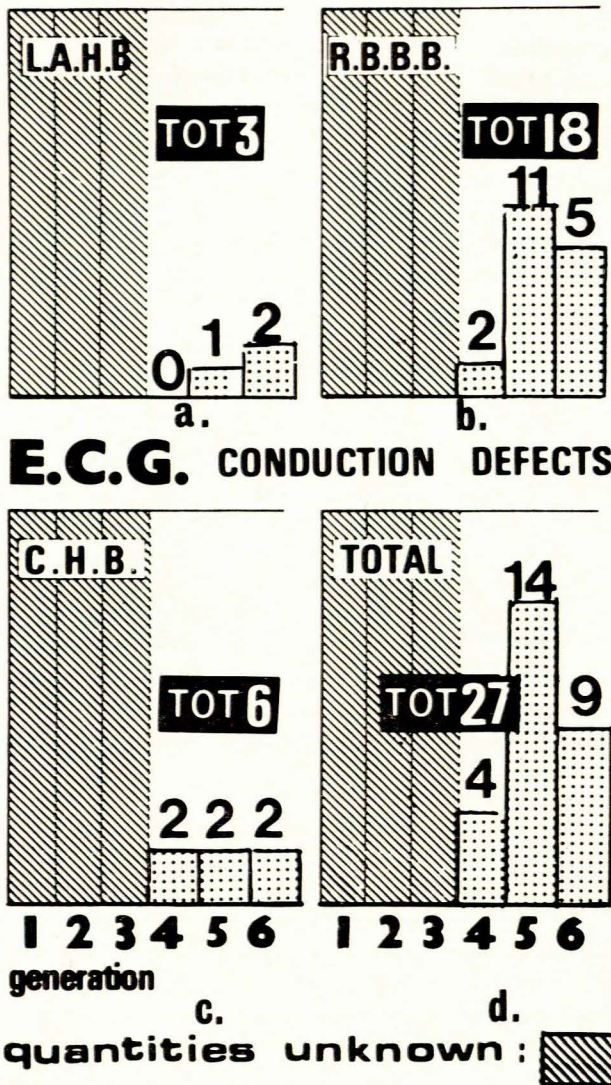
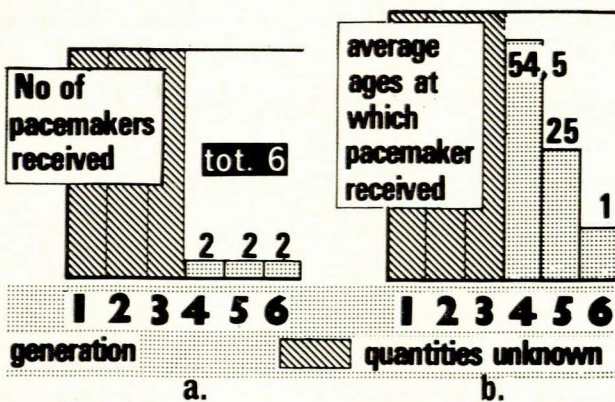Fig. 5. Types of ECG conduction defects in type I heart block.

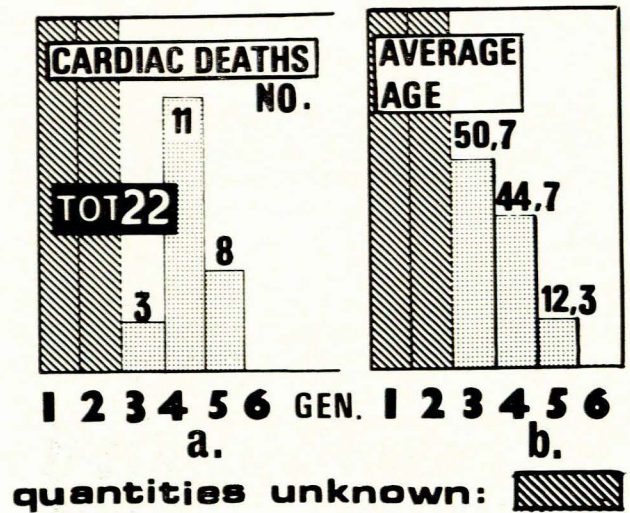Fig. 6. Patients in type I conduction defect with pace-makers.

