De Subitaneis Mortibus

XXVIII. Apoplexy of the Heart

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SUMMARY Apoplexy of the heart can be responsible for sudden and for recurring instability of cardiac rhythm and conduction, and for the clinical counterparts of syncope and sudden death. Every pathophysiological mechanism which produces cerebral apoplexy has its counterpart in apoplexy of the heart. Among the mechanisms documented are thrombosis, embolism and rupture of those special vessels supplying the sinus node, atrioventricular (A-V) node and His bundle. Apoplexy of the heart can occur either with or without significant or recognizable ventricular myocardial infarction. Acute vascular accidents within the critical centers of cardiac impulse formation and conduction deserve more frequent consideration in the explanation of unusual cases of "epilepsy" or seizure disorders of the elderly, of neurologic manifestations (which may be secondary as well as primary) of systemic diseases such as lupus erythematosus or thrombotic thrombocytopenic purpura, and indeed of every case of otherwise unexplained syncope or sudden death at any age.

APOPLEXY IS A TERM most often used in discussing vascular accidents of the brain. Its literal definition includes hemorrhage into any organ; furthermore, sudden anemia is included with sudden hemorrhage as a suitable mechanism to produce apoplexy.1, 2 A crucial feature of the condition is its sudden onset. Apoplexy can be caused either by rupture of a vessel or by its abrupt occlusion. Phrases in clinical use such as pituitary apoplexy and adrenal apoplexy describe events which in many ways resemble apoplexy in the brain.

Numerous functions of the brain and the heart bear remarkable similarity, such as the intricately complex electrical activity, the essentiality of proper behavior of each organ for survival of the individual, the responsiveness of both brain and heart to a very large number of neural and humoral signals from elsewhere in the body, and the important reciprocal influences of the brain and heart on each other. With all these and other similarities, it is surprising that the concept of apoplexy of the heart has not been developed. Sudden vascular accidents can and do occur in the heart, and they can be caused by rupture or by embolism or thrombosis in a coronary artery, exactly as occurs in the cerebral circulation. There is one great difference in the clinical consequences, due to the function of the heart as a pump and the frequent impairment of this special function when the coronary circulation fails. On the other hand, the electrical centers of the heart are often involved during myocardial infarction. Additionally, disordered electrical activity of the heart can be the consequence of a vascular accident which may or may not be associated with ventricular myocardial infarction. With or without myocardial infarction, apoplexy of the heart can cause abrupt loss of consciousness and even sudden death.

While there has been growing clinical recognition that syncope and sudden death can be primarily as well as secon-

darily attributed to an arrhythmia or conduction disturbance, there has been a regrettable lag in the performance of suitable anatomical studies of the cardiac conduction system in fatal cases. This lag is all the more conspicuous in cases of sudden unexpected death which remain unexplained even after a careful "routine" (including toxicological studies) autopsy, despite the fact that Schwartz and Walsh3 have called attention to the importance of examination of the conduction system especially in such cases.

Previous reports in this series of clinicopathological correlating studies appearing in Circulation have illustrated the wide variety of anatomical abnormalities which may be present in the sinus node, atrioventricular (A-V) node and His bundle of victims of sudden unexpected death. Although these various abnormalities include processes which are not vascular in nature, more often it is a critical narrowing or complete obstruction of certain special arteries which must be considered as either a contributing or sole cause of the sudden death. The purpose of the present report is to illustrate how vascular accidents within the electrical control system of the heart closely resemble analogous events in the brain, and to propose that apoplexy of the heart is a useful clinical concept.

Pathophysiologic Mechanisms in Apoplexy of the Heart

Occulsion of Large Coronary Arteries

Sudden deficit (either relative or absolute) of flow through a major coronary artery usually leads to ventricular myocardial infarction. Many factors serve to modify the size of such infarcts and their clinical consequences. One of these is the stability of cardiac rhythm or conduction. Instability of cardiac electrical activity can be a major factor enlarging the infarct size, but some forms of electrical instability of the heart may be lethal independent of the size or even the presence of ventricular myocardial infarction. Whether electrical instability of the heart happens when a large coronary artery becomes critically narrowed or occluded depends to a great extent on two things: 1) exactly where the point of occlusion is; 2) the site of origin of the sinus node artery and the A-V node artery.4 Possible sources of collateral circula-
tion, the presence or absence of anemia or hypoxia, the pattern of anatomical distribution of the large coronary arteries, and the presence or absence of multiple other sites of coronary narrowing all contribute to the pathogenesis of ischemic malfunction of the conduction system, but these and still other factors must be interpreted first in the light of the relationship between the point of coronary occlusion and the site of origin of blood supply to the conduction system.

