

## Information

### CLINICAL CARDIOLOGY SERIES

## The Stokes-Adams Syndrome

ROBERT A. O'ROURKE, M.D.

*Material Supplied by the American Heart Association*

### Part I—Definition and Etiology

THE STOKES-ADAMS SYNDROME is defined as an abrupt, transient loss of consciousness due to sudden but pronounced decrease in the cardiac output, which is caused by a sudden change in the heart rate or rhythm. This definition does not include vasovagal syncope or epilepsy although patients with Stokes-Adams syncope may have seizures during periods of cerebral ischemia. Although partial or complete heart block is usually present during asymptomatic periods, many arrhythmias may produce syncopal episodes with or without the presence of previously established complete heart block. "Arrhythmia-induced syncope" is a more specific term and includes the primary cause of the decreased cerebral blood flow.

### Clinical Features

The clinical manifestations of arrhythmia-induced syncope depend upon the duration and type of underlying arrhythmia as well as the status of the cerebral circulation. Symptoms of arrhythmia-induced syncope vary from slight faintness to loss of consciousness, with or without convulsions.

Characteristically, during the attack there is an initial pallor. Following resumption of the normal circulation there is usually a facial flush due

Dr. O'Rourke is from the Department of Medicine, University of California, San Diego, School of Medicine.

to reactive hyperemia. The absence of an aura tends to separate seizures occurring during Stokes-Adams syncope from seizures of primary cerebral origin. Stokes-Adams seizures usually commence and terminate abruptly. The patient may resume a previous conversation or activity without being aware of the pause produced by the period of arrhythmia-induced cerebral ischemia. A slow or very rapid pulse during the period of unconsciousness points toward the correct diagnosis. Electrocardiographic monitoring during a syncopal episode demonstrates the responsible rhythm and makes appropriate therapy possible.

### Etiology

Since most patients with arrhythmia-induced syncope have some impairment of atrioventricular (A-V) conduction either during or between attacks, the causes of Stokes-Adams syncope are often the causes of complete heart block.

*Structural Lesions of the Heart.* Approximately 7 percent of the cases of complete heart block in adults are congenital in etiology, with or without associated cardiac defects. Syncopal episodes complicating congenital heart block are uncommon but do occur and may necessitate pacemaker insertion.

Myocarditis of various causes may involve the conduction system, resulting in complete heart block and syncopal episodes. Diphtheria has long been known to be associated with conduction defects, particularly complete heart block.

Heart block, occasionally with Stokes-Adams syncope, has been reported during the course of connective tissue disease and in association with degenerative skeletal muscle and nervous system disorders. In valvular heart disease valve calcification or endocarditis may involve the conduction system and produce incomplete or complete heart block.

Acute myocardial infarction is complicated by complete heart block in approximately 2 to 7 percent of cases. Complete heart block complicating inferior wall myocardial infarction usually proves to be transient and restoration of normal conduction occurs within two to three weeks. The conduction defect involves the A-V junctional tissue. When an anterior wall infarction is the cause of complete heart block the mortality rate is extremely high even with pacemaker insertion. In this situation the complete heart block is fre-

quently due to extensive myocardial necrosis involving the right bundle and the two divisions of the left bundle (trifascicular block) rather than to a conduction defect in the A-v junction.

In a considerable number of patients no cause can be established for complete heart block. Careful pathological examination has shown that many such patients with heart block do not have extensive coronary artery disease but have areas of fibrosis involving the conduction system distal to the common bundle (trifascicular block), either alone or in association with scattered areas of fibrosis throughout the myocardium. In elderly people this has been attributed to "sclerosis of the left side of the cardiac skeleton" which presumably results from wear and tear due to the repeated pull of the contracting left ventricular musculature.

Primary and metastatic neoplastic disease, metabolic disease and infiltrative disorders of the myocardium may produce heart block. Complete heart block is a potential risk during corrective heart surgery, particularly during repair of ventricular septal defects. Surgical heart block frequently reverts to sinus rhythm within three to four weeks following operation. If it continues beyond this period a permanent pacemaker is usually inserted. Non-penetrating chest injury is an occasional cause of complete heart block.

Heart block has been reported in association with Reiter's syndrome, amyloidosis, Paget's disease and sarcoidosis. The myocardium is involved in approximately 20 percent of autopsy-proved cases of sarcoidosis. Conduction disturbances, Stokes-Adams syncope and sudden death are known to occur in sarcoidosis and this entity is an important consideration in the differential diagnosis of acquired complete heart block in young adults.

