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Electrical Reversion of Cardiac Arrhythmias*[†]

BERNARD LOWN

From the Department of Nutrition, Harvard School of Public Health, and the Medical Clinics of the Peter Bent Brigham Hospital, Boston, Mass., U.S.A.

I consider it a great honour to be chosen as Thomas Lewis Lecturer of the British Cardiac Society. The work of Sir Thomas Lewis on the heart beat surely ranks as one of the outstanding achievements in experimental physiology. I can claim a greater kinship to Thomas Lewis than that of merely being a distant admirer, for he can be regarded as the godfather of American cardiology. His students are to be found throughout the American continent where they have been instrumental in laying the foundation for the study of heart disease: White, Levine, Landis, Blumgart, and Bland in Boston; Oppenheim and Master in New York; Stroud in Philadelphia; Frank Wilson in Michigan; Katz in Chicago; Prinzmetal in Los Angeles; Graybiel in Florida-to name but a few.

From Thomas Lewis they obtained above all else a scientific approach to medical experimentation. This displaced the then prevalent and shopworn ideas based on the subjectivity and the intuition of the chosen few. The hallmarks of Thomas Lewis's method of work were the application of precisely controlled and exacting methods, the assiduous gathering of evidence, the rigorous censorship of data, and the recognition of the role of animal experiments as a proper domain for inquiry into many complex clinical problems. The yield of his legacy is not a harvest for a single season, and the rich fruit is still being gathered. This very lecture was initiated by his student and my teacher, Doctor Samuel A. Levine.

Yet there is a more intimate kinship I wish to expose for your consideration: namely, that the work on cardioversion represents a therapeutic culmination of Lewis's ideas on the nature of ectopic arrhythmias, especially his theories of the circus movement and the concept of the "excitable gap".

THE PROBLEM AND A POSSIBLE SOLUTION

Drugs have been the mainstay in treating rhythm disturbances of the heart. The use of drugs, however, presents a number of formidable limitations. In the first place, in the individual patient neither the effective nor the toxic dose can be predicted. It has therefore been essential to administer what are considered to be safe increments of the drug at frequent intervals until the arrhythmia either terminates or toxicity supervenes. Such biological titrations generally require hours, days, or even weeks. Intensive observation of the patient and frequent electrocardiographic monitoring are necessary to prevent untoward reactions. However, whatever the precautions, serious side-effects frequently occur. In the second place, the antiarrhythmic drugs, especially when given in large doses or to critically ill patients, often depress myocardial contractility and reduce peripheral resistance at the very time when the cardiac reserve is already maximally compromised. In the third place, these drugs not only depress excitability of ectopic sites but also that of the normal pacemakers of the heart, thereby at times inhibiting restoration of sinus rhythm.

Analysis of the developmental process of ectopic arrhythmias indicates that once an abnormal mechanism is initiated it may be self-sustaining. Continuation of the disorder may be due to the existence of a re-entering wave front of excitation, which traverses either a fixed or variable pathway a concept in large measure the result of the many elaborate and ingenious experiments of Thomas Lewis (1925). If this is indeed true, then all that is required to extinguish an arrhythmia is but a

^{*} The Thomas Lewis Lecture delivered on November 26, 1965, before the British Cardiac Society, London.

[†] The studies reported were supported by funds from grants of the National Institute of Health, the Life Insurance Fund, and the Fund for Research and Teaching, Department of Nutrition, Harvard School of Public Health.

momentary depolarization of the heart with the abolition of the abnormal circuit. The sinus node, having the highest degree of automaticity within the heart, then resumes as the dominant pacemaker. It would follow that an extrinsic electrical discharge perhaps by depolarizing the entire heart might abolish the abnormal pathway and with it the arrhythmia. This was a majestically simple idea that needed exploration.

HISTORICAL CONSIDERATIONS

The history of electrical application to the heart begins in the 18th century with a direct current derived from a Leyden jar. Priority belongs to Abilgard (1775). He relates that he shocked a single chicken into lifelessness, and upon repeating the shock, the bird took off and eluded further experimentation. Benjamin Franklin, one of the leaders of the American Revolution, at about the same time as Abilgard, not only shocked goats and killed fowl with charges of static electricity but also was a subject for his own experiments. During his kiteflying studies he was knocked senseless several times by lightning. Medical history does not recount whether any arrhythmias were induced. From his experiences he commented, "If there is no other use discovered for electricity, this, however, is something considerable that it may help make a vain man humble".

With the introduction of the dynamo and the development of commercially available electric power, a new industrial hazard appeared. The first industrial accident involving electrocution occurred in 1879. By the end of the second decade of this century, about 1000 people annually lost their lives in the United States of America due to accidental electrocution. It was soon realized that a majority of such deaths were due to ventricular fibrillation.

The utilization of electrical discharge for terminating ventricular fibrillation dates to the turn of the century. In 1899, Prevost and Battelli applied strong currents directly to the heart of dogs to induce ventricular fibrillation, and only in a footnote do they mention incidentally that these electrical discharges were also capable of terminating ventricular fibrillation. Scant attention was paid to their work. More than 30 years elapsed before the subject of electrical defibrillation was re-opened by the studies of Kouwenhoven, Hooker, and Langworthy (1932). These investigators tried various electrical discharge circuits including direct current shock. After much experimentation, they concluded that alternating current (A.C.) gave superior results. Their apparatus employed 60 cycle A.C. of 1.5 to

2.0 amperes and 120 to 130 volts. Electrode paddles were applied directly to the heart (Hooker, Kouwenhoven, and Langworthy, 1933).

The efforts of Kouwenhoven extending over three decades clearly defined the electrical and other technical conditions for defibrillating the heart with alternating current and promoted the general acceptance of "countershock" as an experimental and clinical tool. The extensive investigation of Wiggers (1940) confirmed the effectiveness of such current in defibrillating the exposed heart. These studies culminated in the successful defibrillation of the human heart by Beck, Pritchard, and Feil in 1947, the patient recovering completely. Nevertheless, the need for a thoracotomy and direct application of electrodes to the heart limited the clinical use of this method. In 1936, Ferris et al. succeeded in defibrillating sheep hearts by sending currents of 25 amperes through the intact chest. The studies of Zoll and co-workers (1956) clearly demonstrated the effectiveness of A.C. discharge for the transthoracic defibrillation of the human heart.

While the use of alternating current became the favourite method for defibrillation in the United States, the pioneering experimental work of Gurvich and Yuniev (1946, 1947) in the Soviet Union laid a basis for the use of direct current or capacitor discharge (D.C.). The more recent investigations of Peleška (1957, 1963, 1966) in Czechoslovakia demonstrated the physiological consequences of electrical discharge and suggested some of the characteristics required to produce safe cardiac de-Until 1960, electrical discharge, fibrillation. whether A.C. or D.C., was not employed for terminating arrhythmias other than ventricular fibrillation. Lown and colleagues were the first to employ A.C. electively in a patient with coronary artery disease to terminate an episode of ventricular tachycardia that had proved resistant to antiarrhythmic drugs (Alexander, Kleiger, and Lown, 1961). This successful accomplishment led to the transthoracic use of alternating current shock for terminating refractory arrhythmias. This was the level of development up to 1960.