Not all occlusions of large coronary arteries need lead to ischemic malfunction of the conduction system. For example, occlusion of the left anterior descending branch alone virtually never does. Another exception would be the development of a gradual occlusion of the right coronary artery proximal to the origin of the sinus node artery (and/or A-V node artery) when there is time for collateral circulation to become established. At the other extreme are the examples of hemorrhagic destruction of the A-V node and His bundle (fig. 1) as part of the chaotic events surrounding infarction and rupture of the interventricular septum, wherein the heart block compounds the size and clinical consequences of the infarction, and the hemodynamic disturbances compound the extent of ischemia and destruction within the A-V node. Between the example of gradual coronary occlusion with preservation of normal cardiac rhythm and conduction, and the occurrence of multiple coronary occlusions with hemodynamic and electrophysiological disaster coexisting, there is a spectrum of either mechanical or electrical complications. Electrophysiological abnormalities may be transient or prolonged or permanent, they may be innocuous (a few atrial premature beats) or more serious (multiple closely coupled ventricular premature beats, various degrees of heart block) or fatal (untreated or untreatable ventricular fibrillation).

A characteristic infarction occurs at the atrionodal junction when a major coronary artery is occluded proximal to the origin of the sinus node artery. Similar effects on the A-V node are associated with fatal heart block during acute posterior myocardial infarction caused by occlusion of the major coronary artery supplying that region (fig. 1). However, among survivors of such coronary occlusions structural changes in the sinus node or A-V node would either be much less or not exist, since survival itself indicates suitable adaptation by mechanisms such as more generous provision of collateral circulation to the ischemic region. Exactly the same consequences follow apoplexy in the brain, since some victims die while others recover with either partial or complete restoration of function.

**Occlusion of Small Coronary Arteries**

There may be no clinically significant consequence after the occlusion of a left ventricular artery no more than one

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**Figure 1.** These two photomicrographs illustrate thrombotic occlusion of the right coronary artery (RCA in A) associated with acute posterior myocardial infarction, hemorrhagic destruction of the A-V node, complete heart block and rupture of the interventricular septum. The markedly narrowed A-V node artery (AVNA in B) is shown with adjacent hemorrhage within the posterior margin of the A-V node. Other details of this case have been reported previously, as have the cases shown in all the following illustrations as indicated. Goldner trichrome stain here and in subsequent photomicrograph unless otherwise indicated. Magnifications are marked with reference bars.
millimeter in diameter, but occlusion of the A-V node artery (rarely more than 1 mm diameter) is a different matter. The difference is directly attributable to the greater importance of the A-V node and His bundle in the effective function of the heart. Among examples of sudden unexpected death, it is not unusual to find a markedly narrowed or occluded A-V node artery, sometimes with documented heart block. While the A-V node artery may become occluded as part of a widespread disease affecting many small coronary arteries, it can also be selectively affected alone.

It is not difficult to visualize how failure of A-V conduction or the generation of troublesome re-entrant tachycardias can follow the onset of acute ischemia in the A-V node or His bundle. It is more difficult to understand why sudden death is sometimes associated with isolated occlusion of the sinus node artery. Whether the deaths were actually caused by sinus node malfunction is uncertain, although the frequency of this association and the logical expectation that disordered sinus impulse formation should facilitate various forms of electrical instability of the heart make this seem a probable causative relationship rather than coincidence. Intermittent sinus arrest can cause syncope and in rare circumstances death. One might anticipate that an escape A-V junctional rhythm would readily emerge and be efficient if the sinus node failed, and that is sometimes the case. Reasons why it is sometimes not the case include the coexistence of disease in both the sinus node and the A-V node or His bundle, including the simultaneous presence of narrowings within the sinus node artery and the A-V node artery. Other reasons why an effective A-V junctional rhythm might fail to emerge include unbalanced or distorted autonomic neural influences. For example, excess vagal discharge could suppress both normal sites of automaticity. Absence of adrenergic neural input to the A-V junction seriously impairs its efficiency as an escape automatic center, and this adrenergic neural insufficiency may be due to local disease, or to the effect of pharmacological therapy, or to central nervous system disease.

