THE CAUSE OF FIBRILLATION

BY

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For the past 50 years workers have investigated the phenomenon of cardiac fibrillation, but, despite the many observations made, the number of theories of its cause has remained gratifyingly small. That which has attracted the widest attention has been the theory of atrial fibrillation put forward by Lewis (1920), in which he ascribed it to a circus movement, a wave of excitation travelling continuously around the base of the great veins at a sufficiently slow rate to find the tissue in front of it always excitable. Lewis's paper indicates that he was greatly impressed by the experiment of Mines (1913), who cut a ring of muscle from the auricles and ventricles of the heart of a tortoise. This ring did not include the sinus, and Mines saw that after applying a few stimuli a contraction began which passed round and round the ring. Lewis's theory, supported as it was by a great weight of evidence, remained unchallenged for about 30 years.

A notable contribution to the observations on atrial fibrillation was made by Andrus and Carter (1930). They showed that, during vagal stimulation of the dog heart, fibrillation could be produced by a single shock applied early in the relative refractory period following a preceding contraction. About 10 years later a similar observation was made in the ventricles. Wégria and Wiggers (1940) produced ventricular fibrillation by one localized induction shock also applied during the relative refractory period. They called the brief time during which this was possible the vulnerable period: it coincided with the rapid fall of threshold during the period of returning excitability.

In 1948 Scherf, Romano, and Terranova put forward a different view of atrial fibrillation from that of Lewis. They injected the alkaloid aconitine into the sinus node and observed that it caused atrial tachycardia. This tachycardia sometimes changed spontaneously into atrial fibrillation, or it could be made to do so by stimulating the vagus. If the site where the aconitine was injected was cooled, the fibrillation was abolished, but it reappeared when the cooling stopped. The authors considered that their results, particularly the reappearance of fibrillation after the end of cooling, could not be explained on the circus-movement theory. They thought that flutter and fibrillation were initiated by rapid impulse formation from a single centre. "As the impulse thus formed moves into the larger mass of auricular muscle, islands of refractory tissue appear which cause a weaving and interweaving of the contraction process characteristic of fibrillation."

About the same time Prinzmetal and his colleagues (1952) were studying atrial fibrillation by the aid of the

high-speed cinematograph and the cathode-ray oscillograph. They initiated fibrillation by electrical stimulation or by the application of aconitine at a single focus in the auricles. Their general conclusion, based on work in dogs and in patients over a period of four years, was similar to that of Scherf and his colleagues, for they concluded that auricular fibrillation originated from, and was perpetuated by, a single rapidly discharging ectopic focus. They were unable to obtain evidence of a complete circle of movement around the great veins.

Experimental Production of Fibrillation

A few years later we were carrying out experiments in Oxford which led us to a simpler method of causing atrial fibrillation (Burn, Vaughan Williams, and Walker, 1955). We worked on the Starling heart-lung preparation of the dog, and applied electrodes to the tip of the right atrium. The electrodes were held in place by a spring and did not pierce or damage the atrium. We also prepared a burette containing acetylcholine, and we could drive the solution into the superior vena cava at a slow uniform rate. When we stimulated the atria for 30 seconds (using square wave pulses of 1 mA strength, 0.75 msec. duration) at a frequency of 800 per minute, this had no lasting effect on the rhythm as recorded on the E.C.G. So soon as the stimulation stopped the normal rhythm returned. When we infused the solution of acetylcholine into the blood at about 1 mg. per minute, the rate was somewhat slowed but the rhythm was otherwise unaffected. If, however, we stimulated the atria during the infusion of acetylcholine, so soon as the stimulation stopped we saw that the atria were fibrillating. They continued to fibrillate without further stimulation for so long as the infusion of acetylcholine continued. If, however, the infusion was stopped, fibrillation gave place to flutter and then to the return of the normal rhythm within one minute.

We had hit on a means of producing fibrillation and of maintaining it for as long as we wished. We could stop it after it had continued for 90 minutes by a turn of the burette tap. We could start it again 10 times in one experiment. Seen under these circumstances in many experiments, atrial fibrillation scarcely appeared to be a pathological phenomenon. It seemed rather to be the physiological state appropriate to the conditions imposed.

Ventricular Fibrillation

Attention was turned later to the ventricles to see if a similar combination of the two factors would also

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produce fibrillation in them. In the whole animal, ventricular fibrillation cannot be studied, since its onset leads to a cessation of the coronary flow and so to death of the heart. Observations were therefore made in the isolated rabbit heart, perfused through the coronary system with a modified Ringer's solution. The perfusion then continued through the coronaries whatever the ventricular rhythm. Electrodes were applied to the muscle of the left ventricle; these could be used for stimulation or, alternatively, as leads to the E.C.G. We applied stimulation at rates varying from 12 per second in earlier experiments to 25 per second in later experiments, continuing for three minutes, at a temperature of 37° C. This stimulation almost always caused fibrillation, but when the stimulation stopped the fibrillation reverted to a normal rhythm within half a minute in the majority of hearts.