ANIMAL EXPERIMENTS

Alternating Current (A.C.). As long as defibrillation was but rarely attempted, the problem of finding an optimal form of electric shock did not press for solution. With the increasing application of defibrillation, and with the introduction of electrical shock for treating arrhythmias other than ventricular fibrillation, it was essential to define the physiological as well as the pathological consequences of electrical discharge. Animal experiments (Smith



FIG. 1.—Wave form of capacitor discharge without inductance. At a setting of 30 watt seconds (ws) a single discharge across the intact chest evokes ventricular arrhythmia. The median energy required for defibrillating the heart transthoracically is 70 ws.

et al., 1965) have shown that as few as five A.C. shocks of 350 volts-the setting necessary to defibrillate transthoracically a majority of dogs with ventricular fibrillation-when delivered across the limbs result in unique skeletal muscle lesions. These are characterized by focal sarcolemmal proliferation. loss of striation, vacuolization, and ultimately frank necrosis in the individual fibres. When A.C. discharge is delivered across the intact chest of animals in sinus rhythm, there is a consistent provocation of a diversity of cardiac arrhythmias, including ventricular fibrillation (Lown et al., 1962b). When the experimental animal is given as many as 20 successive transthoracic shocks at defibrillatory voltages, 90 per cent exhibit currents of injury and 50 per cent develop the sequential changes of transmural infarction. When A.C. shocks are applied directly to the heart, there is substantial deterioration in ventricular function (Main, Aberdeen, and Gerbode, 1963; Yarbrough, Usserv, and Whitley, 1964). Since the production of ventricular fibrillation after A.C. shock is inversely related to the voltage of the discharge, this method is especially hazardous for the operator and attendant personnel. It may be concluded that A.C. shock was not a very suitable method for correcting arrhythmias in man.

Direct Current (D.C.). Capacitor discharges which deliver a monophasic pulse were studied next. By modifying the parameters of the discharge circuit, one could obtain an endless variety of electrical wave forms. There was no a priori physiological basis for selecting one particular wave form

suitable for human use, except that two preconditions had to be satisfied: that the discharge should be able to depolarize the entire heart upon transthoracic application, and that this should be accomplished with a wide margin of safety. A simple capacitor without inductance was initially employed. This gives rise to a spike wave with exponential decay (Fig. 1). Though such a discharge is as effective as A.C. in defibrillating the heart, it results in protracted ventricular arrhythmias even when low energies are employed. Repeated transthoracic shocks induce electrocardiographic changes which are those one sees with hyperkalæmia (Fig. When multiple shocks are given to a limb, 2). massive skeletal muscle necrosis develops, which may be followed by death.

The inclusion of an inductance in the discharge circuit of the capacitor decreases the peak voltage and peak current, and lengthens the duration of discharge. The reduction in energy dissipation per unit time lessens the damage to subjacent tissues. Even so, such attenuated capacitor discharges may disrupt cardiac rhythm, impair conduction, and induce other deleterious biological effects. After extensive studies, it became clear that tissue damage, potassium release from skeletal muscle, and the provocation of arrhythmias were related to four variables: (1) a rise time of the wave front of 500 microseconds or less, (2) a voltage greater than 3000, (3) a discharge energy exceeding 400 watt seconds (ws), and (4) the absence of oscillatory recovery or "ringing" in the tail end of the wave (Lown and Beeuwkes, 1967). On the basis of these findings an underdamped impulse was









chosen (Fig. 3) which has a duration of 2.5 msec. and is released from a 16 microfarad capacitor through a 100 millihenry inductance. This form of modified capacitor D.C. discharge was found to be both safe and effective in defibrillating the heart. While it takes 70 ws for transthoracic defibrillation of the dog heart, arrhythmias other than ventricular fibrillation are produced only with levels of 400 ws. It provides thereby a five- to sixfold factor of safety. An additional advantage is that cardiac standstill has not resulted after many thousands of high energy shocks.

A factor limiting the elective clinical use of this type of D.C. discharge was the occasional development of ventricular fibrillation. While this occurred after random shocks in less than 2 per cent of normal dogs, there was no certainty that a much higher incidence would not result in patients with organic heart disease.

Vulnerable Period. Physiologists have previously reported on the existence of a vulnerable period in the cardiac cycle during which the heart is susceptible to fibrillation (de Boer, 1923; Andrus, Carter, and Wheeler, 1930; King, 1934; Wiggers and Wégria, 1940). In exploring the basis for the sporadic occurrence of this arrhythmia, it was found that D.C. shock produced ventricular fibrillation only when the discharge fell during the inscription of the initial portion of the T wave. This brief vulnerable period, measuring 30 milliseconds in duration, preceded the apex of the T wave. An appropriate test shock placed within the vulnerable period consistently produced ventricular fibrillation. When the discharge was triggered outside this interval, ventricular fibrillation did not occur. A similar period of vulnerability for the atrium was demonstrated during inscription of the downslope of the R wave or the S wave of the surface electrocardiogram. Discharge during this phase of the cardiac cycle resulted in atrial fibrillation. Vulnerable periods have now been identified in such diverse mammalian species as rabbits, cats, dogs, sheep, and subhuman primates (Lown et al., 1963a). In all animals tested, the ventricular vulnerable period was of the same duration and location whether studied transthoracically, determined from the surface of the heart, or from within the myocardium. These findings suggest that ventricular vulnerability is a physiological property of the mammalian heart.

The vulnerable period, coinciding with the inscription of the apex of the T wave of the surface electrocardiogram, represents the terminal position of the refractory state. Asynchronous recovery from the refractory state has been entertained as a precondition for fibrillation (Brooks *et al.*, 1955; Hoffman and Cranefield, 1960; Moe and Mendez, 1962). When an impulse is delivered to the heart during the vulnerable period, it encounters an irregularly excitable field and is forced to propagate at a subnormal velocity and over a tortuous pathway. This favours re-entry of the depolarization wave and initiation of self-sustained activity. Each successive re-entry augments the initial non-uniformity. Fibres responding early will exhibit a shorter refractory period than those responding later; this further contributes to inhomogeneity and results in increased dispersion both in the duration of refractoriness and in the velocity of conduction. This, then, explains the hazard of randomly triggered electrical discharge which might fall during the vulnerable period and precipitate ventricular fibrillation.

Do these physiological relations apply to man? It has been observed that patients who have extrasystoles occurring early in the cardiac cycle with interruption of the T wave, the so-called R on T phenomenon, are liable to sudden death (Smirk and Palmer, 1960; Palmer, 1962). When pacemakers are implanted and thereafter A-V conduction is restored, repetitive ventricular arrhythmias may follow. These arrhythmias occur only when the artificial pacemaker acting as a parasystolic focus discharges during the inscription of the T wave (Tavel and Fisch, 1964; Holmes et al., 1963). More recently, deliberate testing of the vulnerable period in man by means of an artificial pacemaker has elicited repetitive firing and ventricular fibrillation when the test stimulus was delivered at the apex of the T wave (Castellanos, Lemberg, and Berkovits, 1966). These findings indicate that vulnerability to fibrillation is also an attribute of the human heart. It would follow that the occurrence of ventricular fibrillation following depolarizing electrical shocks in man could be completely prevented by triggering the discharge to avoid the apex of the T wave.

Thus, by employing a capacitor discharge with a specific underdamped pulse and synchronizing the release of this pulse with a safe part of the cardiac cycle, the twin dangers of electricity, namely ventricular standstill and fibrillation, can be avoided (Lown, Amarasingham, and Newman 1962a). It has, therefore, become possible to employ electrical currents for terminating a diversity of ectopic arrhythmias. This method has been designated "Cardioversion" (Lown *et al.*, 1963b).