Fig. 7. Cardiac deaths in members of the family with type I conduction defects.

Types of Electrocardiographic Conduction Defects (Fig. 11)

A sinus bradycardia (SB), defined as a heart rate of 60/min or less, was present as an isolated finding in 3 patients and was associated in both patients with a CHB which we had personally seen. An isolated left posterior hemiblock (LPHB) pattern (Fig. 12) was present in 3 other patients. Five patients were known to have had pace-makers implanted: the proband and his sister, in whom CHB was discovered as a result of our investigations (Fig. 13), and 3 other members not seen by ourselves. The 3 patients not examined had pacemakers implanted, yet died at the relatively young ages of 41, 39 and 16 years. The circumstances surrounding their deaths despite the presence of a pacemaker (Fig. 8) are uncertain and a cause for concern.

The proband, who has a CHB and SB, also has a LAHB pattern. The SB appears to run parallel to the ventricular rhythm, the P waves appearing at approximately the same rate (Fig. 13). In one elderly patient (Fig. 14) an atrial fibrillation (AF) was present, yet the ventricular rate was spontaneously slow at between 40 - 60/min, suggesting that she has a ventricular escape rhythm.

GENEALOGY

Type I

The original settler arrived in South Africa about 1696 from Lisbon, Portugal. He married in Stellenbosch in 1735 a girl of French origin and they obtained, some 13 years later, land rights in the vicinity of the Gouritz river in the eastern Cape.

The original couple (Gen. 1) were both found to be descendants of the original settler; a great number of the descendants still live in the area where their ancestor settled.

TYPES of CONDUCTION DEFECTS	NO. of PATIENTS			
S.B.		0	1	2
L.P.H.B.		0	0	3
S.B. + L.P.H.B.		0	0	1
C.H.B.		0	2[†]	1[††]
C.H.B. + S.B.		0	1	0
C.H.B. + S.B. + L.A.H.B		0	1	0
A.F.		1	0	0
TOTAL		1	5	7
GENERATION	1	2	3	4

▨ quantities unknown

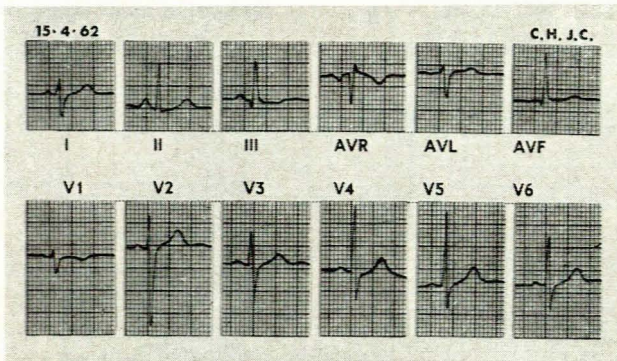Fig. 11. Types of ECG conduction defects in type II heart block.

Fig. 12. ECG of a member of type II family with LPHB.

From generation 4 onwards, however, a movement away from the eastern Cape started. Many moved in a westerly direction, while others sought new environments in other provinces of the Republic of South Africa. Today a large branch of the family lives in the Orange Free State, while others are spread over the whole of the Republic of South Africa. Investigations aimed at tracing and treating the affected members are continuing.

Type II

The original settler arrived in South Africa in 1713 from Amersfoort, Holland, and in 1720 he married a girl from Cape Town. They had 4 children, of whom only
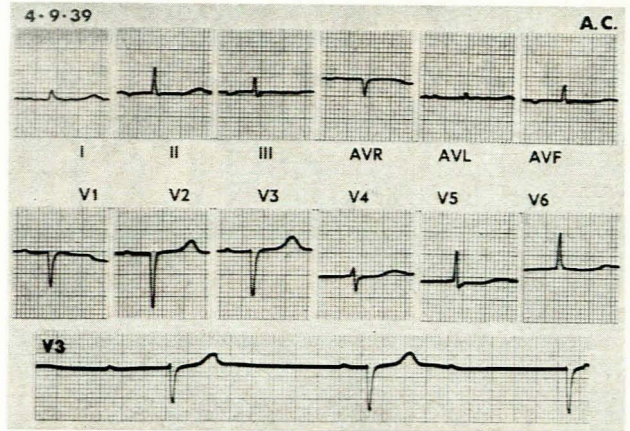