We were then able to test the effect of acetylcholine, to see whether in its presence stimulation would cause a long-lasting fibrillation as it had been found to do in the atria. In actual experiment we used carbamylcholine rather than acetylcholine, as this would have been destroyed in the alkaline perfusion fluid. We found that the results were quite different from those in the atria. The presence of carbamylcholine did not alter the effect of stimulation and did not result in long-continued fibrillation (Armitage, Burn, and Gunning, 1957).

Acetylcholine and the Action Potential

We were thus faced with a different situation in the two parts of the heart. Under conditions in which stimulation at a high rate did not by itself cause fibrillation in either the atria or the ventricles, the presence of acetylcholine caused fibrillation to occur in the atria but not in the ventricles. We therefore considered what other change there might be which acetylcholine caused in the atria which it did not cause in the ventricles.

By the use of intracellular electrodes it has been possible for some years to study the changes which take place in the potential difference across the cell membrane in tissues in which excitation can occur. Thus in nerve and skeletal muscle and in cardiac muscle during the resting phase there is a transmembrane potential difference of about 80 to 90 mV, the inside being negative to the outside. The membrane is said to be polarized. The concentration of sodium ions within the cell is lower than outside, and the concentration of potassium ions is much higher than outside. When excitation occurs the membrane becomes permeable to sodium ions, and these enter the cell depolarizing the membrane. By some means at present unknown this depolarization initiates the contractile process. Before the cell can be excited again the greater part of the transmembrane potential difference must be restored, and the membrane must be repolarized. This is accomplished by a flow of potassium ions to the outside of the cell.

Now cardiac muscle, whether atrial or ventricular, differs from skeletal muscle and from nerve in requiring a long time for repolarization. Whereas in skeletal muscle and nerve repolarization may take 2 to 3 msec., in atrial and ventricular muscle it may take 150 to 300 msec. This is approximately the time required before the muscle is re-excitable, and it is therefore

approximately equivalent to the refractory period. The changes in transmembrane potential during excitation and until repolarization is complete are called the action potential. We see that in cardiac muscle the duration of the action potential and therefore of the refractory period is very long compared with that of skeletal muscle and nerve.

In 1914 Samojloff showed that stimulation of the vagus shortened the refractory period of the atria, and in 1953 Hoffman and Suckling observed a result essentially similar using modern methods. They determined the effect of acetylcholine on the action potential of the atria of the dog; they found that acetylcholine greatly hastened repolarization in the atria, shortening the duration of the action potential from 150 msec. to as low a figure as 10 msec. At the same time they found that acetylcholine had practically no effect on the duration of the action potential in the ventricle.

It seemed that these observations might provide a clue to the effect of acetylcholine on fibrillation. In the atria in which acetylcholine shortened the action potential a high rate of stimulation in the presence of acetylcholine caused fibrillation; in the ventricles in which acetylcholine did not shorten the action potential a high rate of stimulation in the presence of acetylcholine did not cause fibrillation.

Substances Affecting the Atrial Action Potential

Working on the hypothesis that substances or factors might influence fibrillation according to their effect on the duration of the action potential, this being as a rule a measure of their effect on the effective refractory period, we proceeded to investigate the effect on fibrillation of those factors whose action on the duration of the action potential was known. Adrenaline was shown by Webb and Hollander (1956a) to prolong the duration of the action potential in the atria of the rat. They observed that a concentration of 5×10^{-7} M increased the duration by 13%. We therefore studied the action of adrenaline on the atria of the dog heart-lung preparation. In the ventricles adrenaline causes fibrillation during chloroform anaesthesia (Levy, 1914) and it facilitates fibrillation after stimulation of the perfused ventricles (Goodford, 1958). However, when an infusion of adrenaline was driven at a uniform rate into the superior vena cava, stimulation of the atria did not cause fibrillation. On the other hand, such an infusion delivered into the blood at the same time as an infusion of acetylcholine prevented stimulation from causing fibrillation.

We carried out experiments in which stimulation was applied during infusion of acetylcholine alone, and then during infusion of acetylcholine and adrenaline together; we could alternate the single and the double infusion several times, and found that whereas fibrillation followed stimulation during the infusion of acetylcholine it did not follow stimulation during the infusion of both solutions (Burn, Gunning, and Walker, 1957). Thus adrenaline, which lengthened the action potential, was antifibrillatory in effect.