OVER-ALL RESULTS

Cardioversion was first employed in 1961 at the Peter Bent Brigham Hospital. The patient, an

Bernard Lown



FIG. 4A.—Ventricular tachycardia refractory to anti-arrhythmic drugs. Marked intraventricular blockfand slow rate due to large doses of quinidine and procaine amide.



tachycardia.

elderly woman in the throes of an acute myocardial infarction, developed drug refractory ventricular tachycardia accompanied by hypotension and pulmonary cedema (Fig. 4A). Large doses of quinidine and procaine amide slowed the ventricular rate but provoked profound shock. The patient kept on muttering, with adequate reason, that she was dying. A single 100 watt second (ws) synchronized discharge resulted in prompt reinstatement of sinus rhythm (Fig. 4B), with immediate clearing of the pulmonary cedema and restoration of normal blood pressure. The patient exuded a sense of well-being; the only problem was to assure her that she was in the hospital recovery room, not in the Hereafter. Over the past four years cardioversion was employed to terminate 601 episodes of diverse arrhythmias in 470 patients (Table I). The success rate was 94 per cent. This result is the more impressive since 100 patients were refractory to large doses of drugs and were restored to sinus rhythm by cardioversion. In the 601 cardioversions, 1088 electrical shocks were administered, yet there was not a single episode of cardiac asystole or ventricular fibrillation. Although many of the patients treated were in critical condition, a number in the early stages of acute myocardial infarction and some even terminally ill, none died as a result of the procedure. Serious immediate complications were limited to five episodes of ventricular tachycardia. These were of brief duration, in four not exceeding 30 seconds. In the remaining patient an additional cardioversion discharge was required to terminate the ventricular tachycardia. This clinical experience validates both the theory and experimental inferences on which cardioversion is based.

To date, many thousands of patients have been reverted by this method. The results as given in published reports have been nearly identical to those cited above (Killip, 1963; Oram et al., 1963; McDonald, Resnekov, and O'Brien, 1964; Morris et al., 1964b; Hurst et al., 1964; Mathivat et al., 1964; Pantridge and Halmos, 1965; Towers et al., 1965). The complications have been relatively few and related to the following factors: presence of electrolyte derangements or overdigitalization, improper use of antiarrhythmic drugs prior to countershock and for maintenance, inadequate use of sedation and reliance on large doses of anæsthetic agents, failure to synchronize properly the discharge within the cardiac cycle, and employment of excessive energies. These points will be discussed more fully.

TABLE I

FOUR YEARS' EXPERIENCE WITH CARDIOVERSION IN 470 PATIENTS AT THE PETER BENT BRIGHAM HOSPITAL

| Arrhythmia | No. of episodes | Per cent success | |
|------------------------------|--------------------|---------------------|--|
| Atrial fibrillation | 456 | 93·7 | |
| Atrial flutter | 70 | 97·2 | |
| Supraventricular tachycardia | 15 | 74·0 | |
| Ventricular tachycardia | 60 | 98·4 | |

TECHNIQUE OF CARDIOVERSION

The procedure employed is essentially the same. irrespective of the mechanism of the ectopic disorder. Since the most common arrhythmia encountered is chronic atrial fibrillation, the steps to be described will specifically apply to this disorder (Lown, Kleiger, and Wolff, 1964). However, the same procedure with but slight modifications is applicable to other arrhythmias. In the case of elective reversion, one or more days before the procedure is carried out, maintenance quinidine therapy is instituted in a dose of 0.3 g, every six hours. The objective of administering quinidine is threefold: (1) to build up an adequate cardiac tissue level in order to prevent prompt recurrence of the arrhythmia; (2) to determine whether quinidine is well tolerated; and (3) to obtain a small dividend of reversions which result in about 10 per cent of patients with chronic atrial fibrillation on such maintenance doses of quinidine alone. Rossi and

Lown (1966) have found that prior treatment with quinidine improves the chance of remaining in normal rhythm immediately after reversion, reduces the number of shocks, decreases by about 40 per cent the energy required to restore sinus rhythm, and diminishes the incidence of post-cardioversion arrhythmias. If quinidine in any form is not tolerated, the advisability of cardioversion of chronic atrial fibrillation should be reconsidered.

Digitalis drugs are withheld one or more days before the procedure. If digoxin is the glycoside employed, omission for one day is sufficient. No premedication is required except for a sedative. The use of pentobarbitone sodium ("nembutal") one or more hours before the procedure may reduce the energy for reversion. On several occasions the administration of this drug facilitated restoration of sinus rhythm. The accuracy of the synchronizing circuit should be checked several times before the procedure. The patient is then given 25 to 75 mg. methohexital ("brevital") intravenously. The object is to induce transient amnesia rather than anæsthesia or unconsciousness (Shephard and Vandam, 1965). Muscle relaxants are not necessary. The two electrode paddles are coated with thick layers of conductive paste. The patient lies on the flat posterior paddle which is applied in the left infrascapular region, while the anterior paddle is held with pressure over the upper sternum at the level of the third intercostal space. This anteroposterior position, compared with the previously employed antero-lateral placement, shortens the pathway between electrodes and augments the density of the electrical field which traverses the heart, thereby diminishing by about 50 per cent the energy required for reversion (Lown et al., 1964).

An important aspect of the procedure is to begin with low energy settings of 25 to 50 ws and then increase the energy in successive shocks until sinus rhythm is restored. The occurrence and gravity of arrhythmias is not related to the number of shocks employed but rather to the energy content of the shock (Fig. 5). By beginning with a low setting and increasing the level of discharge progressively, only the minimum energy to restore a normal rhythm is employed. If arrhythmias develop before reversion is achieved, one has the option of discontinuing the procedure or else administering appropriate anti-arrhythmic drugs. When frequent ventricular ectopic beats occur after a discharge of 50 ws, a single injection of 50 mg. 2 per cent xylocaine ("lidocaine") intravenously is promptly effective. It is then possible to employ higher energies. If the ectopic beats are not suppressed, procaine amide is next employed. Using this approach, we have never observed serious and pro-



FIG. 5.—With discharge of increasing energy more serious arrhythmias follow: after 100 ws, recurrent ventricular ectopic beats; after 200 ws, salvos of ventricular extrasystoles; after 300 ws, sustained ventricular tachycardia.

gressive ventricular arrhythmias; furthermore, it has not proved necessary to abandon the procedure because of increasing ventricular irritability.

The use of lead II for monitoring the cardioversion may give rise to an erroneous impression that the ectopic mechanism is still present when it has already been abolished. Transitional nodal mechanisms are common and are difficult to differentiate from atrial fibrillation. The difficulty in interpretation may be compounded by the presence of ventricular irregularity, recurrent atrial premature beats, and instability of the baseline due to body movement or muscle tremor. A brief strip of lead V1 recorded before successive shocks generally helps to identify the nature of the cardiac mechanism (Fig. 6). Reversion itself takes but a fraction of a second. A typical example is illustrated in Fig. 7. The electrical discharge induces a shock artefact consisting of an isoelectric baseline which lasts 1.2 to 2.0 seconds. When systemic pressure



FIG. 6.—The pattern in lead II suggests the rhythm to be atrial fibrillation after shocks of 50 ws and 300 ws. In lead V1 it is evident, however, that sinus rhythm had been restored following a shock of 300 ws.



FIG. 7.—A single 50 ws discharge reverts atrial fibrillation to sinus rhythm. The isoelectric line between the two mechanisms is an artefact lasting 1.5 seconds in order to protect electrocardiographic circuitry.

is recorded during cardioversion, the change in pressure contour simulates that of ventricular extrasystole and results in a compensatory pause which equals about two cycles. The patient's response consists of a single twitch of thoracic muscles, a jerk of the arms, and at times an audible sigh. When repeated shocks are employed, there appears a thin ring of erythema demarcating the outer circumference of the paddle electrodes. The patient does not experience pain but the area may be tender for 24 hours. The entire procedure requires about 30 minutes and usually the patient is awake in one to five minutes.

A better appreciation of the application of cardioversion can be derived by considering specific arrhythmias.

