Sinus bradycardia

Autonomic influences and clinical assessment

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Twenty-four patients with sinus bradycardia and 16 control subjects were investigated using various autonomic reflex manoeuvres and drug response tests.

Two groups of patients are suggested by the results: 1) Bradycardia due to atrial disease (sinoatrial disease/sick sinus) – poor autonomic responses, 16 patients. Of those with poor autonomic responses, 9 had additional AV conduction defects, and half had experienced Adams-Stokes syncope. 2) Bradycardia of physiological origin – normal or supernormal autonomic responses. a) Those with normal autonomic function, 7 cases. The dominant atrial pacemaker in this group is possibly set at a lower rate than normal. Such patients were not found to be liable to Adams-Stokes syncope, but may have vasomotor syncope. b) Vagotonia, 1 case. On the basis of one patient it is suspected that sinus bradycardia may be due to 'vagotonia' or due to an unusual sensitivity of the atrium to vagal influence. All autonomic responses were supernormal. Such patients, though probably rare, may be especially liable to vasomotor syncope.

It is suggested that the investigations presented are useful in the routine assessment of patients presenting with syncope and sinus bradycardia. Those patients with symptoms and poor autonomic responses may require pacing while those with physiological responses may need no treatment or may be helped by drugs.

Although most patients presenting with sinus bradycardia are asymptomatic, some present with syncope or dizzy spells. Physiological bradycardia is usually of no clinical significance except when seen in association with vasomotor syncope. When a patient presents with Adams-Stokes syncope and sinus bradycardia the problem is to differentiate the bradycardia of physiological origin from that which may be associated with some atrial pathology.

The aim of the present work has been to investigate the autonomic influences acting in sinus bradycardia and to develop routine tests useful in differentiating the physiological from the pathological type of bradycardia caused by atrial disease. The tests described have developed from the need to assess the clinical significance of sinus bradycardia in patients with syncopal attacks.

The sinoatrial node and atrium are richly innervated by both sympathetic and parasympathetic nerve fibres (Grodner *et al.*, 1970; James, 1967), the pacemaker cells being directly affected by the release of the acetylcholine and catecholamines (James and Nadeau, 1963; Hoffman and Cranefield, 1960; Toda and Shimamoto, 1968; Toda and West,

1967; Grodner *et al.*, 1970). The presence of the enzyme cholinesterase may be of importance in the control of the heart rate since it is responsible for the hydrolysis of acetylcholine and can be demonstrated in active form in the sinoatrial node and atrium (James and Spence, 1966).

Patients presenting with sinus bradycardia have been investigated by using various reflex tests and by infusion of drugs acting on the autonomic system and atrial pacemaking sites.

Selection of subjects and methods

Sixteen healthy adults volunteered as control subjects after being fully informed about the nature of the investigation.

Twenty-four patients with a persistent bradycardia at rest of less than 55 a minute were investigated after giving fully informed consent. No patient was admitted to the investigation if the bradycardia could be related to drug therapy, untreated hypothyroidism, raised intracranial pressure, recent cardiac infarction, or cerebrovascular accident. Some patients presented with symptoms while others were found to have a persistent resting sinus bradycardia on routine electrocardiography. Patients with fixed rate pacemakers were excluded while some with demand pacemakers were

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included. This selection was necessary since only demand pacemakers may be externally inhibited allowing the underlying spontaneous rhythm to manifest itself.