Changes in Potassium Concentration

The effect of changes in the concentration of potassium ions on the action potential of cardiac tissues

has been investigated several times. Earlier work indicated that raising the external potassium shortened the action potential, but the increases in concentration were large (Weidmann, 1955a, 1956). More recently Vaughan Williams (1959), working on rabbit atria, found that the effect of raising the external potassium was biphasic. From a low concentration of 1 mM upwards to 5 mM, the duration of the action potential was increased as the potassium concentration increased. The effect on duration of concentration above 5 mM was not clear, since few points were studied. At 10 mM the duration was less, but whether the maximum lay at 5 mM or at 8 mM is uncertain, since in some experiments the duration increased between 5 mM and 8 mM.

The effect of changes of potassium concentration on atrial fibrillation produced in the heart-lung preparation was observed by infusing a solution of potassium chloride intravenously. This infusion arrested the fibrillation, and the mean amount required to do this was 226 mg. infused into 1 litre of blood. This would have caused a rise from 5 mM to 8 mM if all the potassium remained in the plasma (Burn, Gunning, and Walker, 1956).

Fibrillation in Isolated Atria

When the concentration of potassium was reduced below normal, fibrillation was facilitated, as was observed in isolated rabbit atria. These were set up in a bath with stimulating electrodes in the expectation that stimulation would cause fibrillation if acetylcholine was added to the bath. Fibrillation, however, did not occur. The concentration of potassium was then reduced from 5.6 mM to 1.4 mM, and when the effect of low potassium was added to that of acetylcholine, stimulation caused fibrillation (Holland and Burn, 1957). Thus a fall in potassium concentration below 5.6 mM shortened the action potential and facilitated fibrillation. In agreement with the observation that a rise in concentration (certainly above 8 mM) also shortened the action potential is the observation that high concentrations of potassium also cause fibrillation (McWilliam, 1887; Hering, 1915).

Effect of Temperature

When fibrillation was studied in isolated rabbit atria it was found that it could be arrested by lowering the temperature. Atria which were fibrillating at 37° C. ceased to fibrillate when the temperature was reduced to 27° C. In some experiments the atria began to fibrillate again on merely raising the temperature to 37° C. (Beaulnes and Day, 1957). Now Marshall (1957) found that the effect of lowering the temperature of isolated rabbit atria was to lengthen the duration of the action potential, so that these somewhat unexpected results also agreed with the hypothesis.

Effect of Quinidine

Quinidine was shown by Lewis and Drury (1926) to prolong the effective refractory period, and this finding was confirmed by Dawes (1946) and Gold (1960). The method used by Dawes in which the maximum rate at which atria would follow an electrical stimulus was observed, showed that quinidine greatly reduced this rate and thus delayed the return of excitability. Vaughan Williams (1958a) and Johnson and Robertson

(1958) have shown that quinidine diminishes the rate at which depolarization occurs, and this action by itself, as these authors have shown, must delay the return of excitability. Further observations are, however, still required, since pharmacological studies have shown that quinidine is an antagonist of acetylcholine in all forms of muscle (Dawes, 1946). At present we do not know what is the effect of quinidine on the action potential when this is first made very short by acetylcholine. If quinidine opposes acetylcholine here, it may prolong the action potential greatly.

Observations on Ventricular Fibrillation

Effect of Oxygen Lack

Using the isolated rabbit heart, we investigated a series of factors diminishing metabolic activity, and were able to obtain results showing that these factors facilitated fibrillation. Oxygen lack is known to shorten the action potential and therefore the refractory period. Trautwein, Gottstein, and Dudel (1954) found that in cat papillary muscle stimulated at 140 per minute the duration of the action potential was diminished by oxygen lack, repolarization occurring very much more quickly. This work was confirmed in a later paper (Trautwein and Dudel, 1956). Webb and Hollander (1956b) showed that the action potential of the rat atrium was diminished by anoxia; after 4 minutes the diminution was 13%, after 10 minutes it was 47%, and after 17 minutes it was 81%.

Experiments on fibrillation were performed by stimulating the ventricles of hearts perfused with a solution saturated with a gas mixture containing 95% oxygen and 5% CO₂. Fibrillation did not continue for more than a minute or so after stimulation stopped. When, however, the solution was changed to one saturated with a gas mixture containing 47.5% oxygen, 47.5% nitrogen, and 5% CO₂, stimulation caused persistent fibrillation, which was observed for at least 15 minutes before it was terminated by pouring cold saline over the ventricles (Dirken, Gevers, Heemstra, and Huizing, 1955). The experiment was then repeated with the solution saturated with 95% oxygen. It was thus possible to test the effect of stimulation several times by using alternately a perfusing solution saturated with a mixture containing 95% oxygen and a solution saturated with only half this amount. The latter solution caused persistent fibrillation in nearly all trials (Burn and Huković, 1960).