ATRIAL FIBRILLATION

Atrial fibrillation represents the most frequent chronic disorder of the heart beat. In the present series it constituted 76 per cent of the arrhythmias treated by cardioversion. Sinus rhythm was reinstated in 94 per cent of the 456 episodes of atrial fibrillation in 350 patients. The atrial fibrillation was due to rheumatic valvular disease in 70 per cent, coronary artery disease in 12 per cent, "lone fibrillation" (Evans and Swann, 1954) in 10 per cent, and miscellaneous conditions in 8 per cent. In the majority of episodes, sinus P waves were immediately apparent. Atrial ectopic beats were not uncommon during the first minutes after reversion. In a small percentage of patients, the sinus node required a "warming up" period during which time the A-V node was the dominant pacemaker. In one patient nodal rhythm persisted for three weeks before the sinus node reasserted its role. Ventricular ectopic beats were common sequelæ especially after high energy shocks, in patients with coronary artery disease, and in the presence of digitalis intoxication or electrolyte derangement.

Another finding of interest was the frequent occurrence of prolonged A-V conduction. In 75 per cent of the patients the P-R interval measured 0.17 sec. or more. In an analysis of 125 consecutive patients with atrial fibrillation studied immediately after reversion, 37.5 per cent exhibited first-degree heart block, with a mean duration of P-R interval of 0.21 sec. (Lown *et al.*, 1963b). Prolongation of atrio-ventricular conduction was not due to the procedure itself or to overdigitalization, for in the majority of patients the P-R interval remained prolonged even after discontinuation of A-V block with atrial fibrillation was noted 25 years ago by 2

Altschule (Klainer and Altschule, 1942; Altschule, 1945) in patients with thyrotoxicosis and coronary artery disease, as well as in patients with rheumatic valvular disease. In prospective studies we have observed that progressive prolongation of the P-R interval may precede the onset of atrial fibrillation in patients with mitral valvular disease. We have also noted that the degree of prolongation in A-V conduction was directly related to the duration of the atrial fibrillation. When the A-V conduction time was very prolonged, it was more difficult to maintain sinus rhythm.

Once the decision is reached to revert atrial fibrillation, should quinidine ever be employed? Cardioversion is by far the superior and safer method. In close to 100 patients in the present series, cardioversion was undertaken only after large and even toxic doses of quinidine proved unavailing. Yet 96 were readily reverted electrically and without any complications.



FIG. 8.—The energy for reversion from atrial fibrillation to sinus rhythm in 200 consecutive patients. The paddle placement was antero-posterior.

Energy Requirement. By titrating the energy necessary to restore sinus rhythm, it was possible to determine the minimum effective energy for reversion. Body weight, sex, type of heart disease other than rheumatic, and age were not significant factors. When antero-posterior paddle placement was employed, the mean energy for reverting 200 consecutive patients with chronic atrial fibrillation was 100 ws, while 40 per cent of these patients were reverted with 50 ws or less (Fig. 8). Ninety-five per cent of those responding to cardioversion were restored to sinus rhythm with energies of 200 ws or less. The energy requirement and success of ENE

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| Group | No. of patients | Duration (yr.) | | Reversion energy | Per cent failure | |
|------------------|----------------------|--------------------------|----------------------------|-------------------------|----------------------------|--|
| | - | Range | Mean | - (ws) | | |
| 1 2 3 4 | 50 50 37 18 | <1 1-5 6-10 >10 | 0·25 2·2 6·6 17·0 | 87 103 145 240 | 2·0 2·0 27·8 38·8 | |

cardioversion were directly related to the duration of atrial fibrillation (Table II). Thus, when the arrhythmia had been present for only three months, there were only 2 per cent failures and the mean effective energy was 87 ws. By contrast, when the arrhythmia had been present for over 10 years, with a mean duration of 17 years, the mean effective energy was 240 ws, with a 39 per cent incidence of failure. When atrial fibrillation had been present for less than one year, 10 per cent of patients were reverted with 25 ws and none required discharges of over 200 ws. On the other hand, when fibrillation had lasted over 10 years, none were reverted with 50 ws, and in many patients 400 ws was the effective energy. Of 18 patients having fibrillation for more than 10 years, seven could not be reverted at all and five had sinus rhythm only transiently.

The energy requirement and success of cardioversion appeared to be related to the size of fibril-

TABLE III

AMPLITUDE OF F WAVES IN LEAD VI IN RELATION TO ENERGY REQUIRED FOR CARDIOVERSION

| | Amplitude of f waves | | | |
|-----------------|----------------------|-------------|-----------|--|
| | Small | Medium | Large | |
| | <1∙0 mm. | 1·0-2·0 mm. | > 2.0 mm. | |
| No. of patients | 50 | 50 | 50 | |
| Energy (ws) | 140 | 118 | 92 | |

TABLE IV

ENERGY FOR CARDIOVERSION OF ATRIAL FIBRILLATION OF SAME DURATION IN TWO GROUPS OF 15 PATIENTS EACH HAVING SMALL AND LARGE F WAVES

| • | Groups | | |
|---|--------------------|--------------------|--|
| | Α | B | |
| f wave size (mm.) Duration of fibrillation (mth.) Energy (ws) | > 2·0 2·9 61 | <1.0 2.8 118 | |



FIG. 9.—Size of f waves in lead V1 in relation to success of cardioversion and energy requirements to restore sinus rhythm.

latory (f) waves in lead V1 (Fig. 9 and Table III). When f waves were small, i.e. less than 1 mm. in amplitude, 140 ws were required and there were 20 per cent failures. By contrast, when f waves were large, 2 mm. or greater, 92 ws sufficed and only 4 per cent failures were encountered. The size of f waves was inversely related to the duration of the fibrillation; the longer the arrhythmia, the smaller the amplitude of f waves. It may therefore be that the decisive factor is the duration of fibrillation. However, when patients were selected having the same duration of arrhythmia but with differing amplitudes of f waves, there was still a significant difference in the level of energy for reversion (Table IV). The significant variable, however, is the duration of fibrillation. When two groups of 15 patients each were compared, one having long duration of fibrillation but exhibiting large f waves, the other having short duration of fibrillation but small f waves, the energy was significantly higher in the group with long-lasting arrhythmia (Table V).

TABLE V

ENERGY FOR CARDIOVERSION IN TWO GROUPS OF ATRIAL FIBRILLATION (Group A with large f waves but long duration of arrhythmia;) Group B with small f waves but short duration of arrhythmia.)

| | Groups | | |
|---|----------------|-----------------|--|
| I | Α | B | |
| Mean duration of atrial fibrillation Energy (ws) | 8·8 yr. 158 | 2.8 mth. 118 | |

In addition to the duration of arrhythmia and size of f waves in lead V1, failure to restore sinus rhythm was associated with the presence of predominant mitral regurgitation. While 42 of the 350 patients with chronic atrial fibrillation, or 12 per cent, had pure mitral insufficiency, 11 of the 29 failures, or 38 per cent, had this lesion. Among the 96 patients with mitral stenosis as the sole valvular lesion, there was a 6.2 per cent incidence of failure as contrasted to 11 failures among 42 patients with mitral valvular regurgitation, or 26.2 per cent. Whether the patient had been subjected to valvular operation was an additional factor determining the ease of reversion. In the absence of any valvular operation, the incidence of failure was only 4.0 per cent. After a single operation, whether valvotomy or valve replacement, it rose to about 11.0 per cent and to 36 per cent in patients with two or more operations (Table VI). These factors related to the ease of cardioversion also provided an index of the facility in maintaining a normal mechanism. The size of f waves, the presence of mitral incompetence, and the duration of atrial fibrillation probably exert their effect indirectly through atrial size. Valvular operation probably diminished the success rate of cardioversion by inducing injury and fibrosis in the left atrium.