Many different diseases and a very wide variety of histological abnormalities can cause narrowing and occlusion of small coronary arteries. These include focal fibromuscular dysplasia which may occlude either the sinus node artery or the A-V node artery. This focal fibromuscular dysplasia closely resembles that described in renal arteries and carotid arteries. Other processes which may cause apoplexy of the heart include dissecting aneurysm rupturing the sinus node artery, embolism into the sinus node artery, thrombosis of the sinus node artery, or mixtures of these and related processes. For example, during either thrombotic thrombocytopenic purpura or disseminated intravascular coagulation there are numerous small emboli or thrombi associated with focal degeneration and hemorrhages within the sinus node or A-V junctional

**Figure 2.** Platelet aggregations in small left ventricular arteries (A) occlude their lumens and cause focal degeneration of left ventricular myocardium as shown with the arrows in B. For the effect on the cardiac conduction system of the same heart see figure 3.

**Figure 3.** Focal degeneration and fatty replacement of the His bundle (open arrows) are shown from a patient with recurring intractable arrhythmias and disseminated intravascular coagulation. Acute degeneration of cells within the sinus node of this patient is illustrated.
tissues (figs. 2–5). During the progressive evolution of coronary disease characteristic of most victims of congenital homocystinuria, both the small and large coronary arteries become narrowed; however, the abnormally sticky platelets (which may contribute to the pathogenesis of the vascular mural disease) may even occlude otherwise patent vessels (fig. 6).\(^2\) Without belaboring the number and variety of illustrative examples, it is apparent that abrupt hemorrhage or abrupt anemia of the sinus node or of the A-V junctional tissues may be just as frequent as cerebrovascular accidents, and that every cause of apoplexy of the brain has its counterpart in apoplexy of the heart.

**Neuropathology of the Heart**

Except for the notable contributions of Lino Rossi,\(^2\) there has been far too little attention to this subject. Neural control of the heart facilitates its successful hemodynamic performance, but it is even more important to the intricately organized system for normal impulse formation and conduction.\(^1, 2\) We should not be misled by the fact that transplanted hearts do function, and that electronic pacemakers may be lifesaving, matters which no one now can deny. But for the heart to be optimally responsive to the body’s needs under the widest span of challenges and burdens, and for prolonged effective electrical stability in good health, there is little question that the normal heart beat is preferable and in almost every way superior. For this optimal performance, the heart must be responsive to the neural regulation which causes it appropriately to accelerate or to slow down.

Virtually all neural disturbances in cardiac control can occur secondary to disease in the brain, particularly the medullary centers, so that true apoplexy of the brain has powerful influence on the heart.\(^3, 4\) How often this secondary effect on the heart compounds or renders irreversible the consequences of cerebral apoplexy, by the occurrence of inefficient cardiac rhythm or hypotensive states which would impair any cerebral perfusion, is a matter about which too little is known. Furthermore, one may suspect that some (perhaps many) examples of stroke actually began because of sudden hypotension or other cardiovascular irregularities originally caused by a primary process in the heart. In this regard it is probably unsuitable to use the phrases “apoplexy of the heart” and “cardiac apoplexy” interchangeably, since the latter could refer to principal damage in the brain which was initiated by a transient malfunction of the heart. Apoplexy of the heart refers to both primary events and consequences within the heart itself.

As part of the damage which occurs during acute focal hemorrhage within the heart and particularly its centers of...
control of rhythm and conduction, the local nerves and ganglia are not spared (figs. 7 and 8). Consequently, delivery of efferent signals from the brain must be impaired or interdicted. This impairment might be focal and asymmetrical or more diffuse. Asymmetry of local vagal control may have its own distorting influence on cardiac electrophysiological function, and imbalance between local vagal and sympathetic effects could have still a different form of impairing influence. Asymmetry of sympathetic neural influence can cause serious derangement of normal ventricular repolarization processes. Any form of autonomic neural asymmetry can be produced by inhomogeneous disease affecting cardiac nerves (e.g., myocardial infarction) as well as by disease within the brain. Finally, local neuropathology could also be the source for the generation of afferent signals such as those producing reflex responses either in the heart or elsewhere.