All subjects were examined and weighed before investigation. Those with demand pacemakers had their units inhibited by an external pulse generator attached at least 15 minutes before investigation.

a) Reflex tests

With a continuous electrocardiographic recording (lead chosen to show largest P waves), all subjects performed simple manoeuvres designed to stimulate the dominant atrial pacemaker by autonomic reflexes. Recording started 10 to 15 seconds before the reflex test and was continued throughout and for 10 seconds after each manoeuvre. Recordings were made with quiet respiration, forced inspiration (with breath held in inspiration for a minimum of 15 seconds), a Valsalva manoeuvre, using a sphygmomanometer blown up to 40 mmHg, for a minimum of 15 seconds and continued for as long as possible; right and left carotid sinus pressure continued until maximum response was obtained (up to 10 seconds usually); and straight leg raising for 30 seconds. All the tests were performed in the sitting position on a couch or bed. The electrocardiograms obtained were analysed for atrial rate using a standard rate calculating ruler averaging two consecutive PP intervals. The control rate was taken as the average of three measurements. The maximum or minimum rates during and after the manoeuvres were noted and expressed as the rate difference above or below the control rate. Any changes in P wave morphology or changes in rhythm were noted. As far as possible recordings were made only during regular sinus rhythm. Recordings with nodal rhythm or some irregular rhythm were rejected and the manoeuvre repeated.

b) Drug tests

After the reflex tests, with the patient supine and at rest, intravenous bolus injections of the following drugs were made into a normal saline intravenous infusion. i) 5 µg isoprenaline per 70 kg body weight (prepared in 2 ml vials, 5 µg/ml containing sodium metabisulphate); ii) 0.02 mg atropine sulphate per kg body weight; iii) 0.8 mg prostigmine per 70 kg body weight given 20 minutes after the dose of atropine.

The drugs were given in the order shown and flushed in with not more than 2 ml normal saline. A period of approximately 10 minutes elapsed between the doses of isoprenaline and atropine while the heart rate returned to previous control level. Only one dose of each drug was given.

The doses given were chosen to give an easily measurable response without resulting in undue side effects. The dose of prostigmine was suggested by the work of Fielder *et al.* (1969).

Electrocardiograms were made continuously, 10 seconds before and 1 minute after the dose of isoprenaline. Only regular sinus rhythm was accepted as suitable during the control period. The same procedure was followed for the atropine dose but further electrocardio-

grams (5 to 10 second strips) were taken every 5 minutes until 20 minutes after injection. At 20 minutes after atropine the dose of prostigmine was given. After the dose of prostigmine, 10-second recordings were made every minute for 10 minutes.

The electrocardiograms were analysed for atrial rate with a standard rate calculating ruler. The control rates were taken as an average of five measurements during the control period before each dose, only regular sinus rhythm being acceptable during this period. In the case of both atropine and isoprenaline the atrial rate was analysed with one measurement at every 3-second interval during the first minute. Further measurements were made at 15-second intervals for a further 2 minutes. Thereafter, in the case of atropine, measurements of atrial rate were made at 5-minute intervals until prostigmine was given. During this analysis changes in rhythm or P wave morphology were noted. During the prostigmine response an average of five measurements was made at one minute intervals.

The results were plotted as atrial rate against time in each case. Atrial response was assessed in two ways: i) the maximum or minimum rate obtained above or below the mean control rate, and ii) the maximum rate of rise or fall in atrial rate during the response. This was estimated from a gradient drawn through the steepest four points on the response curve.

Results

The ages, sex, mean resting heart rates, electrocardiographic features, clinical features, and past history of both controls and those with sinus bradycardia are given in Table 1.

Seven patients presenting with sinus bradycardia were found to have P wave abnormalities; 4 having flat or bifid P waves (voltage less than 0.1 mV) with 3 others having P waves of greater duration than normal (0.16 sec). A PR interval greater than 0.2 sec was seen in 8 patients, no higher degrees of AV block being seen. A QRS duration greater than 0.1 sec was seen in 5 patients each with right bundle-branch block and left axis deviation. His bundle electrograms showed normal His to ventricular activation times in these patients.

Reflex tests

The changes in atrial rate with the various reflex manoeuvres are shown in Table 2. No significant quantitative difference could be shown between the control responses to quiet breathing, forced inspiration or straight leg raising, and those presenting with sinus bradycardia. While the increase in rate during a Valsalva manoeuvre was not significant, the total drop in rate after the manoeuvre was significantly less in the sinus bradycardia group.