TABLE VI

ANALYSIS OF FAILURE OF CARDIOVERSION IN 29 PATIENTS AMONG 350 WITH CHRONIC ATRIAL FIBRILLATION

| | Failure to restore nodal sinus rhythm (%) |
|--|---|
| Duration of arrhythmia 5 years 5 years | 33·0 30·0 |
| Actiology of heart disease Rheumatic Mitral stenosis Mitral insufficiency Mixed Coronary Lone Miscellaneous | 8·8 6·3 26·2 4·0 4·8 4·6 20·0 |
| Valvular operation None Single Valve replacement Repeated | 4·0 11·0 12·6 36·0 |

Advantages of Sinus Rhythm. Is reversion of atrial fibrillation indicated ? For the patient who experiences uncomfortable palpitation, the quieting of the heart is a welcome relief from chaotic thumping. Even patients who have not been aware of the presence of arrhythmia frequently note a "calm in the chest" when a sinus mechanism is restored. For the patient who has had embolic recurrences, sustenance of sinus rhythm provides the best guarantee against the potentially disabling consequences of further episodes. In the patient with reduced cardiac reserve, restoration of atrial activity can enhance ventricular filling (Gesell, 1911; Wiggers and Katz, 1922; Linden and Mitchell, 1960), maintain a low mean atrial pressure relative to ventricular end-diastolic pressure (Braunwald and Frahm, 1961), and close the atrio-ventricular valve before ventricular isometric contraction (Little, 1951). These hæmodynamic alterations are translated into an increased cardiac output (Hecht, Osher and Samuels, 1951; Morris et al., 1965). In patients with mitral valve disease, the mean cardiac index increased by 32 per cent following cardioversion (Killip and Baer, 1966).

Atrial fibrillation, in addition to reducing stroke output, also impairs regulation of heart rate especially during exercise and emotional excitement. Cardioversion has made possible the nearly simultaneous recording of heart rate during atrial fibrillation and at the very onset of sinus rhythm. In 21 of 25 consecutive patients the heart rate was slowed (Lown et al., 1963b). The average rate before reversion was 110 ± 33 ; 10 seconds later with sinus rhythm it was 79 ± 22 . The degree of slowing was a function of the ventricular rate during fibrillation; thus in two groups, one with a mean heart rate above 110 and the second below 110 a minute, the reduction was 52 and 14 beats a minute, respectively. The continued stability of the heart rate after reversion indicates that the reduced rate was not due to electrical evoked vagal discharge. Even in fully digitalized patients the rate may be extraordinarily rapid with excitement or exertion. In sinus rhythm, rate is regulated by neuro-humoral release from sympathetic and parasympathetic nerves which modulate automaticity of the sinus node. This permits careful regulation of the heart rate. In atrial fibrillation, rate control can only be achieved by the development of atrio-ventricular block, a much less sensitive mechanism. Perhaps herein resides the major hæmodynamic disadvantage of atrial fibrillation.

Contraindications to Cardioversion. The essential criteria which determine whether the procedure should be undertaken are certainty of reversion and anticipation of maintenance of sinus rhythm. The ease of restoring sinus rhythm is not related to the type of heart disease, prior resistance to quinidine reversion, age or sex of the patient, presence or absence of heart failure, occurrence of embolism, degree of ventricular enlargement, chest circumference, or presence of pulmonary emphysema. A number of electrocardiographic features at the time of reversion have been associated with rapid resumption of atrial fibrillation. These include a P-R interval greater than 0.28 sec., numerous and persistent atrial premature beats, atrial premature beats occurring early in the cardiac cycle (Killip and Gault, 1965), failure of the sinus node to generate a consistent impulse within several minutes following reversion, and the development of sinus tachycardia. The presence of terminal P wave forces in lead V1 (Morris et al., 1964a), extreme right axis deviation, intraventricular block, ST segment deviations or Q-T interval prolongation does not affect the chance of maintaining sinus rhythm. Such information is but hindsight and cannot serve as a basis of selection of patients for cardioversion. It emphasizes, however, that even when it is possible to depolarize the heart electrically, resumption and maintenance of sinus rhythm are not assured.

Experience to date indicates that the following categories of patients with chronic atrial fibrillation are not suitable candidates for cardioversion.

(1) Patients who had previously been reverted with quinidine, and, despite adequate maintenance doses, had recurrence of fibrillation. This also applies to patients who exhibit idiosyncrasy or developed serious untoward reaction to quinidine. At the present time no other anti-arrhythmic drug has proved effective in maintaining sinus rhythm for prolonged periods. Exceptionally, when the indication for reversion is pressing, the use of procaine amide either alone or in conjunction with other agents such as diphenylhydantoin, propranolol, and antazoline is worthy of trial.

(2) The patient with free mitral regurgitation displaying a giant left atrium is difficult to revert and sinus rhythm is frequently short lived. If the atrial fibrillation has been present for over two years, cardioversion is futile. Yet these are the very patients who derive the most striking benefit from a normal heart rhythm.

(3) The elderly, asymptomatic patient with coronary artery disease, with a slow ventricular rate without the benefit of digitalis drugs is an unsuitable subject. The slow rate indicates the presence of an advanced degree of A-V block. The hazard from quinidine in patients with heart block outweighs the possible hæmodynamic benefit of a normal rhythm.

(4) Patients who are lone fibrillators (Evans and Swann, 1954), with small hearts and slow ventricular rates, should not be reverted if the arrhythmia is of long duration. They are not only difficult to maintain, but do not profit from reversion (Killip and Baer, 1966).

(5) Patients who before the onset of sustained atrial fibrillation had recurrent diverse atrial arrhythmias, such as described by Parkinson and Papp (1947), should not be reverted. These paroxysmal disorders are not readily prevented; furthermore, the rapid ventricular rate during attacks may prove refractory to slowing by digitalis drugs. Sustained atrial fibrillation is a blessing.

(6) Patients with atrial fibrillation for longer than five

years who then undergo valvular operation usually do not persist in sinus rhythm. On the other hand, if the arrhythmia has had its onset immediately after operation, long-lasting reversion can be achieved.

(7) Patients immediately before or during valvular operation are poor subjects for cardioversion. If reversion is accomplished before operation, the manipulation of the atria during the surgical procedure almost invariably precipitates atrial fibrillation. If the reversion is carried out upon completion of the operation, 80 per cent will have recurrence of arrhythmia within 72 hours, notwithstanding full maintenance doses of quinidine and procaine amide. A more suitable time for cardioversion is two weeks later.

A number of patients having some of the above contraindications were nevertheless treated. The problem was usually intractable heart failure. It was deemed that even a brief spell of sinus rhythm might be of benefit. This practice is especially warranted in patients in dire circumstances who are being prepared for valve replacement procedures.

Maintenance of Sinus Rhythm. Though atrial fibrillation can now be readily terminated, maintenance of sinus rhythm continues as the central problem. In about 10 per cent of patients in whom the arrhythmia was successfully reverted, the ensuing sinus mechanism lasted for only one to two minutes before fibrillation recurred. In accounting for these transient reversions, as well as for the failure in some patients to restore any sinus activity, it should be emphasized that cardioversion consists of two distinct processes. The first is electrical and external, and consists of delivering adequate energy to depolarize the heart; the second is physiological and internal, and consists of effective pacemaking by the sinus node. Even when it is possible to depolarize the heart electrically, resumption and maintenance of sinus rhythm are not assured. There are several reasons for failure. If the factors originally precipitating the abnormal mechanism are still operating, this method cannot prove successful. Failure may also occur when the sinus node or the atria are injured or depressed by drugs, inflammation, infiltration, or infarction. Whether cardioversion is to be carried out depends not so much on the ability to terminate the arrhythmia, but rather on the capacity to sustain a long-lasting sinus rhythm.

