 Treatment of Cardiac Arrhythmias

By David Scherf

SIMPLE and fairly satisfactory rules have been established for the treatment of cardiac arrhythmias, but many problems remain unsolved. The latter chiefly concern those arrhythmias which are refractory to the generally accepted therapeutic measures. Patients still die from cardiac arrhythmias. Since readers of this journal are well acquainted with the routine aspects of the subject, emphasis in this discussion will be placed on the controversial points.

Disturbances of Impulse Formation

General Discussion

Two forms of disturbances of impulse formation are differentiated. Automatic impulses, originating in an ectopic center may interfere with those formed by the normal pacemaker as in paroxysmal tachycardia, flutter and fibrillation are coupled to the preceding beat. Fibrillation differs from the other arrhythmias in that it appears to represent a situation in which many centers often are active. Only rarely do ectopic abnormal impulses arise spontaneously, that is, independent of the last preceding beat of the basic rhythm.

This concept makes it easier to understand why arrhythmias can be influenced by a great variety of agents. Whatever influences the enzyme systems, the ionic environment and the membrane structure and function may abolish or create these arrhythmias. Extrasystoles or ectopic tachycardias may be arrested by such different ions or compounds as potassium or calcium, or by atropine and acetylcholine, neostigmine and banthine, epinephrine or ergotamine. This makes it also more comprehensible why the same substances (digitalis, quinidine, fagarine, potassium, epinephrine, calcium, acetylcholine and procaine) which abolish extrasystoles may also initiate them.

The therapy of this group of arrhythmias centers around quinidine, digitalis, vagotonic agents and procaine amide. Potassium, calcium, fagarine, magnesium, and procaine hydrochloride have less importance but will also be discussed. These measures either suppress the tachysystolic center, whereupon the sinus node resumes its role as pacemaker, or they slow the ventricular rate. The deleterious hemodynamic action of an arrhythmia is proportional to the ventricular rate.

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Quinidine remains the chief drug for suppressing ectopic arrhythmias. Recent investigations have correlated the blood concentration with the dosage and with the clinical effect.12-17,31 The therapeutic effect and the blood level reach a maximum two hours after an oral dose. Significant was the finding that cumulation is definite though limited. When the drug is administered every two hours the peak concentration is attained after the fifth dose. Thereafter, the intake of the drug equals its disposal by the body. With intervals of four to six hours between doses the cumulative effect may be observed for several days so that the peak concentration may appear after two to four days. If increased blood levels are desired after the time limits just mentioned, it is necessary to increase either the size of the individual dose or the frequency with which it is administered.

A blood concentration of 6 to 8 mg. per liter is effective in successfully converting a majority of cases of auricular flutter or fibrillation into sinus rhythm. Data for ventricular arrhythmias are not available but clinical experience shows that in most instances a satisfactory response is obtained to small doses of quinidine. The doses at intervals of two hours are given five times, during daytime only. If quinidine is given every four hours the administration is best continued also through the night around the clock. The individual doses vary between 0.2 and 0.6 Gm. and depend on the weight of the patient. If the smaller dose is ineffective it is increased. It is of interest, that even the administration of large individual doses three times daily was no less effective than the small doses given more often.22 These new results are thus in full agreement with the clinical experience gained many years ago. Considerable variations from the above cited averages may occur.

Blood levels of over 10 mg. per liter are occasionally necessary to convert an arrhythmia, but the incidence of toxic effects is very high. Determination of the blood level may sometimes aid in the management of a patient. If a relative large dose of quinidine is ineffective and there are no signs of toxicity, knowledge of the blood level may be helpful. If it is low, poor absorption may be assumed and the dose may be safely increased.

Quinidine often widens the QRS complex by decreasing the velocity of myocardial conduction. If the duration of the QRS complex becomes 0.11 second or more, caution is in order and it is best to stop the drug. If such patients and those with A-V block receive quinidine, sudden death from ventricular fibrillation has been observed repeatedly. Usually this is explained by the development of a circus movement, which is said to be facilitated by the appearance of block areas. However, increased excitability and formation of local potentials and oscillations distal from a block area have been observed in the nerve (Wedensky facilitation). It is probable that the response of the heart muscle fiber is similar.31

Administration of quinidine should also be interrupted when extrasystoles appear during therapy; usually they are of ventricular origin.

Effective therapy with quinidine is often prevented by the well known signs of hypersensitivity. Of these, diarrhea is most common and relatively harmless.

Often the vagolytic action12 of quinidine, which appears after administration of normal therapeutic doses, is not fully appreciated. It abolishes the effect of carotid pressure. The sympatholytic effect is also of clinical importance. Accordingly, vasodilatation is a common and often beneficial consequence of quinidine therapy.