*Electrolyte Disorders.* Potassium is the most important electrolyte in relation to A-v conduction. Isolated instances of advanced A-v block have occurred in patients during or following the admission of large doses of potassium salts. Hyperkalemia decidedly decreases the ventricular rate in pre-existing heart block.

Acidosis depresses the ventricular pacemaker in complete heart block and may precipitate Stokes-Adams syncope. Alkalosis, hypokalemia and hypernatremia increase A-v conduction and may reverse heart block. However, alkalosis and

hypokalemia may increase ventricular ectopic activity, leading to ventricular tachycardia or fibrillation.

*Toxic Effect of Drugs.* Digitalis is the drug most frequently responsible for producing complete heart block. Syncopal episodes are uncommon during heart block due to digitalis toxicity because the ectopic pacemaker frequently originates in A-v junctional tissue and the ventricular rate is faster than in complete heart block of other cause. The supraventricular rhythm in patients with digitalis toxicity is often atrial fibrillation.

The antiarrhythmic agents quinidine and procaineamide depress the conduction system as well as pacemaker rhythmicity and are contraindicated in complete heart block. Diphenylhydantoin and lidocaine may also depress the ectopic pacemaker and are therefore contraindicated in the presence of high degree A-v block. However, any of these antiarrhythmic drugs may be safely employed to suppress premature contractions in the presence of heart block if an adequately functioning electrical pacemaker has been inserted.



## Part II—Mechanisms and Treatment

DURING THE PAST FEW YEARS improved cardiac monitoring has more precisely elucidated the underlying electrocardiographic mechanisms producing Stokes-Adams syncope. Moreover, the rapid advances in electrical pacemakers have contributed significantly to the prevention of arrhythmia-induced syncope.

### Electrocardiographic Mechanisms

At one time ventricular standstill was thought to be the sole mechanism responsible for Stokes-Adams syncope and it is still considered the most frequent underlying rhythm disturbance. However it is now established that Stokes-Adams attacks may also be due to extreme bradycardia or to a variety of tachyarrhythmias, particularly ventricular tachycardia and ventricular fibrillation. Continuous monitoring has demonstrated that several electrocardiographic mechanisms may produce syncope in the same patient.

The arrhythmias responsible for Stokes-Adams syncope may be divided into seven groups:

1. *Sudden interruption of atrioventricular impulse transmission causing transient asystole.* When the cardiac rhythm changes from a sinus mechanism or incomplete A-V block to complete heart block, a period of asystole often occurs before the junctional or ventricular pacemaker assumes rhythmicity at its inherent rate. This "warm-up period" varies from ten to ninety seconds and is termed the "preautomatic pause."

2. *Atrial standstill with failure of the junctional pacemaker resulting in ventricular asystole.* When sinoatrial node impulse formation ceases and the A-V junctional tissue fails to assume rhythmicity, ventricular asystole results. This mechanism for Stokes-Adams syncope may occur in patients with inferior wall myocardial ischemia and may be influenced by vagal hyperactivity. This is an uncommon mechanism of arrhythmia-induced syncope.

3. *Asystole in the presence of established heart block.* This arrhythmia may result from a shift in the pacemaker below the area of non-conduction to still a lower focus resulting in a period of asystole resembling the "preautomatic pause."

4. *Paroxysmal ventricular tachycardia or fibrillation in the presence of complete heart block.* A slow heart rate during complete heart block predisposes to rapid impulse formation from ectopic foci. Either ventricular tachycardia or fibrillation may then ensue with syncope resulting.

5. *Paroxysmal ventricular tachycardia or fibrillation during normal A-V conduction.* These arrhythmias are most frequently observed in patients with acute myocardial infarction but have also caused syncopal episodes in patients with apparently normal hearts.

6. *Supraventricular arrhythmias.* Supraventricular tachycardias and bradycardias associated with syncopal episodes have been demonstrated by continuous electrocardiographic monitoring in many patients with the Stokes-Adams syndrome. Frequently the sinus bradycardia predisposes to episodic supraventricular tachycardia ("bradycardia-tachycardia syndrome"). In patients with coronary artery disease tachycardia increases myocardial oxygen demands and decreases left coronary artery diastolic blood flow, often decreasing cardiac output despite the increase in heart rate. Syncopal episodes may result.

Sinus bradycardia, sinoatrial block and sinoatrial arrest may cause syncope in patients with heart disease who are unable to increase stroke volume sufficiently to maintain adequate cerebral blood flow.

7. *Combined forms.* Uncommonly, paroxysmal tachyarrhythmias may be followed by a period of asystole due to a delay in automaticity of pacemakers which have been suppressed during the tachycardia.

The recognition that different electrocardiographic mechanisms may produce syncope in the same patient on different occasions is important in therapy.