Of the first 100 patients reverted, 23 per cent have remained in sinus rhythm. The first patient with atrial fibrillation was treated on November 2, 1961, and continues to have a sinus mechanism. With improvement in patient selection the incidence of long-lasting sinus rhythm should increase. At present, 50 per cent of patients subjected to cardioversion remain in sinus rhythm for at least one year. Yet we have reverted patients with lesser expectations of retaining a normal mechanism. The patient with mitral regurgitation and an enlarged left atrium who has been in atrial fibrillation for more than a year is unlikely to maintain sinus rhythm even with optimal doses of quinidine. Yet these are the very patients who derive the greatest benefit from sinus rhythm and may be taken from invalidism to full occupation. Our policy has been to revert such patients periodically if they remain in normal rhythm for at least three months. The procedure is carried out on an out-patient basis, entailing minimal loss of work. Such a practice is preferable to and carries less risk than mitral valve replacement.

ATRIAL FLUTTER

Chronic atrial flutter has been one of the most difficult arrhythmias to terminate with drugs. The disorder is commonly refractory to quinidine. Digitalis glycosides, the more effective agents for this arrhythmia, need to be employed in large and sometimes toxic doses. When the arrhythmia manifests a 1:1 atrio-ventricular response, it may prove disabling and at times even jeopardize survival. Chronic atrial flutter has, however, been the easiest disorder to terminate by means of cardioversion. It generally responds to a single lowenergy shock (Fig. 10). To date, we have treated 70 patients with atrial flutter and 30 patients who have been in atrial fibrillation but on precardioversion quinidine maintenance doses reverted to atrial flutter. The effective energy was 50 ws or less. Patients ranged in age from 19 to 84. There was a preponderance of men. The duration of arrhythmia varied from several hours to nine years. The arrhythmia in many of these patients had proved resistant to massive doses of digitalis and quinidine. A number were in serious difficulty because of an uncontrollable ventricular rate. One patient, though receiving large doses of digitalis, had to remain recumbent, for whenever in an upright position he experienced syncope associated with a 1:1 atrio-ventricular response and a ventricular rate of 200 a minute. On the basis of the experience in a number of medical centres, it can be concluded that cardioversion is the treatment of choice for chronic atrial flutter.

Cardioversion has one additional use in patients with atrial flutter. When the arrhythmia can be restored to a sinus mechanism only transiently, cardioversion can be employed to induce atrial fibrillation. The latter arrhythmia is much easier to manage. This also applies to the occasional patient with atrial fibrillation, who after cardioversion, remains for only a brief interlude in sinus rhythm and then manifests atrial flutter. The deliberate induction of atrial fibrillation is accomplished by administering a low energy shock of 5 to 10 ws delivered anywhere in the cardiac cycle but outside the ventricular vulnerable period (Fig. 11). This manœuvre has been successful in 14 out of 15 such attempts. This experience supports the theory proposed by Lewis (1925) that atrial flutter is due to a circus movement, since every point in the atrial cycle is equally vulnerable.

SUPRAVENTRICULAR TACHYCARDIA

Cardioversion is also a proper method for terminating certain atrial and nodal tachycardias. To date 18 patients have been treated, including



FIG. 10.-Drug refractory atrial flutter reverted with a single discharge of 25 ws.



FIG. 11.—Atrial flutter is reverted to atrial fibrillation by a 5 ws discharge. Experience indicates that this results irrespective of where in the atrial cycle the discharge is triggered.

five with paroxysmal atrial tachycardia with block, four of which were not due to digitalis. These atrial and nodal tachycardias had proved resistant to vagal manœuvres, digitalis glycosides, and a number of anti-arrhythmic drugs. Thirteen of the 18 were restored to sinus rhythm, or 72 per cent. This represents the lowest success rate of any of the arrhythmias treated with cardioversion. One patient who had digitalis-induced paroxysmal atrial tachycardia with block developed ventricular bigeminal rhythm after a low energy shock of 5 ws, which was controlled with a combination of intravenous xylocaine and procaine amide. Thereafter shocks of higher energy failed to provoke ventricular ectopic beats, but also proved ineffective in restoring a sinus mechanism. The arrhythmia persisted for several days and eventually responded to potassium administration. Cardioversion should be reserved for treating refractory supraventricular tachycardias which do not respond to vagal manœuvres or sedative drugs. It should not be employed when there is reason to believe that digitalis has precipitated the arrhythmia.

VENTRICULAR TACHYCARDIA

The use of anti-arrhythmic drugs such as procaine amide and quinidine for treating ventricular tachycardia may reduce cardiac contractility and peripheral resistance, thereby adding to the burden of the arrhythmia and further compromising an already limited cardiac reserve. With cardioversion, restoration of a normal mechanism is instantaneous and is not accompanied by depression of the cardiovascular apparatus. The most dramatic results of cardioversion are observed in patients with ventricular tachycardia. Indeed, several patients with severe heart failure and hypotension felt well enough to request food soon after reversion. Restoration of effective cardiac action characterized by rise in blood pressure and return of compensation was evident immediately after reversion in all except those patients who were given large doses of antiarrhythmic drugs. Patients with recurrent ventricular tachycardia who previously required weeks of hospitalization to control the disorder were now readily treated in the out-patient department.

Sixty episodes of ventricular tachycardia were treated by means of cardioversion. The success rate was 97 per cent. The duration of arrhythmia ranged from 1 to 33 days. In 10 patients the arrhythmia occurred in the early stages of acute myocardial infarction. Fifteen were refractory to anti-arrhythmic drugs, though employed in large and toxic doses.

The single failure occurred in a patient who had

frequent recurrences of ventricular tachycardia over many years without any apparent heart disease. He weighed 100 kg. and had a chest circumference of 112 cm. (44 in.). He had been successfully treated with cardioversion on a number of occasions, but required 600 to 800 ws to extinguish the arrhythmia. The higher energies were obtained by connecting two cardioverters in series. On one occasion even these large energies proved inadequate. He was therefore given 15 g. of procaine amide, 9 g. intravenously and 6 g. intramuscularly over an 18-hour period. This resulted in re-establishment of sinus rhythm. While on previous occasions, when cardioversion proved successful, he was discharged within an hour after the procedure and drove himself 100 miles to his home, when he was treated with drugs several weeks in hospital were required before he was free of hypotension, weakness, and dizziness.

It is our present view that cardioversion is the treatment of choice of the critically ill patient with ventricular tachycardia (Lown, 1964). When the arrhythmia is accompanied by severe hypotension, or the patient is in pulmonary ædema, or the disordered rhythm is sustained and occurs in the wake of an acute myocardial infarction, cardioversion should be considered as the initial treatment. When the patient does not appear to be critically ill, drugs are to be preferred. One has the choice of using either xylocaine or procaine amide. In the patient with acute myocardial infarction xylocaine is employed because of a lesser tendency to produce hypotension. Xylocaine is given intravenously in a dose of 50 mg.; if it is ineffective it can be repeated in a dose of 100 mg. Procaine amide is given in 100 mg. increments every five minutes, with repeated checks of blood pressure. If reversion does not occur after a total dose of 1.0 g. of procaine amide, or if a substantial fall in blood pressure or widening of the QRS complex develops, drug administration is halted and cardioversion is employed.

COMPLICATIONS

Complications following cardioversion generally relate to technical errors in procedure, the occurrence of pulmonary œdema and embolic manifestations, and the improper use of drugs.

Errors in technique include the use of an instrument with an improper capacitor wave form, failure to synchronize the discharge, or release of the shock in the presence of electrocardiographic artefacts which may trigger the electrical pulse during the vulnerable period. Initiating the procedure with a large energy setting is an additional factor favouring serious ventricular arrhythmias. Yet errors may be committed long before the paddles are applied to the chest. For example, failure to explain to the patient the nature of the procedure may result in agitation and anxiety, release circulating catecholamines, and thereby increase cardiac susceptibility to arrhythmias while diminishing the likelihood of reversion.