Qualitative changes during the reflex responses were not seen in the control group. In the sinus bradycardia group various changes were seen.

TABLE 1 Clinical features sinus bradycardia

	Controls	Sinus bradycardia
Number of patients	16 $\begin{cases} 8 \text{ male} \\ 8 \text{ female} \end{cases}$	24 $\begin{cases} 12 \text{ male} \\ 12 \text{ female} \end{cases}$
Age range	17-70 yr mean 52 yr	29-77 yr mean 61 yr
Mean resting atrial rate	74.5/min	47.1/min
Number with past history of:		
Adams-Stokes syncope	0	10
Vasomotor syncope	0	6
Cardiac pain	0	5
Myocardial infarction	0	3
Diphtheria	0	3
Rheumatic fever	0	1
Epilepsy	0	1
Hypothyroidism (treated)	0	1
Electrocardiographic features		
Atrial arrhythmia	0	12
Atrioventricular conduction defect	0	12
Ischaemia	0	4
Cardiac infarction	0	3
Number requiring pacemakers (permanent systems)		
	0	9

During forced inspiration atrioventricular nodal rhythm was seen in 4, while sinus arrest was seen in one. During right carotid sinus pressure atrioventricular nodal rhythm was seen in 3, with sinus arrest occurring in 1 patient. Similar responses were observed with left carotid sinus pressure, atrioventricular nodal rhythm occurring in 2 and sinus arrest occurring in 2 others.

Drug tests (Table 2)

1) Isoprenaline response Both the increase in atrial rate and the maximum rate of change of atrial rate were significantly lower in the sinus bradycardia group than in the control subjects ($P < 0.01$) (Table 2). No P wave changes were seen in the controls during this response nor were any arrhythmias observed. The PR interval did not vary in any control subject. In one control subject the T wave became flat.

Of the 22 subjects with sinus bradycardia, 14 failed to achieve atrial rates within control range (Table 2) (Cases 1, 3, 5, 6, 8, 9, 12, 13, 15, 17, 18, 20, 22, 24). One patient (Case 10) spontaneously reverted to atrial fibrillation after the reflex tests and was therefore not tested further. In another

TABLE 2 Results of reflex and pharmacological tests in sinus bradycardia

Investigation	Change in atrial rate relative to control rate				
	Controls		Sinus bradycardia		P
	Mean	Range	Mean	Range	t-test
Respiratory arrhythmia	9.17/min	3, 18/min	5.5/min	2, 20/min	> 0.1
Forced inspiration	- 4.75	+ 7, - 26	- 2.67	+ 23, - 26	< 0.1
Valsalva (during)	+ 23.64	+ 10, + 47	+ 14.2	- 21, + 44	< 0.1
(after)	- 38.9	- 19, - 78	- 17.6	0, - 53	< 0.01
Right carotid sinus pressure	- 22.36	- 2, - 47	- 11.1	- 3, - 22 + sinus arrest	< 0.02
Left carotid sinus pressure	- 14.7	0, - 32	- 7.3	- 1, - 19 + sinus arrest	< 0.05
Straight leg raising	+ 16.6	+ 2, + 30	+ 13.2	+ 1, + 38	> 0.2
Isoprenaline	(a) + 30.5	+ 22, + 39	+ 19.1	+ 4, + 40	< 0.01
	(b) + 1.9	+ 0.9, + 3.0	+ 1.07	+ 0.01, + 3.0	< 0.02
Atropine	(a) + 34.75	+ 14, + 53	+ 31.46	+ 12, + 70	> 0.2
	(b) + 1.97	+ 0.85, + 2.8	+ 1.99	+ 0.3, + 8.7	> 0.2
Prostigmine	(a) - 25.6	- 15, - 46	- 16.8	- 5, - 57	> 0.1
	(b) - 3.9*	- 3, - 5.7*	- 2.9*	- 0.28, - 10*	> 0.2

(a) Increase in atrial rate (beats/minute).