Lack of Glucose

A lack of glucose has also been shown to shorten the action potential in the rat atria, the shortening becoming greater the longer the time of glucose deprivation (Webb and Hollander, 1956b). Goodford (1958) found that when he perfused rabbit hearts with glucose-free solution for some time, stimulation caused persistent ventricular fibrillation. Some hearts perfused with glucose-free solution for two and a half hours began to fibrillate spontaneously; this fibrillation was arrested when the perfusion fluid was changed to one containing glucose. In experiments in which readmission of glucose in low concentration did not stop the fibrillation, the addition of insulin, which assists the uptake of glucose by cardiac muscle (Burn and Dale, 1924) was successful in causing arrest of fibrillation.

Effect of Metabolic Inhibitors

The first substance known to interfere with metabolic processes that was examined was dinitrophenol. Macfarlane and Meares (1955) found that dinitrophenol increased the rate of repolarization in the atrium and in the ventricle of the frog, reducing the "plateau" to about one-third of its normal length. Kuschinsky, Lüllmann, and Muscholl (1958) found that it reduced the duration of the action potential in the atrial muscle of the rat. Dinitrophenol was found to facilitate fibrillation in the rabbit ventricles, stimulation causing persistent fibrillation in its presence. The effect was reversible (Armitage *et al.*, 1957).

Another metabolic inhibitor is sodium azide, which Macfarlane (1956) found would reduce the duration of the action potential in the frog ventricle; in keeping with this, Goodford (1958) found that, in the presence of sodium azide, rapid stimulation of the ventricles led to persistent fibrillation. The effect of sodium azide was reversible.

A third metabolic inhibitor is sodium moniodoacetate. Lüllmann (1959) found that in its presence the duration of the action potential in the atria of the rat was shortened, and Goodford (1958) found that in its presence rapid stimulation of the ventricles caused fibrillation. This effect was not reversible.

Effect of High Calcium Solutions

In solutions containing a higher concentration of calcium than normal, Schütz (1936) found that cardiac muscle became re-excitabile at a relatively early stage of repolarization and the effective refractory period was shorter. Weidmann (1955b) confirmed this observation. When isolated rabbit hearts were perfused with solutions of increasing calcium concentration, Milton (1959) observed that the proportion in which stimulation caused persistent fibrillation also increased in approximately linear relation. In the same experiments he observed that the reverse was true for potassium, and that the proportion in which stimulation caused persistent fibrillation increased as the concentration of potassium diminished below normal.

Comments on the Evidence

An account has been given of all factors of which the effect is known both on the duration of the action potential and on the occurrence of fibrillation. In all cases there was some correlation between the effects. The correlation was, however, less certain for potassium, which has many effects on the heart. Vaughan Williams (1958b) has suggested, for example, that the arrest of atrial fibrillation in the heart-lung preparation by infusion of potassium chloride may be explained not by a lengthening of the action potential but by a diminution of the resting potential, which would diminish the rate of sodium entry (increased in the presence of acetylcholine).

The effect of a reduction of temperature in arresting fibrillation, observed in the ventricles (Goodford, 1958) as well as in the atria, must appear strange to those engaged in thoracic surgery, where work at low temperature is attended by the risk of fibrillation. The effect of low temperature, like that of potassium, is certainly complex. Scherf, Blumenfeld, and Terranova (1953) produced ventricular fibrillation by focal cooling,

but in some cases the cooling of the ventricles led to the abolition of atrial fibrillation; this remained absent only as long as the cooling continued. So far as ventricular fibrillation in the theatre is concerned, Churchill-Davidson and his colleagues (1953) considered that the risk arose only when the body temperature fell below 26° C. Without discussing the many aspects of cooling further, the point can be stressed that cooling, which lengthens the atrial action potential, was also found to stop atrial fibrillation.

Explanation of Fibrillation

The combination of an infusion of acetylcholine and rapid stimulation produced fibrillation in the atria but not in the ventricles. Since acetylcholine shortened the action potential in the atria but not in the ventricles, the contribution of acetylcholine to fibrillation in the atria was probably due to the shortening of the action potential. Once fibrillation began, the presence of acetylcholine was sufficient to maintain it; when the infusion was stopped the fibrillation stopped also. We may then ask why the lengthening of the action potential stopped the fibrillation.