Systemic or pulmonary embolism may complicate cardioversion of atrial fibrillation. About 20 per cent of all patients with chronic atrial fibrillation experience one or more serious embolic episodes during the course of this arrhythmia (Daley et al., 1951; Goldman, 1960). The incidence of embolism is increased immediately following reversion to sinus rhythm. According to Sokolow (1939), the danger of embolism is especially striking when the atrial fibrillation recurs. In a series of 400 patients reverted from atrial fibrillation to sinus rhythm with quinidine, Goldman (1960) encountered six embolic events, an incidence of 1.5 per cent. In the 450 episodes of atrial fibrillation treated with cardioversion the incidence of embolism was nearly identical, or 1.2 per cent. None of the 100 patients who received anticoagulant drugs experienced any embolic complications. However, this does not provide decisive proof for the efficacy of anticoagulant drugs, since the incidence of embolism is too small to lend significance to the observation. The use of anticoagulant drugs is at present limited to two high-risk groups, namely patients who have had prior recurrent embolism, and women with asymptomatic mitral valvular disease with atrial fibrillation of recent onset. When anticoagulant drugs are employed, treatment is started three weeks before reversion and continued for one week thereafter.

Pulmonary œdema was observed in four patients within 24 hours after cardioversion by Resnekov and McDonald (1965). It responded rapidly to the usual therapy. We have noted five episodes of pulmonary œdema in four patients. The clinical appearance suggested pulmonary embolism. In the one patient who experienced two such episodes, there were no further recurrences with adequate anticoagulation. It may very well be that emboli dislodged from the right atrium are the initiating event of this syndrome.

Complicating Arrhythmias. The majority of abnormal rhythms immediately following cardioversion are atrial in origin and trivial. They generally represent one of three mechanisms: (1) delayed warm-up of the sinus node manifested by sinus bradycardia, nodal rhythm, or escape beats—the so-called "somnolent sinus"; (2) increased atrial automaticity as demonstrated by individual or multiple atrial premature beats occurring either singly or

in paroxysms of tachycardia; (3) the "sick sinus" syndrome, a defect in elaboration or conduction of sinus impulses characterized by chaotic atrial activity, changing P wave contour, bradycardia, interspersed with multiple and recurrent ectopic beats, with runs of atrial and nodal tachycardia (Fig. 12 and 13). "Sick sinus" is noted in less than 5 per cent of patients who have had atrial fibrillation for less than one year; however, when the arrhythmia had been present for 10 years or longer the incidence was 45 per cent. The first two mechanisms are transient and generally result in stable sinus rhythm within one to five minutes. The third mechanism almost invariably reverts to atrial flutter or fibrillation.

The ventricular arrhythmias following cardioversion are less common but more threatening. These are of two types: the first develops immediately after the shock and consists of ventricular fibrillation, usually the result of improper synchronization. The second type occurs after several or more normal beats, or as late as one to two hours after reversion. It varies from unifocal infrequent recurring ventricular premature beats to prolonged runs of arrhythmia. The latter may consist of ventricular bigeminy, salvos of multifocal beats, ventricular tachycardia, or even ventricular fibrillation, at times ending in death (Rabbino, Likoff, and Dreifus, 1964).

Clinical Studies of Digitalis and Cardioversion. Early in the experience, it was noted that patients receiving large doses of digitalis or those on maintenance digitalis therapy who had substantial diuresis immediately before cardioversion were likely to show post-reversion ventricular arrhythmias (Lown, 1964). To determine the role of digitalis, 100 consecutive patients with atrial fibrillation who were subjected to cardioversion were analysed (Kleiger and Lown, 1966). Of this group, 18 patients showed frequent ventricular ectopic beats, ventricular bigeminy, or ventricular tachycardia (Group A), and the remaining 82 were free of such disorders (Group B). Electrocardiograms before cardioversion were compared in these two groups. The appearance of serious ventricular ectopic mechanism following electric shock was correlated with the presence of certain arrhythmias in the precardioversion electrocardiograms. Of the 18 Group A patients, 17 manifested abnormalities in the precardioversion electrocardiogram suggestive of digitalis intoxication, as compared to 41 of the 82 in Group B. Before cardioversion, nodal mechanisms were nearly three times as frequent in Group A as compared to Group B (Table VII).



FIG. 12.—Long-standing atrial fibrillation after electrical discharge results in depolarization of atria with emergence of "sick sinus". Note irregular, bizarre P waves with frequent nodal beats.



FIG. 13.—"Sick sinus", showing marked changes in P wave morphology as recorded from lead II, superior vena cava, and from within right atrium.

Further support for the role of digitalis in predisposing to post-cardioversion arrhythmias is provided by the following observations. Six of the 18 Group A patients and none of the 82 Group B patients had well-confirmed manifestations of digitalis intoxication either shortly before or after cardioversion. In addition, in 10 patients of Group A there developed immediately after the electrical shock atrial arrhythmias suggestive of overdigitalization. Two had episodes of paroxysmal atrial tachycardia with block, a disorder which when associated with multiform ventricular ectopic beats almost invariably denotes digitalis intoxication (Lown and Levine, 1958) (Fig. 14). In 7 of the remaining 8 there was nodal rhythm with A-V dissociation. Furthermore, first-degree heart block was more common in Group A than in Group B patients. Thus, the majority of Group A patients had in addition to ventricular ectopic beats other findings suggestive of digitalis intoxication following cardioversion. If the heart rate is less than 70 a minute and runs of nodal rhythm are present, the

 TABLE VII

 INCIDENCE OF ARRHYTHMIAS BEFORE CARDIOVERSION IN PATIENTS WITH AND WITHOUT ECTOPIC VENTRICULAR ACTIVITY FOLLOWING ELECTRICAL DISCHARGE

| | | | | Incidence of arrhythmias before cardioversion (%) | | |
|--------|-------------------------------------|-----------------|--------------------------------|---|--------------------------|------------------------------|
| Group | Post-cardioversion ectopic beats | No. of patients | Evidence of digitalis toxicity | Nodal rhythm | Wenckebach conduction | Ventricular ectopic beats |
| A B | Present Absent | 18 82 | 17 41 | 27·0 6·7 | 22·0 10·0 | 54 34 |



FIG. 14.—Before cardioversion, rhythm was atrial fibrillation with regularized ventricular response. Within 36 seconds after restoration of sinus rhythm by 100 ws discharge, there developed paroxysmal atrial tachycardia with block and ventricular bigeminy.

patient with atrial fibrillation has nearly a 50 per cent chance of developing serious ventricular arrhythmias following cardioversion. The occurrence of such arrhythmias does not depend on the restoration of sinus rhythm, but on the magnitude of the electrical discharge. It may manifest as a rare ectopic beat after a discharge of 50 ws, multiple and multiform ventricular extrasystoles after 100 ws, and ventricular tachycardia and fibrillation after 400 ws (Fig. 5). All three patients reported by Rabbino et al. (1964), who developed ventricular fibrillation following cardioversion, had arrhythmias due to excessive digitalis and were subjected to high energy electrical shocks. This experience emphasizes the extreme hazard of trying to terminate digitalis toxic arrhythmias by means of cardioversion.

Animal Experiments. In view of the clinical experience suggesting that digitalis may have an adverse effect in the patient undergoing cardioversion, the issue was examined in the experimental laboratory (Lown, Kleiger, and Williams, 1965). Two questions were posed: (1) can digitalis-induced arrhythmias be treated successfully by cardioversion? (2) does overdigitalization alter the cardiac response to electric discharge?