The action of quinidine in these arrhythmias, which is so often incorrectly attributed to changes of the refractory phase, is due chiefly to an alternation of the center suppressing the firing of abnormal stimuli; there is also a diminution of the excitability of the myocardium. Actually certain drugs such as rawolphia abolish auricular fibrillation without exhibiting any influence on the duration of the refractory phase.36

Because of the occasional scarcity of quinidine, it is worthwhile to emphasize that quinine, although somewhat weaker than quinidine, is also effective in the treatment of ectopic arrhythmias.

Digitalis has a direct suppressive action on ectopic centers and readily abolishes extra-
systoles and tachycardias. It may rarely convert flutter or fibrillation to sinus rhythm. Its ability to prolong A-V conduction is valuable in controlling harmful effects of rapid ventricular activity in auricular tachycardias. On the other hand, digitalis is notorious for its propensity for provoking ventricular extrasystoles, ventricular tachycardia and, ultimately, ventricular fibrillation. Although it very rarely causes auricular extrasystoles, it does induce, on occasion, auricular tachycardias and even auricular fibrillation.

Before the physician employs digitalis for the treatment of an arrhythmia, he must be sure that this drug did not cause the arrhythmia. Ventricular extrasystoles and tachycardias caused by digitalis are characterized by a continuous change of form of the ventricular complexes, while the auricular tachycardias show A-V block. An arrhythmia caused by digitalis may persist for several weeks after the drug is stopped.

The manner in which digitalis is used in the individual arrhythmias depends on the type of the arrhythmia (see below).

**Cocaine derivatives** depress the excitability of the heart. Instillation of procaine or other derivatives into the pericardium diminishes ectopic beats during cardiac surgery. Since many substances are absorbed from the pericardium with the greatest speed, the effect is no better nor more prolonged than that of intravenous injection of the same drug. The local inhibitory effect of direct pericardial instillation may be detrimental. Novocaine applied to the sinus node of the dog abolishes immediately the activity of the node. Intravenous injections of procaine hydrochloride have been proposed for the treatment of cardiac arrhythmias which appear during anesthesia with cyclopropane. Its usefulness under such circumstances and in clinical arrhythmias is very limited because of the brevity of its action. Within five minutes hydrolysis occurs in the blood stream. Procaine amide is more stable and therefore also more active after oral administration. Clinically and experimentally, procaine amide has been found to be about one-fourth to one-third by weight as strong as quinidine. Therefore, one may substitute one for the other according to the rule that 0.25 Gm. (one capsule) of procaine amide is equivalent to 0.065 Gm. (one grain) of quinidine.

For practical purposes, the action of procaine amide on the heart is identical with that of quinidine. It suppresses tachysystolic or extrasystolic centers, depresses myocardial conduction, prolongs the Q-T interval and is prone, on the other hand, to create new ectopic centers. Also similar to quinidine, the maximum effect is observed clinically and electrocardiographically two to four hours after an oral dose. Neither the blood levels nor cumulative characteristics have been adequately investigated. However, the clinical impression prevails that in this respect both drugs are similar.

Undesirable extracardiac effects of procaine amide are nausea, vomiting, headache, and diarrhea. These occur with distressing frequency as the oral dose exceeds 4 Gm. daily. In cardiac action this is equivalent to only 1 Gm. of quinidine. Accordingly, it appears that for effective doses oral procaine amide is more toxic than quinidine. Disturbances of hearing and vision, which are so common with quinidine if doses exceed 2 Gm. daily, have not been observed with procaine amide. However, it is difficult to give equivalent doses of this drug orally. Many instances of hypersensitivity to procaine amide have been reported. These include, like quinidine, urticaria, dermatitis, agranulocytosis, aplastic anemia, fever, muscle pains and mental disturbances. Extrasystoles and ventricular fibrillation appear. However, a given patient often is only sensitive to one of these drugs. Since sensitivity to quinidine is so common, the availability of a substitute is of importance. When quinidine must be discontinued because of its side-effects in a given patient, procaine amide may be substituted without interruption of schedule. Occasionally the additive action of the two drugs on the heart achieves therapeutic success otherwise impossible.

In direct proportion to the rate of the intravenous injection, procaine amide reduces the blood pressure to shock levels. This is not seen with oral administration. Quinidine acts
similarly. Therefore, when the intravenous route is used with either drug, not only the electrocardiogram but also the blood pressure must be concurrently observed. The injection should be performed very slowly, over at least a period of five minutes. It should be emphasized that the intravenous route is only rarely indicated. With the exception of unconscious patients and those unable to ingest medicines, oral administration is preferable.