(b) Rate of change of atrial rate (beats/min/sec)

(*beats/min/min)

patient (Case 14) the rate achieved was above control range.

On the basis of decreased rate of change of atrial rate 11 patients had responses below normal range (Cases 1, 3, 5, 6, 12, 13, 15, 16, 17, 19, 23). One had an above normal response (Case 14), the remaining responses falling within control range.

In 2 patients frequent change in P wave shape occurred (Cases 11, 23), with atrioventricular nodal rhythm occurring at times in 5 (Cases 6, 11, 12, 13, 16). Supraventricular ectopics were frequently observed in three (Cases 1, 3, 6).

2) Atropine responses No significant difference ($P > 0.2$) was found with either the increase in atrial rate or in the maximum rate of change of atrial rate between the control and sinus bradycardia groups. Only one patient had a response below the normal range (Table 2) (Case 12) and one had a response above normal range (Case 14). With respect to the rate of change of atrial rate with atropine, 5 patients had responses below the control range (Table 2) (Cases 1, 13, 15, 20, 24), 3 of whom exhibited atrioventricular nodal takeover (Cases 1, 13, 20).

In the control group atrioventricular nodal takeover occurred in one subject. In most subjects the PR interval decreased by 0.04 sec. Nodal takeover was observed in 8 patients (Cases 1, 3, 6, 12, 14, 16, 19, 20), with P wave variation occurring in one case (Case 23).

3) Prostigmine responses Prostigmine was seen to return the atrial rate to preatropine levels only. When those with sinus bradycardia are compared with controls, the differences between the drop in atrial rate and the rate of change of atrial rate fail to reach significant levels ($P > 0.1$).

In 13 of the sinus bradycardia group the decrease in atrial rate observed was below the normal range (Table 2, Cases 2, 3, 5, 6, 7, 8, 12, 16, 17, 20, 21, 23, 24). One patient (Case 14) decreased his atrial rate greater than any control subject.

Fourteen patients had a decrease in the rate of change of atrial rate below the control range (Cases 1, 2, 3, 5, 6, 12, 13, 16, 17, 20, 21, 22, 23, 24). Four patients had responses greater than the control range in this respect (Cases 4, 9, 14, 19).

Results and clinical features

Of the 10 patients that had both reduced reflex and drug responses (Cases 3, 6, 8, 13, 16, 17, 20, 21, 23, 24), 5 had a history of Adams-Stokes attacks (Cases 3, 6, 13, 17, 20) and 2 a history of fainting attacks (Cases 3, 8), with 5 requiring pacing (Cases 6, 13,

17, 20, 23). Two were satisfactorily controlled with long-acting isoprenaline (Cases 3, 16). These patients all had below normal atrial responses and are therefore likely to have sinoatrial disease or 'sick sinus syndrome'.

Of the 10 patients with both reduced reflex and drug responses, 5 had an abnormality of either P wave voltage or morphology (Cases 3, 8, 13, 17, 23), 2 had evidence of sinoatrial block (Cases 6, 16), 2 of sinus arrest (Cases 8, 17), one of paroxysmal atrial fibrillation (Case 13), and 4 had atrioventricular nodal rhythm at times (Cases, 16, 17, 21, 23). Of the 10 cases with reduced responses, 4 had evidence of right bundle-branch block with left axis deviation but no prolongation of His to ventricular activation time. There was, therefore, no electrophysiological evidence of trifascicular bundle-branch disease in these cases. Since one patient also had first-degree atrioventricular block with a PR interval of 0.32 to 0.4 sec, 5 of the 10 patients with reduced reflex and drug responses had evidence of abnormal atrioventricular conduction.

