The Sick Sinus Syndrome

Adams-Stokes syncope results from ventricular arrest or fibrillation, usually complicating failure of atrio-ventricular conduction. The treatment of this previously fatal form of heart block by electrical pacing is now well established. Bradycardia and syncopal attacks associated with failure of sino-atrial conduction are a less widely recognized condition, even though disordered function of the sinus node was well described over half a century ago.\(^1\)

Failure of impulse formation in the sinus node (sinus arrest) or failure of transmission of the sinus impulse to depolarize the atrial myocardium (sino-atrial exit block) causes bradycardia, but symptoms are unlikely unless there is also delay or failure of subsidiary specialized cells in the atrium or atrio-ventricular junction to take over (“escape”) and pace the heart. Symptomatic sinus node disease therefore implies disease of the conducting tissue beyond the sinus node. A common association between sinus bradycardia and paroxysmal atrial tachycardia was first described by D. S. Short in 1954.\(^4\)

The term “sick sinus syndrome” was coined by B. Lown in 1967,\(^2\) and its attractiveness has secured its adoption. In a recent review from King's College Hospital R. H. Lloyd-Mostyn and colleagues suggested the term “sinu-atrial disorder,” which is less catchy but more accurate.\(^6\) “Lazy sinus syndrome”\(^7\) makes the condition sound benign, but sudden death does occur, though it is certainly much rarer than in atrio-ventricular block. The occurrence of several types of bradycardia and tachycardia in some patients with the sick sinus syndrome has earned the apposite term “brady-tachycardia” for this group.\(^8\) The clinical spectrum in 56 patients seen at the Massachusetts General Hospital has recently been described by J. J. Rubenstein and colleagues.\(^9\)

Symptoms may be absent and bradycardia may be intermittent. Differentiation from physiological sinus bradycardia can be guessed from its inappropriateness in the patient and confirmed by the failure of a normal tachycardic response to exercise or atropine. Sino-atrial block results more often from organic heart disease than simply from excessive vagal tone.\(^10\)

In elderly patients, who predominate, there is usually other evidence of organic heart disease, but the condition occurs also in young people and is sometimes familial, with an autosomal dominant inheritance.\(^11\)

Sinus rhythm, sinus bradycardia, junctional rhythm often with reciprocal beats, supraventricular ectopic beats, and supraventricular tachycardia may all be seen in the same patient, but ventricular ectopic activity is surprisingly rare despite sometimes profound bradycardia. The tachycardias may be paroxysmal atrial tachycardia, atrial flutter, or atrial fibrillation, and their frequency in association with bradycardia is all the more remarkable because the electrophysiological mechanism is still not understood.\(^9\) Probably depression of automaticity and delay in conduction through parts of the junctional tissue set the stage for the reciprocating rhythms now thought to be the basis of most paroxysmal tachycardias. Since the bradycardia is more frequent the attacks of tachycardia may be missed.\(^6\) Drugs used in the treatment of one extreme of rate may precipitate the opposite one and bring to light the underlying disorder.\(^12\) Many patients with the sick sinus syndrome have coronary artery disease, and they may present with angina precipitated by either extreme of heart rate. Patients with brady-tachycardia are greatly at risk from systemic embolism, presumably because of the changing atrial rhythms.\(^9\)

Associated electrocardiographic abnormalities are common\(^13\) and were found in 37 out of the 56 patients described from the Massachusetts General Hospital. Thirty-three patients showed some other disturbance of conduction, either at the atrio-ventricular (A-V) node or in the peripheral bundle branches. Nineteen patients showed first-degree A-V block and 20 patients left axis deviation.\(^9\) Impaired A-V conduction is frequently detectable by bundle-of-His electrography, the recording being taken from an electrode catheter introduced via the tricuspid valve. Abnormalities of conduction, automaticity, and excitability in specialized tissue other than the sinus node have been found\(^14\) as well as impaired A-V conduction in 8 out of 15 patients with symptomatic sick sinus syndrome.\(^5\)

The sick sinus syndrome is far more common than is generally realized. The basic pathology is usually degenerative change in the sino-atrial node (and other specialized conduction tissue), but there seems to be a far commoner association with coronary artery disease than is true for chronic atrio-ventricular block.\(^6\) An occasional association with almost every kind of heart disease has been described, but surgical injury\(^13,16\) and association with the Jervell-Lange-Nielsen familial syndrome of congenital nerve deafness and syncope are worth bearing in mind.\(^17\)

The workers at King's College Hospital stressed that cardiac catheterization, and particularly coronary angio-graphy, may be hazardous. The sino-atrial node is supplied by the right coronary artery in 55% of patients and the atrio-ventricular node in 90% of patients and contrast injection into this artery may precipitate dysrhythmia or asystole.\(^6\)

Angina caused by persistence of bradycardia during exercise has been described,\(^18,19\) and it may also be precipitated by tachycardia in this syndrome.\(^6\)

Drug treatment of the sick sinus syndrome is usually unsuccessful. Atropine generally produces side effects which preclude the continued use either of atropine itself or of similar drugs, and anyway it rarely speeds the bradycardia. Sympathomimetic drugs tend to increase the number of attacks of tachycardia. Antiarrhythmic drugs usually fail to stop these attacks and may aggravate symptoms related to bradycardia through depression of the already sluggish atrio-ventricular junction escape mechanism. Though direct-current cardioversion may be used to correct symptoms producing tachyarrhythmias, its use may be hazardous, because DC shock is known to suppress pacemaker activity\(^20\) and may be followed by sinus arrest or another dysrhythmia.\(^5\)