The treatment of cardiac arrhythmias is often of great importance. False confidence in the safety of a drug can lead to its excessive use. It is, therefore, imperative to correct the erroneous impression that procaine amide is more effective and safer in the treatment of ventricular arrhythmias than quinidine. It is claimed that procaine amide may be effective when quinidine fails, but it is not always realized that acute ventricular tachycardias vary in their stability. Others overlook the additive effect of procaine amide given immediately after quinidine. Controlled investigations have failed to produce sufficient evidence for the superiority of procaine amide. On the other hand, occasionally ventricular tachycardias following acute coronary occlusion fail to respond to quinidine even if given in the largest permissible doses. In such instances, one occasionally obtains a prompt response from procaine amide.

Potassium, injected intracardially, has been known for almost 50 years to abolish ventricular fibrillation. On the other hand, an intravenous injection of potassium may readily induce fibrillation. Since hypokalemia is now recognized in a great variety of conditions and potassium salts, administered intravenously, are often recommended, extreme caution must be exercised. Even therapeutic doses of potassium salts given orally may cause A-V block with irregular ventricular complexes, supraventricular tachycardias or auricular standstill. Renal function should be normal if potassium salts such as potassium chloride or acetate are employed. Many investigations have demonstrated that the diseased myocardium contains less potassium than normal cardiac muscle. The low potassium content may be a causal factor in the propensity of the diseased myocardium to develop tachysystolic centers, particularly following digitalis. This is suggested by the readiness with which oral doses of potassium inhibit such arrhythmias. The potassium content of the heart muscle of dogs following toxic doses of digitalis was found markedly diminished.?

Fagarine. The scarcity of quinidine during the Second World War stimulated research on other substances with antifibrillatory effects. One of the most interesting new drugs is fagarine, derived from a plant of the Argentine. It appeared effective and nontoxic in animal experiments but the clinical results were disappointing. It has the unfortunate tendency to induce ventricular fibrillation. In a limited experience with fagarine several instances of ventricular fibrillation occurred and the drug was abandoned.?

Atabrine, an antimalarial drug, is chemically unrelated to quinidine but has many similar actions. It inhibits cholinesterase, paralyzes the vagal fibers, depresses excitability and may abolish arrhythmias. So far, however, it has been found effective only in paroxysmal arrhythmias. The absence of a therapeutic effect in chronic fibrillation raises the possibility that the acute attacks of tachycardias or fibrillation in which the compound was apparently effective might have disappeared spontaneously. The drug (0.4 to 0.6 Gm.) is dissolved in 10 cc. of a 1 per cent solution of Novocaine and is injected intramuscularly.?

Barbiturates distinctly reduce the propensity of the heart to develop arrhythmias. The excitability of the heart is diminished and extrasystoles caused by epinephrine, cyclopropane and other agents appear less frequently, in diminished numbers or not at all.

Acetylcholine and other choline derivatives play an important part in normal and abnormal stimulus formation. According to Burn and his school, the synthesis of acetylcholine within the cell plays an important part, as a "local hormone," in the normal automaticity of the heart. While in certain doses, ectopic stimulus
formation is inhibited, these substances also initiate heterotopic stimulus formation and may cause flutter and fibrillation.

According to Dawes, quinidine and procaine preparations abolish arrhythmias because of inhibition of the synthesis of acetylcholine and Burn believes that procaine and quinidine exert their effects by competing with acetylcholine or epinephrine.

Comparative investigations led DiPalma and Lambert to stress the importance of the presence of a methoxy group in antifibrillatory compounds. Dawes pointed out that the majority of drugs exhibiting a quinidine-like action contains an aromatic group joined to a basic group by an ester, ether or carbinol linkage. The antifibrillatory and anesthetic action of certain drugs show a good correlation. This research may point the way to the discovery of new synthetic compounds.

Extrasystoles

Extrasystoles appear if impulses spreading over the heart elicit in a cell or a small group of cells (the center) more than one discharge. The supernormal phase which makes it possible, to “pick up” impulses from a sub-threshold background certainly plays a smaller part in the genesis of extrasystoles than is often believed. In the mammalian heart, the phenomenon of the supernormal phase is found only under certain special conditions while extrasystoles persist in some patients for years and are abolished only with difficulty.

Extrasystoles vary greatly in significance. Usually they cause no symptoms. An occasional patient may suffer acutely, for each extrasystole provokes a short period of anginal pain, vertigo or annoying cough; the impact of the sudden irregularity on the psyche of the patient may be great. Most extrasystoles are harmless, but occasionally an extrasystole arriving during the last part of systole and earliest part of diastole (the critical or vulnerable phase) may lead to ventricular fibrillation.

Most extrasystoles seen in practice occur in persons with healthy hearts, but in other instances they constitute important evidence of heart disease or drug toxicity. Treatment of extrasystoles is indicated when they cause significant symptoms or may be the forerunners of more serious arrhythmias.