Fig. 13. ECG of a sister of the proband from type II family discovered during the course of investigation to have CHB.
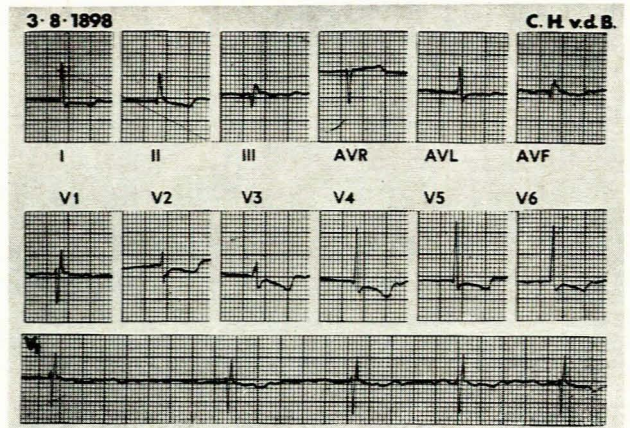

Fig. 14. ECG of the mother of the proband from type II family discovered during the course of investigation to have an AF.

2 were sons. As data are not available for the eldest son, it is presumed that the present branch is directly descended from the second son. They settled in the eastern Cape, where to date many members are still living.

The father of the proband was a member of a sibship of 8, of whom no less than 3, including the father, had died of cardiac disorders (Fig. 8, Gen. 2). The dominant pattern of inheritance is evident. The investigations of different branches of this family are being pursued. In this family the evidence of death in infancy is not present as strongly as in the type I family.

DISCUSSION

Both types of conduction disturbance are serious, are expressed as an autosomal dominant gene, and have been introduced into a large number of families in the Republic of South Africa.

The familial nature of the conduction defects in both families is not open to dispute. It may be questioned whether the conditions are progressive once evidence is present of a lesser degree of conduction disturbance. In the proband of the first family the electrocardiogram showed evidence of a fluctuating high-degree trifascicular block. The fact that pacing devices were required at ages varying from an average of 1 year in the sixth generation to 25 years in the fifth and 54 years in the fourth generation in this family is suggestive evidence of the progression of a condition which, although present at an early age, may also become manifest at a later age.

In the second family (type II) we have similar evidence of conduction disturbances of a lesser degree. The same observations in favour of a progression of events can once again be made.

The literature moreover amply confirms that lesser degrees of different forms of heart block, whether familial, congenital or of unknown association, can progress to complete heart block.[2-9] The evidence is that progression to complete heart block in 2 patients with a type I conduction disturbance similar to that in the proband in our first family occurred within 3 months of birth.[4,9]

A group of 209 patients with bilateral bundle-branch block, of whom a significant number had no known form of heart disease, were followed up for periods of up to 11 years.[3] With an average follow-up period of 2 years it was found that 14,4% progressed to complete heart block, some as long as 10 years after first coming under observation. In type I heart block, progression has been recorded within 2 years[6] and in type II within 2 - 3 years after the detection of the conduction disturbance.[7]

From the indirect evidence obtained, particularly in the type I family, it appears that there are certain ages at which the risk of fatal heart block is greater than at other ages: at or shortly after birth, during puberty and early adulthood, and again in middle age.

The onset of fatal episodes of complete heart block must so far be viewed as unpredictable, but in many patients it is at least reasonable to assume that evidence of progression will be seen electrocardiographically and that careful follow-up is demanded, particularly during these three apparently critical periods in the lifespan of family members.