## Treatment

The aim of therapy for arrhythmia-induced syncope is threefold: (1) prompt restoration of the circulation during cardiac arrest, (2) restoration of an intrinsic cardiac rhythm adequate to maintain cerebral blood flow and (3) prevention of recurrent episodes.

*Medical Treatment.* The medical therapy of complete heart block includes the correction of potential contributing factors such as acidosis and hyperkalemia. The sympathomimetic drugs, which include parenteral epinephrine, oral ephedrine and isoproterenol by either route of administration, are primarily indicated when ventricular asystole or bradycardia occurs in complete heart block and intracardiac pacing is unavailable. These agents act by increasing A-V conduction, increasing the rate of the ventricular pacemaker, and shifting the lower pacemaker to a higher focus in the common bundle or A-V junctional tissue. During an attack of arrhythmia-induced syncope due to bradycardia, isoproterenol should be given by intravenous infusion during electrocardiogram monitoring so that its administration can be rapidly terminated if ventricular irritability results.

The vagolytic agent atropine may increase the ventricular rate in complete heart block complicating a recent inferior wall myocardial infarction. Atropine is often successful in the treatment and prevention of Stokes-Adams syncope due to sinus bradycardia, sinoatrial block and bradycardia-tachycardia syndrome.

Steroids through their anti-inflammatory and hypokalemic effects have been occasionally suc-

cessful in improving A-V conduction in patients with complete heart block due to myocarditis or acute myocardial infarction.

The trisodium salt of ethylenediamine tetraacetic acid, a calcium-chelating agent, has been used in the treatment of complete heart block due to digitalis intoxication when electrical pacing is unavailable.

*Pacemaker therapy.* Because of the unpredictable, potentially fatal nature of Stokes-Adams attacks and the inconsistent results and frequent complications with drug therapy, electrical pacing has become the treatment of choice when syncope occurs in patients with complete heart block.

The general indications for pacemaker insertion include (1) complete heart block associated with congestive heart failure (2) complete heart block with Stokes-Adams syncope (3) complete heart block following acute anterior or inferior wall myocardial infarction (4) partial A-V block (second degree block) complicating anterior wall myocardial infarction and (5) post-surgical complete heart block.

Recent reports have demonstrated the feasibility of suppressing episodes of ventricular tachycardia and fibrillation in patients with normal A-V conduction by pacing the atrium or the ventricle at a rate faster than that present between episodes of ventricular tachyarrhythmia. Electrical pacing has been employed successfully in combination with propranolol and cardiac sympathectomy in the treatment of otherwise unresponsive ventricular arrhythmias. Rapid atrial pacing has been used successfully in the treatment of supraventricular tachycardias including atrial flutter and paroxysmal atrial tachycardia.

In patients with syncopal attacks due to ventricular tachycardia or ventricular fibrillation complicating complete heart block, the emergency insertion of a ventricular pacemaker is strongly indicated. A ventricular pacemaker is the only means available for the long-term prevention of ventricular tachyarrhythmias in patients with heart block. If transient ventricular asystole complicates complete heart block a ventricular pacemaker is also indicated. A single Stokes-Adams attack in a patient with complete heart block is sufficient reason for pacemaker insertion.

## Selected Items from the FDA Drug Bulletin

### Nitroglycerin Packaging Affects Potency

A recent FDA assay survey of nitroglycerin tablets suggests that improper packaging has a crucial bearing on the drug's stability and potency.

The assay involved nitroglycerin tablets stored in a pen-shaped plastic container provided by pharmacies as a convenient means of carrying several days' supply. Dispensers containing the drugs were left standing at room temperature for 1-, 2-, and 3-day periods.

The nitroglycerin was found to have decreased to about 50 percent, 30 percent and 20 percent of initial potency after being left in the dispensers for these periods. FDA has requested recall of the dispensers.

The assay led FDA to conclude that unexplained patterns of therapeutic response by patients to nitroglycerin therapy may be caused by the manner in which the drug is packaged. Physicians should consider this possibility when evaluating patient response to the drug.

To avoid rapid loss of potency, nitroglycerin should be kept at all times in tightly-sealed glass vials. Physicians and pharmacists may wish to tell patients this when prescribing and dispensing the drug.

—FDA DRUG BULLETIN, FEB 1972



### Imipramine and Alleged Birth Defects

Recent alarm about possible implication of imipramine (Tofranil®), an anti-depressant drug, in birth defects (amelia and phocomelia) appears to be without firm foundation. A report of an association between imipramine given pregnant mothers and congenital deformities in their offspring came from Australia in early March.