The presence of asymptomatic extrasystoles should not be mentioned to the patient. For the symptomatic type, avoidance of tobacco, correction of constipation and other simple measures may help. Often informing the patient of the harmlessness of his sensations induces him to forget his complaints. When symptoms are distressing, a careful and sympathetic explanation to the patient and administration of quinidine are advisable. Extrasystoles denote organic heart disease. They may represent an early sign of coronary sclerosis; they may occur only on effort and be recorded during an exercise test; or they may appear at rest or during an attack of anginal pain. They are occasionally precursors of ventricular fibrillation just as auricular extrasystoles may foreshadow auricular fibrillation. They should be treated with quinidine.

Extrasystoles are quite common in acute myocardial infarction. In animal experiments involving ligation of a coronary artery, they are precursors of fibrillation and we assume that this holds for man as well. Accordingly, a determined effort should be made to suppress them or at least to decrease their frequency. Quinidine is the drug of choice with procaine amide as an acceptable substitute. Quinidine sulfate, 0.2 Gm. every six hours, is the usual initial dose. If the extrasystoles persist, the dose is increased. Usually therapy is effective. Some investigators claim that their animal experiments indicate that quinidine did not change or even increased the mortality rate. The fact that quinidine was administered intravenously in large doses in these experiments and caused respiratory standstill or diastolic arrest of the heart is probably responsible for the adverse results. These cannot supplant the mass of evidence, both clinical and experimental, in favor of quinidine. We strongly recommend the use of quinidine in every case of myocardial infarction with ventricular extrasystoles.

Digitalis usually abolishes extrasystoles provided the drug did not originally induce them.
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This holds for normal hearts as well as for diseased ones. If the heart is healthy, even large, sublethal doses of digitalis do not induce extrasystoles. However, in some abnormal hearts it does so readily. Digitalis-induced extrasystoles are characteristically variform and continued exhibition of the drug may produce dangerous ventricular tachycardias and even ventricular fibrillation. Occasionally, even a dose smaller than the therapeutically effective one will induce extrasystoles. If the drug is urgently needed, the dilemma is solved by continuing small doses of digitalis (not more than 0.1 Gm. of the standardized leaf daily) and at the same time examining the patient twice daily before each dose. Should the frequency of the variform ventricular extrasystoles increase, the drug must be stopped. It is extremely doubtful if one form of digitalis will succeed where another has failed in such a case. Because digitalis extrasystoles are common in hearts with certain organic lesions such as the markedly dilated and failing heart of rheumatic mitral lesions, and because they are rare in other lesions, lack of potassium in the heart muscle fibers may well be responsible for their appearance. Potassium chloride and potassium acetate, given orally in the amount of 6 to 10 Gm. daily, actually abolish such extrasystoles, but this therapy is rarely necessary. Occasional extrasystoles or bigeminal rhythm caused by digitalis disappear within a few days or several weeks after the drug is discontinued. Quinidine administered orally is of value in "preterminal" ventricular tachycardias caused by digitalis. An intramuscular injection of 0.25 Gm. of a suitable quinidine preparation has been found to be life saving.

The appearance of digitalis extrasystoles following the injection of a mercurial diuretic has also been attributed to potassium loss during the diuresis. We consider, however, that the redigitalisation phenomenon is a more important etiologic factor.

Extrasystoles arising during digitalis therapy but not variform need not interdict digitalis. Careful observation is in order, however, for if they increase unduly or become variform the drug must be stopped.

Variform ventricular extrasystoles occur during anesthesia with cyclopropane. Ordinarily they are transient so that it is unnecessary to treat them actively. Occasionally ventricular tachycardia ensues and rarely ventricular fibrillation ultimately develops. Though many factors have been accused of favoring the appearance of extrasystoles during this type of anesthesia, the mechanism remains obscure. Anoxia and especially the use of sympathomimetic agents such as epinephrine should be avoided. Experimentally, the combination of cyclopropane plus epinephrine is a favorite method for inducing ventricular fibrillation. Apparently atropine and barbiturates prevent, to some extent, ventricular extrasystoles during anesthesia. The most publicized preventive agent has been intravenous procaine hydrochloride, but its alleged success is difficult to reconcile with its ineffectiveness under controlled conditions. Usually a definite action is obtained only when the doses are so large that neurologic toxicity is seen.