Further studies are contemplated in order to determine how frequently electrocardiographic follow-up should be done. It is clear though, that in South Africa at least, we dare not ignore the potential gravity of a sinus bradycardia or of a chance finding of right bundle-branch block without thoroughly going into the family history. Furthermore, the fatality of both types of conduction disturbance is independent of the question of whether or not the QRS complex is wide, confirming the observations of other workers[5] who also showed that a type II conduction disturbance with narrow QRS complexes did not improve the prognosis. However, in a non-familial setting it has been the experience that a congenital heart block with narrow QRS complexes has a good prognosis, if no other heart anomaly is present.[10]

The pathogenesis of these conditions has been thought to be a degeneration of the conduction paths,[11,12] but the differing pattern of the two types strongly suggests that a vascular lesion may precede the degenerative changes. The association of right bundle-branch block and left anterior hemiblock in type I is in conformity with the known source of the nutrient arteries for these fascicles from branches of the anterior descending coronary artery, while the sinus bradycardia associated with left posterior hemiblock and narrow QRS complexes is in accordance again with the known blood supply of the atrioventricular (AV) node and the posterior inferior division of the left bundle branch from the right coronary artery.[13]

Occlusion of the nutrient vessel to the AV node as a cause for congenital heart block has been described,[14] and a vascular basis for a progressive congenital heart block has been suggested.[15]

It is possible that a similar vascular condition could be responsible for these two types of conduction disturbance. The progression could depend on a progressive occlusion of the small vessels supplying the relevant fascicles.

A suggested alternative explanation for progression has been the modelling of tissues surrounding the conduction bundle of His after birth, or a genetically determined programme for cell death in the conduction tissues.[15]

It also becomes evident from these studies that one cannot view the finding of an isolated right bundle-branch block as an innocent conduction disturbance.

The family with the type I conduction disturbance described in this paper has many branches. Although we have not been able to trace the members of the single family described earlier from this country,[16] it is more than likely that they will be shown to belong to the same group.

The type II conduction defect furthermore shows that a congenital heart block with narrow QRS complexes is not less hazardous than one with wide complexes. In the Republic of South Africa we must take thorough cognizance of any degree of heart block and even of persistent sinus bradycardia, particularly in young people. In any such patient a thorough family history is essential and if there is any suspicion of a familial disease, careful electrocardiographic follow-up is necessary.

REFERENCES

1. Brink, A. J., Torrington, M. and Van der Walt, J. J. (1976): S. Afr. med. J., 50, 2119.
2. Lenegré, J. (1966): Cardiologia (Basel), 48, 134.
3. Scanlon, P. J., Pryor, R. and Blount, S. G. (1970): Circulation, 42, 1123.
4. Kelley, D. T. and Rowe, R. D. (1972): Pediatrics, 50, 333.
5. Sarachek, N. S. and Leonard, J. J. (1972): Amer. J. Cardiol., 29, 451.
6. Husson, G. S., Blackman, M. S., Rogers, M. C. et al. (1973): Ibid., 32, 365.
7. Lynch, H. T., Mohiuddin, S., Sketch, M. H. et al. (1973): J. Amer. med. Ass., 225, 1465.
8. Schaal, S. F., Seidensticker, J., Goodman, R. et al. (1973): Ann. intern. Med., 79, 63.
9. Chan, Tak-Sek, Potter, R. T. and Liu, Lena (1973) Amer. J. Dis. Child., 125, 82.
10. Corne, R. A. and Mathewson, F. A. L. (1972): Amer. J. Cardiol., 29, 412.
11. Lev, M., Cuadros, H. and Paul, M. H. (1971): Circulation, 43, 703.
12. Lev, M. (1972): Prog. cardiovasc. Dis., 15, 145.
13. Frink, R. J. and James, T. N. (1973): Circulation, 47, 8.
14. James, T. N., Hacker, D. B. and Marshall, T. K. (1974): Ibid., 49, 772.
15. James, T. N., McKone, R. C. and Hudspeth, A. S. (1975): Ibid., 51, 379.
16. Combrinck, J. M., Davis, W. H. and Snyman, H. W. (1962): Amer. Heart J., 64, 397.