These experiments were carried out in dogs. To answer the first question, dogs were digitalized to an end-point of ventricular tachycardia with either ouabain or acetyl strophanthidin, a very rapidacting glycoside-like drug. As soon as the arrhythmia emerged, the animals were shocked transthoracically in an attempt to restore sinus rhythm. This was attempted 63 times in 16 animals, and only in one case was reversion of ventricular tachycardia achieved for more than a few seconds. In no case was lasting reversion accomplished even though shocks of 400 ws were administered. This represents over five times the average energy level required to defibrillate the dog's heart with ventricular fibrillation.

When ventricular fibrillation was produced during digitalis-induced ventricular tachycardia by discharging the electrical pulse at the apex of the T wave of the ORS complex of the tachycardia, defibrillation could be accomplished readily. The result, however, was reinstatement of ventricular tachycardia rather than sinus rhythm. The energy required for abolishing ventricular fibrillation was essentially the same, whether the fibrillation was initiated during sinus rhythm or during digitalisinduced ventricular tachycardia. These experiments indicate that digitalis-induced ventricular arrhythmias cannot be terminated by direct current discharges. Furthermore, when an electrical arrhythmia is induced it can be readily reverted even in the presence of a digitalis-induced arrhythmia.

The second question relating to the alteration of cardiac response to electrical discharge by overdigitalization was also examined in dogs. It is possible to induce ventricular tachycardia in normal animals by high energy transthoracic shocks. The median energy in a large group of animals was 400 ws. The lowest shock level which produced ventricular tachycardia and observed in only one animal was 100 ws. However, when animals were retested immediately after recovery from digitalisinduced ventricular tachycardia, the median energy was lowered to 0.2 ws, a 2000-fold reduction (Fig. 15). These episodes of ventricular tachycardia following shock generally lasted from 3 to 30 seconds. When the electrical threshold was tested during incremental digitalization, it required at least 85 per cent of the toxic dose of ouabain before a lowering of the threshold was demonstrated.

The ventricular tachycardia following electric shock in the overdigitalized animal was similar in QRS morphology, direction of ventricular complex, and rate, to the arrhythmia which was produced by digitalis drugs without electrical discharge. It may be concluded that digitalization strikingly



FIG. 15.—Before digitalization a 300 ws transthoracic shock does not result in any arrhythmia. When the animal has received 90 per cent of a potentially toxic dose of ouabain, a discharge of 0.2 ws, after a brief delay results in ventricular tachycardia.

sensitizes the heart to provocation of ventricular arrhythmias by electrical discharge.

Current experiments indicate that the post-shock arrhythmias in the digitalized animal can be completely prevented by pretreatment with procaine amide or quinidine. Potassium is promptly effective in abolishing these arrhythmias. Conversely, when the electric shock no longer evokes ventricular tachycardia and the animal appears to have completely recovered from digitalis intoxication, administration of glucose and insulin, which lowers potassium in the extravascular compartment, reestablishes the phenomenon of electrical sensitization of the heart. It is our view that electrical discharge changes the transport characteristics of the cell membrane for electrolytes and promotes a net loss of potassium from the cell, thereby augmenting the toxic action of digitalis drugs.

Clinical Implications. In the light of the above findings, certain steps need to be followed in order to reduce the risk attending cardioversion of the digitalized patient. Digitalis toxic arrhythmias are treated with drugs and not with cardioversion. If reversion is to be carried out on a patient receiving digoxin, the drug is discontinued for 24 hours. If longer-acting digitalis drugs are employed, they are stopped for two days. It has been suggested (Gilbert and Cuddy, 1965) that cardiac glycosides be withheld for 5 to 10 days. Such a practice is unnecessary and not without danger. When a patient is deprived of digitalis drugs, congestive heart failure may redevelop, and atrial fibrillation may as a result promptly recur. Furthermore, in the undigitalized patient the heart rate may accelerate to a high level once quinidine is instituted before

cardioversion. If the patient has a limited cardiac reserve, decompensation may recur: indeed, such a complication has already been reported (Gilbert and Cuddy, 1965).

Whenever the pre-cardioversion electrocardiogram shows abnormality suggestive of digitalis intoxication, cardioversion is postponed. Digitalis is stopped until the arrhythmia clears. Cardioversion is similarly delayed in the presence of hypokalæmia until the electrolyte derangement is corrected. Diuretics are withheld for one to two days before reversion. It has been our experience that the patient who has received excessive digitalis drugs is more difficult to revert, and may require more energy. Thus, in the group of patients who showed postcardioversion arrhythmias presumably due to digitalis, 72 per cent were reverted as compared to 92 per cent in a control group. This has also been the experience of Stern (1965). Since the development of post-cardioversion arrhythmias is directly related to the energy of discharge, it is advisable to start with an initial shock of 25 ws. If ventricular ectopic beats occur after the first shock and increase in frequency with the next higher discharge, one has the option of either discontinuing the procedure or administering antiarrhythmic drugs before proceeding with still higher energies.

In an emergency situation, when prompt reversion is necessary and the patient has received large doses of digitalis, cardioversion is initiated with a shock of 5 ws. If ectopic beats develop, they can usually be abolished by intravenous administration of the following drugs: licocaine 50 mg., procaine amide 100 mg., diphenylhydantoin 100 mg., or propranolol 5 mg. These drugs can be repeated if ectopic mechanisms recur following successive shocks. If these steps are followed the appreciable risk associated with cardioversion of the overdigitalized patient can be minimized and even avoided entirely.

There remains a group of ventricular arrhythmias which are not related to digitalis and which occur after cardioversion. These are probably the result of quinidine cardiotoxicity (Castellanos *et al.*, 1965). The development of quinidine syncope due to transient bouts of ventricular fibrillation has been noted even in patients receiving small maintenance doses of the drug (Selzer and Wray, 1964). Thus, the major hazard of cardioversion is related to the use of two drugs—digitalis being implicated in the arrhythmias occurring immediately after cardioversion, and quinidine being responsible for the delayed ventricular disorders.

CONCLUSION

Cardioversion is now employed in several thousand centres throughout the world. The prompt acceptance of cardioversion testifies to the fact that a therapeutic need has been met. The method of cardioversion is simple and direct. The physician can observe the entire process. It does not require frequent electrocardiographic monitoring. Being applicable to ventricular as well as supraventricular arrhythmias, differentiation between these disorders, essential with the use of drugs, ceases to be a critical prerequisite for effective therapy. Cardioversion is the most effective method now available for terminating arrhythmias. Its use is not accompanied by a significant occurrence of serious complications. There is no depression of contractility, conductivity, or excitability of the heart, a common sequel after large doses of antiarrhythmic drugs. These features of effectiveness, safety, and simplicity permit cardioversion to be employed by physicians less experienced in the recognition and treatment of arrhythmias.

Cardioversion does not reduce the need for antiarrhythmic drugs. On the contrary, more such drugs will be used to maintain normal rhythm. An additional benefit of this new form of treatment will be the challenge to search for more effective and safer drugs. Finally, the opportunity which cardioversion affords for study of the very process of reversion should provide a deeper insight into the mechanism which underlies abnormalities of the heart beat.

FINAL COMMENT

The burden of the responsibility and the privilege of giving this lecture is allayed by the realization that it provides further confirmation, if such be needed, for the findings of Thomas Lewis. Were he here with us, he would have relished the biological irony implicit in the need to use electricity to close the electrical excitable gap that keeps the arrhythmia pulsing. He would, however, have hastened to the laboratory to devise rigorous experiments to complete the job of keeping the excitable gap closed. Above all, he would have been pleased at the adoption of his methods of investigation, methods that entail continuing research dialogue shifting between bedside and animal experiment, always guided and sustained by the daily promptings of the sick.

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