Extrasystoles are almost invariable during cardiac catheterization and cardiac surgery. They arise when the inner or outer layers of the heart are irritated. Contact with the heart of almost any blunt instrument, particularly if the instrument is of cold metal, may produce extrasystoles. Preventive treatment with quinidine or similarly acting drugs may diminish, but not entirely abolish their occurrence. During intubation, the catheter is to be withdrawn or pushed forward when extrasystoles appear in the electrocardiogram. Usually they then disappear. During cardiac surgery, the finger is left in the orifice of a valve as briefly as possible, and contact between heart muscle and cold instruments is minimized. Instillation of drugs into the open pericardium certainly is no less effective in influencing extrasystoles than medicine administered by injection since drugs are absorbed from the pericardial sac with the greatest speed.

Paroxysmal Tachycardias

These arrhythmias have such a great variety of clinical and electrocardiographic features that no two patients are identical. Many repre-
sent an occasional harmless attack in a healthy person; others are dangerous “preterminal” tachycardias which end in ventricular fibrillation. A paroxysmal tachycardia with a slow rate usually causes no symptoms. Rapid rates, however, particularly in elderly patients, may cause shock, anginal pain or congestive failure. Even hemiplegia and peripheral gangrene have been reported. Pulmonary edema is not rare.

The subjective sensation of a racing heart almost always induces a great deal of anxiety so that reassurance is urgently needed. Before treatment the nature of the tachycardia should be determined with the aid of the electrocardiogram whenever possible. This is important because the significance, prognosis and treatment depend on whether an auricular or a ventricular type is present. In most patients therapy can be postponed until the tracing is taken and read.

One should always try to end the attack by producing one of the vagal reflexes before using drug therapy. This applies also to ventricular tachycardia for occasionally carotid pressure is successful even in this type. If done expertly, the production of vagal reflexes will stop about 50 per cent of the attacks of auricular tachycardia. The patient should be supine; cardiac action should be observed by auscultation. Carotid pressure and not carotid massage should be performed. Pressure on the right side is somewhat more effective than on the left. The pressure should be applied at different levels in order to make sure that the carotid sinus has actually been pressed upon; only this structure contains the receptors specific for the reflex. The pressure should not be exerted longer than 10 to 15 seconds. It is discontinued as soon as the tachycardia stops.

We do not press on the eyeball since upon two occasions we have observed detachment of the retina following this maneuver in patients with myopia. Induction of nausea and vomiting is often successful. The least obnoxious method for accomplishing this is to have the patient thrust two of his fingers into his throat. The use of ipecac is less pleasant and apomorphine should be prescribed only by those physicians who have injected this drug into themselves.

Other maneuvers which are successful at times are compression of the abdomen, Valsalva maneuver, sudden deep inspiration with holding of the breath and bending forward.

In regard to drug therapy there are few disturbances in which the rule “primum non nocere” is so often neglected as in paroxysmal tachycardia. The literature is replete with reports of sudden deaths in this usually harmless condition after an injection of acetylcholine, Mecholyl, neostigmine, epinephrine, quinidine, quinine, procaine amide and other substances. It is not uncommon for the docto rather than the patient to become unduly alarmed and fling common sense to the winds. In the vast majority of cases even an attack lasting several days is well tolerated. Many patients feel only a peculiar sensation rather than palpitation.

Intravenous quinidine abolishes most attacks speedily, often within seconds. This therapy is warmly recommended despite repeated, emphatic and thoroughly justified warnings in the literature that sudden death from cardiac standstill or ventricular fibrillation may immediately follow the injection. A physician experiences great satisfaction if his injection stops an attack within seconds and without any side-effect. This happens in a few patients. In the next one, however, collapse and sudden death may ensue promptly. One can hardly overemphasize the danger associated with the intravenous use of this drug.

If the tachycardia has caused anginal pain or shock, immediate relief is indicated. An intravenous injection of digitalis or strophanthin is the wisest move. This is advised even in the presence of ventricular tachycardia, although we realize that this is contrary to the prevailing opinion. Of course, one must first make sure that digitalis did not cause the tachycardia. Carotid pressure often will abolish the tachycardia after the administration of digitalis although it failed before the injection. One may use 0.4 mg. of digitoxin or Cedinalid or 0.25 mg. of ouabain or Strophosid. Not rarely 20 cc. of a 20 per cent solution
of magnesium sulfate injected intravenously will stop the tachycardia. In patients with shock from a recent myocardial infarction we prefer the intravenous injection of digitalis or strophanthin.

In the vast majority of patients, when there is no urgency, the method of choice is quinidine by mouth. The first and second doses of quinidine (0.4 Gm.) are given one hour apart and are followed by 0.2 to 0.4 Gm. every two hours until the attack subsides.

The situation may be serious in those rare patients who do not respond to the vagal reflexes, to digitalis, to quinidine or procaine amide. This happens particularly in patients with fresh myocardial infarction. Such patients may die because of the tachycardia. A serious problem is also presented by the paroxysmal tachycardia complicating pregnancy when large doses of quinidine are contraindicated. The tachycardia disappears soon after the delivery.