There were 6 patients with reduced drug responses but normal reflex tests (Cases 1, 2, 5, 12, 15, 22). One of these had abnormal P waves with intermittent sinus arrest (Case 5), 3 had nodal rhythm at times (Cases 1, 12, 15), 2 had right bundle-branch block with left axis deviation (Cases 1, 15), and 2 had prolonged PR intervals (Cases 5, 22). None was seen to have either sinoatrial block or atrial fibrillation. Of these 6, 5 had a history of Adams-Stokes attacks (Cases 2, 5, 12, 15, 22), with 3 requiring pacing (Cases 5, 12, 22). This association makes it likely that these patients have sinoatrial disease or 'sick sinus syndrome'. One was controlled with long-acting isoprenaline (Saventrine). One only had a history of fainting episodes.

Eight patients (Cases 4, 7, 9, 10, 11, 14, 18, 19) were found to have no evidence of reduced atrial pacemaker function. Of these, 3 had syncope which was thought to be vasomotor in type (Cases 4, 11, 14) rather than Adams-Stokes syncope. Three had paroxysmal atrial fibrillation, one had occasional atrioventricular nodal rhythm, and one other had periods of sinus arrest (Case 11). While 2 of these patients had first-degree atrioventricular block, none had evidence of bundle-branch block. These patients have either physiological sinus bradycardia or undetectable sinoatrial disease.

Discussion

Several workers have found that there may be reduced reflex and drug responses of heart rate in patients with slow atrial arrhythmias or sick sinus syndrome (Brasil, 1955; Shaw and Eraut, 1969;

Eraut and Shaw, 1971; Easley and Goldstein, 1971; Mandel *et al.*, 1972). Whether the responses so defined were reduced relative to normal is less definite since no control group data have been published. Mandel *et al.* (1971) did however use post-pacing suppression to confirm subnormal atrial pacemaker function in their patients. After atrial pacing, good sinoatrial function is attended by early atrial takeover and poor function by delayed takeover.

The results of the present work show that there are two groups of patients with sinus bradycardia, those with normal reflex and drug responses and those with reduced responses. When these tests are used to differentiate two groups the inclusion of patients with probable physiological bradycardia has perhaps tended to reduce the statistical significance of some results.

The results of this work suggest that those with the presented evidence of reduced atrial pacemaker function are liable to Adams-Stokes attacks. Inadequacy of lower pacemaking sites may be important in the production of Adams-Stokes syncope in these patients. Those with normal atrial pacemaker responses may have been subject to syncope of vasomotor origin, but not to Adams-Stokes attacks.

On the basis of drug responses alone, all patients with Adams-Stokes attacks had evidence of reduced sinoatrial automaticity. Of the 8 patients found to have Adams-Stokes attacks, 4 had no electrocardiographic evidence other than sinus bradycardia to suggest reduced atrial pacemaker function. One other had a P wave abnormality alone while 3 others had both P wave abnormalities and atrioventricular nodal rhythm at times.

P wave abnormalities, atrial fibrillation, sinoatrial block, and sinus arrest have been found to occur commonly in association with defective sinoatrial pacemaker function. The same abnormalities were found, however, in some with normal atrial function, suggesting either the physiological origin of these arrhythmias or defects not detected by the present investigations.

Since no pathological data are available at present, it remains to be shown that reduced responses to autonomic stimuli are associated with recognizable atrial pathology. From the present work one may deduce only that there is a disturbance of atrial pacemaker function in some patients. The available evidence suggests that sinus arrest, atrioventricular nodal rhythm, etc. (sick sinus syndrome) are associated with atrial pathology (Brasil, 1955; Rossi, 1969).

