Congenital Familial Nodal Rhythm

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It has been known for years that the more serious cardiac arrhythmias, atrial fibrillation, atrial flutter, and even ventricular tachycardia, can exist in persons without demonstrable evidence of heart disease. One of the initial comprehensive reviews of this phenomenon was that of Orgain, Wolff, and White in 1936, who reported 47 individuals presenting uncomplicated atrial fibrillation and 5 patients exhibiting atrial flutter.

The much rarer phenomenon of familial cardiac arrhythmias, to our knowledge, has been documented in the literature on only 4 occasions, and in each instance the arrhythmia was atrial fibrillation. Three normal brothers, who were included in the previous review, were subsequently presented in a more extensive report by Wolff in 1943. Additional case reports of atrial fibrillation in 2 elderly but apparently normal brothers were reported by Levy in 1942. Lindqvist and Soderstrom, in 1945, found uncomplicated atrial fibrillation in identical twins, 42 years of age. More recently, Gould described a family covering 5 generations in which, of a total of 113 individuals, 10 men and 12 women were found to have atrial fibrillation without attendant abnormal cardiac findings. The earliest age of occurrence was 32 years. Four cases were described in detail, and in each instance this arrhythmia developed during or after the sixth decade of life. The fairly late onset of the arrhythmia in many of these individuals makes it difficult to eliminate completely the possibility of underlying arteriosclerotic heart disease as a predisposing factor.

A review of the pertinent literature has failed to disclose an example of a familial arrhythmic trait, specifically nodal bradyarrhythmia, so dominant as to express itself congenitally in all the offspring of a given ancestor. It is the purpose of this paper to report an example of such a familial trait. Recently, we have had the opportunity of examining 2 brothers who have manifested nodal bradyarrhythmia apparently since birth or early youth. Through them we have succeeded in obtaining histories and electrocardiograms of their parents, their siblings, and their offspring (fig. 1). Nine descendants exhibit nodal rhythm and probably have done so since birth.

Of further interest is the development of paroxysmal atrial fibrillation in 4 individuals who have attained the fourth decade of life. We shall record and briefly discuss the case histories of 2 family members in detail.

Case Reports

Case 1

G. W. (fig. 1, IV-10) is a 50-year-old civil engineer who was referred to Duke Hospital for the management of a long-standing arrhythmia. During his childhood he was aware that his pulse was always slow, and although asymptomatic, he was restricted from engaging in strenuous athletics. In 1942 after being described as “100 per cent perfect with a pulse of 76 and a blood pressure of 130/80 mm. Hg,” he was accepted for military service. During training, however, he noted transient episodes of “fluttering,” weakness, and dyspnea. When examined for advancement to officer status, he was found to have a slow pulse and a heart murmur, and he was hospitalized with the tentative diagnosis of an interatrial septal defect. After refusing cardiac catheterization, he was given a medical discharge. Because of recurrent bouts of “fluttering” and shortness of breath, he found that he could no longer continue with the physically demanding job of civil engineering. He was then compelled to take a more sedentary position as a draftsman. While taking several medications in 1954, he developed an extensive dermatitis. All drug therapy was then withdrawn. From that time until 1958 he restricted himself to sedentary activities and apparently was
his "heart had stopped." This was followed by vague chest pain, shortness of breath, profuse perspiration, momentary loss of consciousness, and urinary incontinence. Shortly thereafter he was admitted to Duke Hospital. The patient's past history was otherwise unremarkable.

Physical examination revealed a moderately obese white man in no distress. Blood pressures were 130/90 mm. Hg supine and 140/90 mm. Hg standing. The radial pulse was grossly irregular at a rate of 84 beats per minute. There was no overt evidence of decompensation. The lungs were entirely clear. The heart on percussion appeared at the upper limits of normal in size. No thrills or shocks were noted. A grade-I systolic murmur was audible at the apex, and a systolic ejection sound was heard over the pulmonary out-flow tract. P₂ was greater than A₂ but was not split.

Laboratory studies revealed the following pertinent findings: multiple electrocardiographic tracings sent in by the patient's personal physician, covering a 10-year period from 1949 to 1959, recorded predominantly nodal bradycardia and on one occasion sinus bradycardia. Atrial fibrillation was observed in 1958. Subsequently a communication from another physician confirmed the presence of atrial fibrillation by electrocardiogram as early as 1945 and in 1947 nodal rhythm was recorded.

A baseline electrocardiogram on admission revealed atrial flutter-fibrillation with a ventricular rate of 80 and evidence of digitalis effect. Multiple chest x-rays and cardiac fluoroscopy disclosed "large hilar shadows, slight cardiac enlargement
and a prominent pulmonary out-flow tract (fig. 2).