If attacks of paroxysmal tachycardia occur frequently, prophylactic therapy with quinidine is the procedure of choice. The dose is adapted to the requirements of the patient.

Flutter

Auricular Flutter. Of late the justification for separating flutter from paroxysmal tachycardia has become questionable for both origins in a tachysystolic center.27 The other differentiating criteria are not absolute. Carotid pressure frequently abolishes paroxysmal tachycardia but never flutter. It may even increase the flutter rate. In animals, however, flutter may be occasionally suppressed by vagal stimulation.30 The response to vagal stimulation is not entirely a function of rate for in some patients with a tachycardia of 250 per minute carotid pressure may be successful.40

Brief attacks of paroxysmal flutter are treated with quinidine in the manner already described for paroxysmal tachycardia. If the attacks recur frequently the drug should be given every day as a prophylactic.

Opinions are divided as to the best therapy for flutter that has lasted more than a few days. It is agreed that such patients should be treated in the hospital because they require careful supervision. Either digitalis or quinidine can be used and there is no accurate guide which is best for a given patient. Most cardiologists favor the use of digitalis. Flutter is sometimes replaced by sinus rhythm but usually it is converted into fibrillation. Digitalis is best administered in the form of digitoxin, approximated 0.6 mg. daily for one or two days. As soon as fibrillation appears, the dose is reduced and a smaller maintenance dose is given. Usually one attempts to convert fibrillation into sinus rhythm with quinidine. Others prefer administration of quinidine from the start. During quinidine therapy, the ventricular rate may temporarily increase. This results from two mechanisms: (1) a decrease of the auricular rate allows the conduction of more stimuli to the ventricle and (2) the vagolytic effect of quinidine improves A-V conduction. There is no substantial evidence that the administration of digitalis before quinidine ameliorates this complication; digitalis slows A-V conduction mainly through increased vagal tone. The clinical consequences of a change from 3:1 or 2:1 block to 1:1 rhythm are, however, usually negligible in spite of a threefold increase of the cardiac rate.

The program of treatment is guided by the condition of the patient and the heart. Digitalis is used from the start when shock or severe anginal pain is present, after acute myocardial infarction with poor heart sounds and low blood pressure, in congestive cardiac failure, or with a very high initial ventricular rate.

If the general condition is good, some prefer to start with quinidine. The dosage is the same as has been described, since the primary purpose is identical for all tachysystolic arrhythmias, namely, to obtain a blood concentration adequate to suppress the tachysystolic focus.

If a sudden rise in ventricular rate occurs, one should continue to administer quinidine. The additional quinidine will lower the ventricular rate either by decreasing the rate of the tachysystolic center or by decreasing the A-V conduction through its direct action on the A-V node and bundle. The danger of embolism with restoration of sinus rhythm is less in fibrillation since the “fluttering” contractions of the auricles tend to prevent
thrombus formation in the auricles. There is no advantage in administering quinidine by intramuscular injection since no significantly higher blood levels are obtained by this method than by oral administration. The therapeutic levels are, however, reached earlier.

Some patients with auricular flutter have A-V block with a 4:1 or higher A-V ratio. Even after mild exertion, this block usually persists and prevents high ventricular rates. Under these circumstances therapy of the flutter itself is not indicated.

Procaine amide has not proved successful in the treatment of auricular flutter, probably because the required dosage is in the toxic range.

Occasionally, chronic flutter responds neither to digitalis nor quinidine. Antithyroid therapy is occasionally successful. At times flutter resists all therapy and constitutes a serious problem.

**Ventricular Flutter.** The separation of ventricular flutter from ventricular paroxysmal tachycardia is impossible. The treatment would be identical.

**Fibrillation**

**Auricular Fibrillation.** The treatment of paroxysmal auricular fibrillation is similar to that of paroxysmal tachycardia. Quinidine is employed for the attack if the attack is associated with severe exertion, during pneumonia, acute myocardial infarction and hyperthyroidism; it is also used prophylactically. In patients with congestive failure, a course of digitalis should precede quinidine. In some patients who have established auricular fibrillation with a slow ventricular rate, no therapy is indicated. Such patients often exhibit no other signs of heart disease. Mild exercise may increase the rate markedly; under these conditions digitalis is indicated. Small doses, such as 0.1 Gm. of standardized powdered leaf daily, usually suffice.