Some patients in this series were paced up to 15 minutes before investigation. The influence of long-

term ventricular pacing on atrial pacemaker function is unknown. In short-term atrial pacing it is characteristic for atrial rhythm to return within seconds after the cessation of pacing (Mandel *et al.*, 1971). In this series those paced for syncope due to a sinoatrial problem were the most likely to have an abnormality. One paced patient was found to have supernormal autonomic responses whereas others had only minor abnormalities of function. The finding of reduced responses in unpaced patients shows that the phenomenon is not solely pacing induced. In the absence of any known mechanism for atrial pacemaker suppression by ventricular pacing it must be assumed that reduced responses to autonomic stimuli are most probably caused by a disturbance of atrial pacemaker cells themselves.

Nine of the patients with defective sinoatrial pacemaker function were found to have an atrioventricular conduction defect, suggesting that 'sinoatrial disease' is part of a widespread conducting tissue disease. As in complete heart block idiopathic fibrosis may possibly be the commonest cause of sinoatrial disease.

The benefit of performing reflex tests lay in the opportunity afforded to observe the occurrence of arrhythmias. During these tests, nodal escape, implying lesser automatic function in the atrial pacemaking sites, sinus arrest, and supraventricular tachycardias were occasionally seen, often with reproduction of the patients' symptoms. Some clue as to the mechanism of the patients' dizzy spells, palpitations, or syncope was thus discovered. In some cases many hours of ward monitoring had failed to reveal a significant arrhythmia.

Isoprenaline infusion, as a bolus infusion, proved to be the most useful quantitative discriminating test of atrial pacemaker function. With the dose given occasional ectopics were seen and then only for a short period. The response lasted 2 to 3 minutes and at worst caused only brief palpitation. The present results do not support the results of Mandel *et al.* (1972), i.e. that good responses are obtained in all patients with sinoatrial disease or sick sinus syndrome. The doses of isoprenaline used in this study were much smaller however. Their method of continuous drip infusion of isoprenaline was not employed since it is difficult to standardize and is more liable to cause prolonged symptoms and arrhythmia. The results of the present work agree with those of Brasil (1955) and of Eraut and Shaw (1971) in showing that patients with sick sinus syndrome have reduced responses to isoprenaline.

The lack of control data in previous work may have led to the conclusion that atrial responses to atropine are reduced in 'sick sinus syndrome'. In the control subjects studied the range of normal

responses to atropine was large, thus diminishing the usefulness of atropine infusion as a clinical test of atrial pacemaker function. Since atropine competitively inhibits acetylcholine it may be that there is no atrial abnormality in atrial acetylcholine in sinoatrial disease – that is if the heart rate response to atropine is directly related to the amount of transmitter present.

It is possible that atrial cholinesterase activity is reduced in sinoatrial disease, thus leading to a build-up of acetylcholine in atrial tissues. This would cause bradycardia and perhaps result in a change of the dominant atrial pacemaker site. In the presence of a local build-up of acetylcholine, atropine might increase the atrial rate more than anticipated even in the presence of less automatic pacemaker cells. This consideration makes speculation about the role of acetylcholine in sinus bradycardia all the more difficult.

Prostigmine lowers the atrial rate by inhibition of cholinesterase, thereby increasing the availability of acetylcholine. The response is thus determined by the activity of the local enzyme together with the availability and atrial sensitivity to acetylcholine. As there is demonstrable activity of cholinesterase in the atrium of animals and humans (Csapó, 1970; James and Spence, 1966), normal responses to atropine, associated with decreased responses to prostigmine in some patients, may indicate reduced activity of atrial cholinesterase in sinoatrial disease. It is possible that reduced activity of atrial cholinesterase alone could account for some forms of sinus bradycardia. Diphtheria myocarditis, previously a cause of sinus bradycardia in man has been shown to be associated with inactive atrial cholinesterase in rabbits (Maliovanova, 1968).

Whereas, with carotid sinus pressure, sinus arrest might be caused by abnormal carotid sinus sensitivity, it might possibly be caused by either abnormal atrial sensitivity to acetylcholine or by excess local build-up of acetylcholine resultant on the inactivation of atrial cholinesterase. The finding of reduced responses to prostigmine in 3 of the 4 patients found to have sinus arrest on carotid sinus pressure supports the latter theory.