Right heart catheterization and dye-dilution curves failed to reveal any evidence of intracardiac shunting. Right atrial and right ventricular pressures were normal. Pulmonary artery pressures were not obtained because of the development of ventricular irritability associated with mild chest pain and hypotension while the catheter was in the right ventricle. The procedure was therefore terminated and the patient quickly recovered without ill effects. Subsequently, under intense digitalis therapy his ventricular rate slowed to 60. Quinidine was then instituted and after 1.6 Gm. the rhythm reverted to a basic nodal bradycardia with an occasional wandering pacemaker and more rarely, isolated normal sinus beats. After exercise the ventricular rate increased by at least 10 beats above resting levels. Following intravenous atropine sulfate, 1.8 mg., the rate increased from a baseline of 45 beats per minute to a high of 75 beats per minute but nodal rhythm still persisted (fig. 3).

Because of the satisfactory response to atropine sulfate, the patient was discharged on 0.3 mg. of the drug 3 times a day. He returned 5 months later, having stopped the atropine sulfate because of distressing eye symptoms but having continued his quinidine, 0.4 Gm. 4 times a day. He continued to complain of easy fatigability and, on mild exertion, shortness of breath and "fluttering" of his heart. He had previously changed his occupation from draftsman to photographer but now found that he no longer had the energy to continue with either. His physical examination was essentially unchanged. The apical rate was 50 beats per minute and an electrocardiogram revealed wandering of the pacemaker from sinus to node. After 1.6 mg. of atropine intravenously, nodal rhythm appeared at a rate of 70. On the morning of the following day, after 15 mg. of dextro-amphetamine sulfate, in spasmule form, he felt well and somewhat livelier than usual. A tracing showed nodal rhythm at a rate of 60 beats per minute. He was advised to continue dextro-amphetamine and quinidine therapy.

Case 2

R. W. (fig. 1, IV-14) a 42-year-old music teacher and brother of G. W., was admitted 1
month after his brother’s discharge for evaluation of a similar cardiac arrhythmia. Their histories were quite similar. The patient enjoyed good health as a youth and participated in numerous sports, especially tennis. He was aware that his pulse was slow, usually about 50 beats a minute but he experienced normal growth and development without cardiovascular symptoms. At age 19 while in college he was denied life insurance because of an “enlarged heart and a heart murmur.” On 3 occasions he was rejected from the service in World War II because of a “heart condition.” His Selective Service record is quoted as stating “congenital malformed heart, rough systolic pulmonic murmur with thrill and increased pulmonary conus with relative stenosis.” “X-rays showed widening of the upper part of the heart and hilar shadow, very likely cardiac enlargement.” With the advent of war he left school and went to work in a powder plant, but when hostilities ceased he returned to college at the age of 30. It was here, while engaged in the strain of constant study, that he first experienced chest tightness and palpitation, which he described as a “nervous feeling.” It was his impression that his first episode was gradual in onset and was unassociated with shortness of breath or ankle swelling. Symptoms gradually subsided over a 12-hour period during hospitalization. Subsequently numerous such episodes were experienced, oftentimes in the wake of mental stress. Four years prior to admission quinidine prophylaxis was instituted, but he took the medication only sporadically. Despite these distressing episodes, he continued his activities as a band director and was apparently able to play wind instruments without difficulty. One month prior to admission, he developed an upper respiratory infection associated with fever, sweating, aching, and coughing. Then he developed a sudden episode of palpitation, which although controlled by digitalis, nevertheless persisted until his admission to Duke Hospital.

The general physical examination revealed a well-developed, moderately obese man in no distress. The supine blood pressure was 155/95 mm. Hg and standing 145/90 mm. Hg. The chest was symmetrical and expanded well. High-pitched squeaks and rhonchi were readily heard but no moist alveolar rales were heard. The heart was percussed approximately 11 cm. to the left of the midsternal line. No thrills or shocks were noted. The rhythm was grossly irregular with an apical rate of 120 beats per minute and a radial rate of 80 beats per minute. M1 was split but no apical murmurs were heard. A systolic ejection sound was heard over the pulmonary out-flow tract; P2 was greater than A2 but was not split. The remainder of the examination was unremarkable and there were no signs of heart failure.