Whether one should convert chronic fibrillation to a sinus rhythm constitutes a difficult problem. In the current wave of enthusiasm for conversion, one must recall that 2 to 5 per cent of all patients with chronic auricular fibrillation treated with quinidine experience either serious embolism or death. The latter can be caused by ventricular fibrillation, cardiac standstill, cerebral embolism or respiratory failure. Accordingly, if the patient is not suffering appreciably from the fibrillation there is no need for aggressive therapy. The increased danger of embolism in chronic nontreated fibrillation is, of course, a real one. It is, however, by no means absent during sinus rhythm.

After the first instances of sudden death due to quinidine therapy were published, the original enthusiasm for this form of therapy subsided. It was emphasized that fibrillation of the auricle does not seriously affect the circulation if the ventricular rate is reduced to 80 beats per minute or less. Such slowing of the heart is actually possible in all patients unless rheumatic fever, hyperthyroidism or pulmonary embolism is present. The improvement that follows satisfactory control of the ventricular rate is certainly almost as great as that which follows conversion to sinus rhythm.

In recent years it has been shown, however, that in some patients with auricular fibrillation and a slow ventricular rate, restoration of sinus rhythm is accompanied by an increased minute volume and blood pressure and a fall in the venous pressure. The activity of the auricles, therefore, is of greater importance in some patients than was formerly believed. Actually, this might be expected in patients with mitral stenosis where the contraction of the left auricle is helpful; however, in mitral stenosis with marked enlargement of the left auricle, an effective contraction is impossible even during sinus rhythm. In many but not all patients in whom sinus rhythm was restored, the clinical condition improved.

It is certain that the present enthusiasm for conversion of fibrillation will wane in the course of time just as it did in the early 1920's when quinidine was widely used for this purpose. Even anticoagulant therapy for 10 to 14 days before the course of quinidine does not prevent embolism although it may help in some cases. On the other hand, it introduces a new source of danger.

If it had been established that dangerous complications occur more often in fibrillating than in nonfibrillating patients, physicians
would be more willing to accept the risks involved in the use of quinidine. In any case it must be remembered that in patients with chronic heart disease such as mitral stenosis and coronary sclerosis, fibrillation recurs in 50 per cent within six months after successful conversion.

In brief, much of the hemodynamic disturbance caused by fibrillation can be corrected by digitalis alone with slowing of the ventricular rate. However, there is no doubt that a significant proportion of patients will benefit considerably from conversion. The latter however, is always a risky procedure and should be attempted only in selected cases in a hospital.

Definite contraindications to defibrillation exist in patients with mitral stenosis and a large left auricle; the danger of embolism attendant on conversion is especially great. On the other hand, if the patient is already manifesting multiple emboli, a course of anticoagulants followed by quinidine has been successful in preventing further emboli.

Conversion to regular rhythm is also contraindicated in patients with mitral stenosis who have had pulmonary edema or hemoptysis. Fibrillation seems to protect these patients from a recurrence of these incidents. Auricular fibrillation seems also to protect some patients with coronary sclerosis from angina pectoris; the reasons for this are not known.

Conversion of chronic fibrillation may be indicated in spite of all risks in the presence of intractable congestive failure.

All patients with fibrillation should be examined very carefully for the existence of hyperthyroidism.

The method of administration of quinidine has been discussed above. In most instances five daily doses are given at intervals of two hours. In one patient the dose of 2.66 Gm. (40 grains) was given five times daily without therapeutic effect. Sinus rhythm will be re-established in about 80 per cent of the patients. After conversion has been achieved, it is important to prevent recurrence of fibrillation. It is often necessary to administer quinidine four times daily for an indefinite period.

**Ventricular Fibrillation.** This arrhythmia almost always causes death within a few minutes. Measures to abolish it in the experimental animal were recommended more than 50 years ago. The problem became clinically important with the advent of modern thoracic surgery. The principles of treatment of ventricular fibrillation differ considerably from those of the other cardiac arrhythmias. Since irreparable damage is sustained by the central nervous system after an absence of blood flow lasting three to five minutes, the need for immediate therapy is evident. To maintain some blood supply to the brain and to the myocardium the heart must be rhythmically compressed manually 40 to 50 times per minute. Simultaneously measures are invoked to terminate the fibrillation and supply oxygen.

While rhythm compression of the heart is performed, intraventricular injection of an agent which will abolish the fibrillation should be made. The agent used should permit the resumption of rhythmic activity as soon as fibrillation subsides. Potassium chloride, although effective in abolishing fibrillation, is not advocated because it only rarely permits full recovery of the myocardium even if calcium is also used. Even if fibrillation disappears it often recurs.

Two agents which meet the requirements are procaine hydrochloride and electrical shock. Procaine hydrochloride introduced into the fibrillating ventricle in sufficient concentration stops the fibrillation. This compound is quickly hydrolyzed so that the myocardium can resume regular contractions within a few minutes. About 5 to 10 cc. of a 2 per cent solution are injected into the left and, if necessary, also into the right ventricle during the period of manual compression. The fibrillation can also be stopped by the application of electrical current. The heart is placed between two large electrodes and an alternating current of 110 volt and 1.5 amperes is used. Special electrical units have been designed for this purpose.