One patient having sinus arrest with carotid sinus pressure had supersensitive responses to all reflexes and to atropine, isoprenaline, and prostigmine. This supports the possibility of increased sensitivity to both sympathetic and vagal neurotransmitters in this case. Sinus bradycardia might, therefore, be caused by vagal supersensitivity in some cases.

Of the 16 patients found to have reduced atrial pacemaker function on the basis of drug responses,

8 had clinical evidence of probably significant aetiological factors. Two had resting electrocardiographic evidence of ischaemic heart disease (Cases 2, 23), 2 had previous inferior cardiac infarction (Cases 2, 5), 3 had diphtheria as children (Cases 3, 10, 24), one rheumatic fever (Case 2), one was presumed to have influenza requiring admittance to hospital (Case 4), while one other had treated myxoedema (Case 20). Of the 3 patients with ischaemic heart disease, one had first-degree atrioventricular block (Case 5). Since pathological data are not available, the presence, nature, and aetiology of any atrial disease entity has yet to be established.

As a result of this investigation, one might postulate three states of atrial pacemaker function resulting in chronic resting sinus bradycardia (unrelated to drug therapy, cardiac infarction, etc.).

1) Sinoatrial disease (sick sinus syndrome)

Sixteen cases (Cases 1, 2, 3, 5, 6, 8, 12, 13, 15, 16, 17, 20, 21, 22, 23, 24) had sinoatrial disease.

Sinus bradycardia may be due to reduced atrial pacemaker function, the best of the pacemaker sites in the atrium being unable to respond normally either to direct drug or to reflex stimulation. Because of the reduced response to some reflexes in this group, one cannot exclude additional primary disease of the autonomic atrial nerve supply. Histological evidence for atrial autonomic nerve damage has been obtained by Rossi (1969). Reduction in atrial cholinesterase may be important and explain the decreased responses to prostigmine, the often normal response to atropine, and the occasional paradoxical finding of sinus arrest with carotid sinus pressure in patients with otherwise reduced reflex responses. Patients with reduced pacemaker function may have Adams-Stokes attacks, and have an associated atrioventricular conduction disorder. A phase of increased excitability of damaged pacemaker cells may account for associated fast rhythms in some patients.

2) Physiological bradycardia

Seven cases (Cases 4, 7, 9, 10, 11, 18, 19) had physiological bradycardia.

a) Low rate setting: normal pacemaker function Atrial pacemaker function may be normal, with no evidence of either an increased response to atropine or vagal withdrawal to suggest 'vagotonia', or a lack of sympathetic drive as a cause of bradycardia. It is possible that these patients may have atrial pacemaker rates set at a lower rate than normal while retaining normal pacemaker function and

autonomic influence. This group might, therefore, be regarded as having a physiological bradycardia and probably form the commonest naturally occurring group. As with other normal persons, they may be subject to vasomotor syncope, but not to Adams-Stokes syncope. The atrioventricular nodal rhythm and sinus arrest in these cases may be physiological in origin and caused by a spontaneous mechanism involving vagal stimulation (Hoffman and Crane-field, 1960).

Some patients in this group may have sinoatrial disease, but with normal function in the dominant atrial pacemaker. Long-term follow-up may answer this question. Widespread atrial damage is probably necessary to produce an abnormality in the results of the tests described.

b) **Vagotonia:** one case (Case 14) One patient was seen to have 'supernormal' reflex and drug responses. Since the vagal tone usually predominates at rest, this patient may have truly increased vagal tone accounting for his bradycardia. This type is probably rare.

It is suggested that the evaluation of atrial pacemaker function is of clinical value in patients presenting with bradycardia and syncope.

The tests presented are at present in routine use for both inpatients and outpatients of this department.

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