Baseline electrocardiograms revealed atrial fibrillation with a rapid ventricular response and numerous premature ventricular extrasystoles. Electrocardiograms accompanying the patient disclosed nodal rhythm in 1958. An electrocardiogram taken 2 months prior to admission exhibited atrial fibrillation with a ventricular response of 100 and occasional periods of ventricular tachycardia with multifocal extrasystoles. Multiple chest x-rays and fluoroscopy demonstrated the heart to be slightly enlarged in all diameters with a pulsating shadow along the left margin, suggesting an enlarged pulmonary out-flow tract (fig. 4). The secondary pulmonary branches did not pulsate actively. To the radiologist these findings suggested the presence of a possible patent ductus arteriosus.

During hospitalization digitalization was completed and then right heart catheterization was performed. The resulting oxygen samples and dye-dilution curves revealed no evidence of intracardiac shunting. All right-sided chamber pressures were normal and the cardiac output was 5 liters per minute at rest. Following catheterization quinidine administered orally in divided doses to a total of 2.4 Gm. reverted the rhythm to a basic nodal rhythm at a rate of 66, which subsequently slowed to 40 beats per minute. The cardiac rate increased with exercise but increased to a greater degree after atropine (fig. 5). Because of the
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Figure 5
A. Admission electrocardiogram on R.W., showing atrial fibrillation. B. After conversion with quinidine, nodal bradycardia resulted. C. After atropine, the rate increased to 70.

Discussion

In both brothers the presence of an arrhythmia and the striking x-ray findings of an enlarged pulmonary out-flow tract suggested either congenital heart disease or, less likely, pulmonary disease with secondary right heart enlargement. Though pulmonary function studies were not performed, there was no reason to incriminate pulmonary disease in G. W. and less reason in R. W. since, despite his mild chronic bronchitis, as a band director he plays wind instruments without difficulty. Other than nodal rhythm and atrial fibrillation the electrocardiograms in both patients show only minor T-wave changes. In R. W. cardiac catheterization revealed normal right-sided pressures, a normal cardiac output, and no increase in arteriovenous oxygen difference. In G. W. inability to traverse the pulmonary artery prevented us from obtaining samples for arteriovenous oxygen difference and Fick outputs; however, resting cardiac outputs performed by the dye-dilution method were normal. We therefore concluded that we could not incriminate any specific disease process to explain the radiologic findings.

Under normal circumstances, the cardiovascular system responds to peripheral demands with an increase in cardiac output...
Bipolar limb leads taken on the maternal ancestor 2 years prior to death. Atrial fibrillation with a rapid ventricular rate, left bundle-branch block, and multifocal premature contractions are present. B. In contrast this normal electrocardiogram was recently taken on the paternal ancestor who is still living and well at 72 years of age.

primarily through an augmentation in both heart rate and stroke volume. It is suggested that in these individuals, just as in those with congenital heart block, nodal bradycardia significantly limits the tachycardiac response and therefore the increase in cardiac output can only be accomplished through an augmentation in stroke volume. Over a period of years the cardiovascular system may "physiologically adapt" to its limitations and this adaptation may manifest itself by cardiac enlargement.

The family history was striking. The patients' father (fig. 1, III-10) though elderly, enjoyed excellent health and was "healthier than the patient." The father has a normal electrocardiogram (fig. 6B) and is still living and well at 72 years of age without evidence of cardiac disease. The father's family is not included in figure 1 because they did not have any heart disease to the best of our knowledge; one sister age 80 is living and well; one brother age 70 is living and well; and one brother age 73 died of a cerebrovascular accident. Both of the father's parents are dead; the cause of their deaths is not known.

In contrast, many of the maternal family members are reputed to have or have had heart trouble. The mother of our patients (fig. 1, III-9) was informed of heart trouble after her marriage at 22 years of age, and was given only a short time to live. Contrary to prediction, she lived to the age of 71 years, working hard all her life. It is believed that in her early adult years she manifested a
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slow pulse, but during the last 20 years of her life she had documented atrial fibrillation. After years of borderline cardiac compensation she finally died in congestive heart failure. The electrocardiogram taken on the mother 2 years prior to death exhibited a markedly chaotic rhythm with atrial fibrillation and a rapid ventricular rate characterized by complete left bundle-branch block and numerous ectopic multifocal ventricular contractions, which simulate runs of ventricular tachycardia (fig. 6A). All 4 children (fig. 1, IV-10, 12, 14, 15) had nodal bradycardia, known to have been present as early as 9 years of age in one case, and all also developed documented paroxysms of atrial fibrillation. Characteristically this has occurred either late in the third decade or early in the fourth decade of life. Their respective offspring and even the grandchild of G. W. (fig. 1, VI-3), though asymptomatic, manifest a nodal rhythm, which seems to have occurred at birth (fig. 7). Table 1 illustrates in composite form certain characteristics of the arrhythmia as it applies to each member of the family.