If cardiac inhibition with diastolic arrest is the cause of circulatory standstill the employment of procaine hydrochloride or the electric current is unnecessary. Therapy of cardiac arrest is discussed in the following
section. For resuscitation, rhythmic compression of the heart is needed in any case.

**DISTURBANCES OF CONDUCTION**

Intra-auricular and intraventricular conduction disturbances do not lead to arrhythmias. Only on rare occasions does sinoauricular block cause cardiac standstill and require therapy. A-V block, however, occasionally causes disturbances demanding treatment.

No therapy is necessary for prolongation of the P-R interval. One should keep in mind that healthy individuals engaged in strenuous athletics may exhibit a P-R interval of 0.20 or 0.22 second with or without a bradycardia. Periodically dropped beats (Wenckebach phenomenon) as well as 2:1 or 3:1 A-V block do not require special therapy. Most patients with complete A-V block do not need treatment for the block itself; usually the centers in the ventricle take over the function of pacemakers satisfactorily. However, should these centers have an inherent rate too low for circulatory efficiency (24 beats per minute or less), it is necessary to treat the arrhythmia directly, since under these circumstances the heart is unable to increase the rate sufficiently on exertion. Patients with this condition experience marked dyspnea and weakness on slight effort. The administration of 0.032 Gm. of ephedrine three times daily increases the basic rate of the heart and improves the exercise tolerance. Usually, it is advisable for the patient to adjust his activities to his limited capacity.

The most serious complication of A-V block is the Stokes-Adams syndrome. Its prevention and treatment depend on the mechanics present in the particular case. Often the syndrome is caused by cardiac standstill when partial A-V block becomes complete and the ventricular pacemakers are tardy in taking over. In rare instances of permanent A-V block, cardiac standstill may result from an abnormality in the lower pacemakers. In still other cases of A-V block, the appearance of numerous ventricular extrasystoles or tachycardia or even short attacks of ventricular fibrillation interfere with cardiac action. It is not unusual for a patient to exhibit one mechanism at one time and the other at another time, or even tachycardia and standstill in rapid succession. Only an electrocardiogram obtained during an attack permits one to recognize the mechanism of a particular attack. The same disease, often bilateral bundle branch block, which causes the A-V block may lead to the formation of centers rapidly firing impulses. It may be assumed that the excitability of centers beyond a block is increased (Wedensky facilitation).

Since the therapy for Stokes-Adams attack due to one mechanism is harmful when the other mechanism is present, the task for the physician is not easy. The administration of drugs should be postponed until the mechanism of the attacks has been determined with the aid of the electrocardiograph.

To prevent Stokes-Adams attacks during the change-over from partial to complete A-V block, the establishment of permanent complete block by digitalis has been recommended. During an attack of cardiac standstill, the best treatment consists of mechanical stimulation of the heart by punching the chest vigorously with the fist. Ephedrine aids in preventing these attacks. Intracardiac injections have little justification; epinephrine may lead to ventricular fibrillation. If an intracardiac injection is undertaken, caffeine salts are less dangerous. The mechanical stimulus of the needle often suffices to awaken the automaticity of the ventricles.

When ventricular tachycardia or fibrillation causes circulatory standstill, it would seem logical to use quinidine or procaine amide. Experience shows, however, that this is dangerous; quinidine may cause ventricular fibrillation in such cases. Most examples of brief ventricular fibrillation reported in the literature have occurred in patients with complete A-V block who received quinidine.

Aminophylline suppositories appear to have some clinical merit in all forms of Stokes-Adams attacks probably through beneficial action on muscular metabolism. Therefore, this therapy is permissible even when an accurate diagnosis is impossible or where cardiac standstill and tachycardia succeed each other.
Complete A-V block following myocardial infarction requires no therapy and may be a welcome complication. The resulting bradycardia usually improves the relation between oxygen need and oxygen supply of the heart. A fall in blood pressure and pulmonary congestion may occur when the bradycardia is replaced by normal rhythm with an increased rate. The administration of oxygen and of suppositories of aminophylline is indicated.

The use of atropine in heart block, so popular a few years ago, is not justified. With increase in the auricular rate the degree of heart block may be increased and partial change into complete block.

Employment of digitalis in patients with partial heart block as well as in those with complete block should follow the rules that apply to all cardiac patients. When decompensation and myocardial failure are evident, digitalis is indicated. Large doses should not be used, that is, not more than 0.2 Gm. of digitalis daily, and the patient must be watched carefully.

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