Long-term electrical pacing should be given to patients with severe symptoms of recurrent tachycardia or syncopal attacks during extremes of heart rate. Though on theoretical grounds long-term atrial pacing would be desirable, in practice ventricular pacing is usually preferable. Firstly, long-term atrial pacing tends to be erratic, and, secondly, the need for thoracotomy to institute atrial pacing makes ventricular pacing seem wiser.\(^6\)\(^15\) In patients with paro-
ysmal tachycardia the presence of an artificial pacemaker makes it possible to give more effective doses of antiarrhythmic drugs without danger arising from further depression of the natural pacemaker. Large doses of a beta-adrenergic blocking drug are usually the most successful in these patients and may be combined with digoxin in patients with associated cardiac disease and heart failure. The high incidence of systemic embolism in patients with bradytachycardia makes it wise to employ long-term prophylactic anticoagulant treatment.

1 Laslett, E. E., Quarterly Journal of Medicine, 1969, 2, 347.
2 Levine, S. A., Archives of Internal Medicine, 1916, 17, 153.
5 Lown, B., British Heart Journal, 1967, 29, 469.
16 Hudson, R. E., British Heart Journal, 1967, 29, 646.

New Laws for Doctors

Every doctor who prescribes medicines for patients should be aware of new regulations for the control of drugs that come into force on 1 July. Full details of the new regulations will be sent to all general practitioners by the Departments of Health before that date; information will also be available in hospitals and local authority health departments.

The regulations put into force the Misuse of Drugs Act 1971, which has replaced the old Dangerous Drugs legislation. Morphine, heroin, pethidine, and similar drugs are included in schedule 2 of the new regulations. Two important changes have been made in the way that doctors deal with these drugs. Firstly, every prescription for a schedule 2 drug must specify in words and figures the dosage and the total quantity of the drug to be supplied, and the form and strength of the preparation to be dispensed must be stated.

Secondly, the register kept by a doctor of his own use of schedule 2 drugs will in future have to include an entry on every occasion that he administers a dose of the drug or causes it to be administered under his own supervision. The full text of the relevant sections of the regulations should be studied by any doctor who may need to prescribe drugs in schedule 2. As with any new procedure, doctors will no doubt find following the regulations time-consuming and tedious at first. However, both pharmacists (who will have as many problems as doctors) and doctors themselves may take consolation in the thought that the purpose of the increased stringency is the prevention of misuse of drugs, and few of our current medico-social problems deserve higher priority.

Lomotil Intoxication in Children

Tablets of Lomotil consist of 2.5 mg diphenoxylate hydrochloride and 0.025 mg atropine sulphate and are widely used for "traveller's diarrhoea." Indeed, the drug has accompanied man on his longest ever journey, to the moon. But recently there have been several reports of Lomotil poisoning in children from either accidental ingestion of large doses or wrongly prescribed medication. Of 18 children thus poisoned two have died.1-4

Diphenoxylate hydrochloride is structurally related to pethidine, is a powerful antitussive, and prolongs the transit time of the intestinal contents by its action on the smooth muscle of the gut. The onset of action is slow by all routes of administration and the duration of action longer than that of codeine or pethidine. The manufacturers recommend that the preparation should be avoided in the first year of life, by patients receiving barbiturates or anticoagulant therapy, and in cases of hepatic disease. Nearly all the children poisoned were under the age of 3 years. Ten had accidentally ingested toxic doses, and eight were receiving doses in excess of those recommended.

The toxic dose varies widely between children. For example, six tablets rendered a 2-year-old girl moribund before she responded to treatment,1 and 12 tablets produced fatal respiratory depression in a 2-year-old boy.2 Lomotil intoxication produced clinically recognizable atropinism in less than 50% of the children. Though in two cases suggested by M. E. Ament3 there was an early phase of atropinism with high fever, generalized flushing, and tachypnoea for two or three hours. More commonly the first indications of poisoning were drowsiness, constriction of pupils, hypotonia, loss of tendon reflexes, nystagmus, and convulsions. Individual sensitivity to atropine may explain the variation in clinical patterns.

The cardinal sign, however, of Lomotil poisoning was respiratory depression with slowing of the respiratory rate followed by total apnoea. This was the presenting feature in several children in whom ingestion of Lomotil had not been suspected initially, but it also developed later in others known to have ingested toxic doses of the drug. In one case4 apnoea developed 10 hours after ingestion and recurred, despite appropriate therapy, up to 16 hours after ingestion. Similar lapses in time between ingestion and symptoms were reported in other cases, confirming the slow absorption and long duration of action of diphenoxylate. Prolonged clinical observation over 48-72 hours is therefore obligatory in such cases.

Appropriate treatment depends on prompt recognition that Lomotil has been ingested. The child should be admitted to hospital and have his stomach emptied by gastric lavage. The late onset of respiratory depression must be anticipated and facilities for resuscitation made readily available. If respiratory depression occurs, general supportive measures (including the maintenance of an adequate airway and oxygenation) are mandatory, but nalorphine is the vital factor in treatment. The general paediatric dose is 5 to 10 mg/1·73 m², given intravenously or intramuscularly. In infants under 6 months the initial dose suggested is 0·25 mg. Nalorphine's duration of action is brief and the initial dose may need to be repeated several times at intervals of 15 to 30 minutes according to the clinical response. Some caution...