Discussion

Apoplexy of the heart is a clinically useful term to describe those conditions in which sudden hemorrhage or sudden local anemia occurs as the consequence of vascular disease influencing the centers of impulse formation and conduction within the heart. There are not only many similarities between the electrical control system of the heart and the function of the brain, but nearly all vascular accidents known to cause stroke in the brain have their explicit counterparts within the coronary circulation. Just as there are motor control centers in the cerebral cortex which have certain specific functions directly impaired by acute hemorrhage or sudden local anemia, there are centers normally responsible for the provision of efficient cardiac rhythm and conduction which can be similarly influenced by hemorrhage, embolism or thrombosis. But even more useful than the recognition of these similarities are the two following facts: 1) abrupt disorganization of cardiac electrical stability often has a vascular basis in all essential features analogous to apoplexy of the brain, which is far more familiar to most physicians; 2) this cardiac electrical instability can be caused with or without associated ventricular myocardial infarction.

There are many diseases and clinical circumstances where one may predict that apoplexy of the heart occurs more frequently than is presently appreciated. Some obvious examples include coronary disease with or without angina or infarction, hypertension, aortic stenosis and other valvular disease, cardiomyopathies, various collagen diseases and

**Figure 6.** Aggregating platelets within the sinus node artery of a patient with congenital homocystinuria are indicated with arrows in A, where there are a number of additional unmarked aggregates as well. In B there is abnormally heavy focal fibrosis of the sinus node of this patient, compatible with recurring focal degeneration which has healed.

**Figure 7.** Intracardiac neuropathology is demonstrable in this patient dying with diphtheria and both atrial arrhythmias and conduction disturbances. Hemorrhagic and inflammatory destruction of neural elements directly adjacent to the sinus node are shown here at two magnifications, with the boxed area in A being the entire picture in B.
cases of sudden death, failure to examine the brain is rare and most would consider such a study seriously inadequate, particularly if no other suitable cause of death was found. On the other hand, the cardiac conduction system is rarely examined in just the same circumstances, despite abundant evidence that its study may provide an equally convincing explanation of otherwise unexplained sudden deaths. Although there is a totally undeserved aura of mystery about the anatomy and pathology of the cardiac conduction system, its suitable study is neither that mysterious or tedious. The greater mystery is why so few have sought to familiarize themselves with the principles involved, and why there has been no more effort by forensic pathologists to require such studies in cases of otherwise unexplained sudden and unexpected deaths.

Interpretation of anatomic abnormalities within the sinus node, A-V node or His bundle is sometimes straightforward, e.g., a particularly destructive lesion in the His bundle of an individual known to have developed heart block recently. At other times, interpretation is more complex and requires knowledge of how the conduction system functions under normal and various pathological influences. Such knowledge can be obtained by consultation, but this has the disadvantage that the consultant may not understand normal and abnormal anatomy. It would seem more suitable for some individuals knowledgeable about cardiac electrophysiology to become more familiar with normal and abnormal anatomy of the conduction system, or that those who know about the anatomy learn more about normal and abnormal cardiac rhythm and conduction. Until more such individuals are available, there will continue to be an understandable reluctance by many to do the type of study with which this report is concerned.

In the meantime, if physicians come to consider apoplexy of the heart as a useful concept, it should lead to more frequent consideration of electrical instability of the heart as a basis for unexplained loss of consciousness with or without convulsions. Since sudden hemorrhage or acute focal anemia affecting the conduction system of the heart can be caused by so many different diseases which occur at all ages, it is to be hoped that apoplexy of the heart will be considered more often in the differential diagnosis for younger as well as older individuals. It would be as unfortunate as it is incorrect to continue the prevalent misconception that vascular injuries to the conduction system are only caused by atherosclerosis and therefore are to be found exclusively in older patients. It is equally misleading to consider that ventricular ischemia or infarction is a necessary component of syncope or sudden death from coronary atherosclerosis, although it often is. Complications of atherosclerosis are still by far the more frequent basis for apoplexy of the heart, but when either an older or younger individual with unexplained syncopal episodes or unusual "epilepsy" is the object of study, one must begin to consider rare as well as common causes.

One can only admire the ability of the heart to right itself promptly after most forms of electrical instability, and this adaptability probably includes examples of apoplexy of the heart. How many such examples there are may never become known, since the occurrence of one or a few such episodes with full recovery may then be forgotten. The survival and complete recovery of all such patients being the
goal of any physician, it is not to be regretted that anatomical study of the heart is precluded. If such syncopal episodes persist or become more frequent, there can be the analogy to the “little strokes” now a familiar concept about the brain. Ultimately, we will only know how often apoplexy of the heart was responsible for syncope and sudden death if the appropriate postmortem examinations are conducted to answer the question.

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De subitaneis mortibus. XXVIII. Apoplexy of the heart.
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_Circulation_. 1978;57:385-391
doi: 10.1161/01.CIR.57.2.385

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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