Judging from the histories of our documented group, we can venture a prophecy that a very likely series of events occurring in subsequent members of this family might be as follows: a normal childhood and development without evidence of physical disability though characteristically the slow but regular pulse would be evident. Symptoms characterized by sudden transient episodes of a "fluttering or nervousness" in the chest may begin in the late twenties or early thirties. Otherwise these individuals will be asymptomatic. Finally, there may occur established atrial fibrillation requiring definitive therapy for relief. Despite this discomforting picture, the total outlook does not appear distressing and the prognosis for

Figure 7
Representative leads from descendants with documented nodal rhythm. Roman numerals refer to the generation and arabic numerals refer to the individuals; refer to figure 1.
Table 1

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<thead>
<tr>
<th>Certain Characteristics of the Arrhythmia Tabulated for Each Family Member</th>
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<tr>
<td>Generation Member</td>
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<tr>
<td>Age Dead</td>
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<tr>
<td>Subjective estimate of health</td>
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<tr>
<td>History of &quot;fluttering heart&quot; or other suggestive cardiac symptoms</td>
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<tr>
<td>Age of onset of &quot;fluttering&quot;</td>
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<td>Known atrial fibrillation</td>
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<td>Age slow heart rate</td>
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<td>first became apparent</td>
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<td>Documented nodal rhythm</td>
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longevity with proper precautions appears excellent.

The mechanism of this unusual familial characteristic remains highly conjectural. Genetically, it appears to be a dominant autosomal trait with an extremely high degree of penetrance. Initially, it was suspected that through an inherited defect there resulted congenital absence of the sinoatrial pacemaker, but the occasional occurrence of transient sinus bradycardia, seemingly emanating from the sinoatrial node even though infrequent, would tend to militate against this mechanism. Still another possible explanation could lie in the fact that the atrioventricular node and not the sinoatrial node is the dominant pacemaker, again through an inherited aberration. Why atrial fibrillation should subsequently occur in these individuals remains unknown. Recent experimentation by Scherf et al.7 has shown that vagal stimulation under certain circumstances will consistently result in atrial fibrillation in the dog. Accordingly, one may entertain the possibility of nodal rhythm converting to atrial fibrillation in the presence of an inordinate degree of vagal tone. Whatever the exact mechanism is, this last point seems clear: like physical characteristics, unusual disturbances of cardiac rhythm may have a genetic mechanism of expression.

Summary

An unusual family group covering 3 generations is presented, all of whose members manifest a characteristic arrhythmia that appears to be an inherited trait. Each of the 9 known descendants exhibits a nodal bradycardia and each of the 4 descendants who have entered the fourth decade of life have also experienced paroxysms of atrial fibrillation. These paroxysms almost invariably terminate with the re-establishment of nodal rhythm. By history, the majority of these individuals are asymptomatic, and detailed examination of 2 adult members has failed to uncover evidence of specific cardiac disease. The problem of familial arrhythmia is briefly reviewed.

Summario in Interlingua

Es presentate un unusual gruppo familial con membros de 3 generationes qui omnes manifesta un arrhythmia caracteristica que pare esser un tracto de hereditate. Omne le 9 cognoscite descendentes exhibi un bradycardia nodal e omne le 4 descendentes qui ha entrate in le quarte decennio de lor vitas ha etiam experientiate paroxysmos de fibrillation atrial. Iste paroxysmos se termina quasi invariablemente in le restablimento de rhythmio nodal. In lor antecedentes le majoritate de iste subjectos es asymptomatic, e le detaliate examine de 2 membros adulte ha pro-
ducite nulle signo de specific morbo cardiac. Le problema de arrhythmia familial es revistate brevemente.

References

Aneurism of the Aorta; Singular Pulsation of the Arteries, Necessity of the Employment of the Stethoscope

By D. J. CORRIGAN, M.D.

Lecturer on the Institutes and Practice of Medicine; one of the Physicians of the Sick-Poor Institution, Dublin.

"Such, however, was the power of prejudice, that it is observed, by Harvey, that no physician, passed the age of forty, believed in his doctrine; and that his practice declined from the moment he published this ever-memorable discovery." Medical Facts, Vol. 1.

Many of the profession still view with scepticism the utility of the stethoscope, in ascertaining the exact nature of thoracic disease.

I shall not enter into any general discussion on the merits of the instrument. This is obvious, that those who use it have not only all the information to be derived from symptoms, history of the disease, etc., which its opponents enjoy; but that, in the instrument, they have a medium super-added through which to obtain additional knowledge, and they are thus enabled to come to the examination of thoracic disease, as it were, with increased powers of mind.—The Lancet, 1:586, 1829.
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