In fibrillation the muscle fibres are not contracting simultaneously; they are contracting independently and are out of phase with one another. When a muscle fibre contracts, excitation spreads from it to adjacent fibres; when this excitation reaches adjacent fibres it will cause them to contract if they are excitable. Now, in the presence of acetylcholine atrial fibres are repolarized very rapidly, and after contracting can be re-excited very soon. Thus spread of excitation from one fibre to neighbouring fibres which are out of phase will cause them to contract so long as acetylcholine keeps the action potential short. If, however, acetylcholine is withdrawn, the action potential and the refractory period lengthens and an atrial fibre which has contracted remains inexcitable for a long time. When excitation spreads to it from a neighbouring fibre which is out of phase, the excitation has no result. Thus the fibrillation stops.

These considerations explain why atrial fibrillation is arrested by cutting off acetylcholine, and they further explain the reason for the long action potential of cardiac muscle, which may last for 200 msec. or more before repolarization is complete. The purpose of this long period of inexcitability is probably to prevent fibres which are slightly out of step, or out of phase, from stimulating one another.

In order to produce atrial fibrillation, a short period of high-frequency stimulation was necessary as well as an infusion of acetylcholine. Mere reduction of the length of the action potential (in the heart-lung preparation) was not sufficient to set up fibrillation, for in the presence of acetylcholine the pacemaker was slowed. The effect of the short period of high-frequency stimulation was probably to throw the atrial fibres out of phase. A rapid rate of stimulation is known to affect conduction, the velocity being diminished as the rate increases (Mines, 1913). Prinzmetal and his colleagues (1952) observed this in dog atria at rates above 350 per minute, and Brooks and his colleagues (1955) at rates above 250 per minute. Vaughan Williams (1958b) has observed the same thing at still lower rates. A connexion between such a depression of conduction velocity and fibrillation has been stressed by DiPalma and Schults, who pointed out that "the onset of

delay conduction in the auricle often precedes fibrillation, and it may seem that fibrillation only occurs in association with such dysfunction." The slowing of conduction by an increasing rate of stimulation indicates that the rising rate throws an increasing strain on the process of conduction. It is then likely that conduction will not be affected uniformly, but will suffer to a different extent in different parts of the atria.

If the rate of conduction varied along different paths an impulse proceeding to a distant point A might arrive sooner than it would arrive at a distant point B, even though B was adjacent to A. Thus A would contract before B. When B contracted a little later, excitation from B would spread to A. If the action potential was of normal length, excitation from B would not effect A, because A would be inexcitable. If, however, acetylcholine was present, and the action potential was greatly reduced in length, then excitation from B would find A already repolarized and excitable. A would then contract again. Excitation from A would then spread back to B, and B would contract again. Fibrillation in fact would begin, and would continue until the acetylcholine was withdrawn. We thus have a picture of fibrillation which depends on two assumptions: the first that when a fibre contracts there is a spread of excitation from it to neighbouring fibres, and the second that when a high rate of stimulation is applied fibres are thrown out of phase with one another.

The observations on ventricular fibrillation which were made give a fair measure of support to this conception. Here also a high rate of stimulation was used. The high rate of stimulation not only slows the conduction velocity but, as Lewis, Drury, and Bulger (1921) demonstrated in the atria of the dog, it shortens the refractory period as well. If we assume that the rapid stimulation throws fibres out of phase by unequal depression of conduction, then, since it also shortens the refractory period, it can induce fibrillation. When the stimulation is stopped, the fibrillation stops because the refractory period lengthens again, unless a substance is present, such as dinitrophenol, which keeps the action potential, and therefore the refractory period, short.

The occurrence of fibrillation as a result of a single shock applied early in the relative refractory period (Andru and Carter, 1930; Wégria and Wiggers, 1940) may also be related to the slowing of conduction which a shock so placed produces. DiPalma and Schults (1950) say, "It is interesting to speculate why the vulnerable period occurs at the end of the relative refractory period. Might it not be because it is the interval in which a local state of *inequality of recovery* of heart muscle most frequently exists?" It seems unlikely that there is a difference between the effect of a single shock and that of the burst of stimuli which was used in causing atrial fibrillation, since in the experiments in which we recorded the E.C.G. and also the stimuli side by side we saw fibrillation begin with the second stimulus in one experiment and with the seventh stimulus in another.

The results finally emphasize the relation between fibrillation and the amount of energy available. Factors which reduced the energy supply, such as oxygen lack, glucose lack, and metabolic inhibitors such as dinitrophenol, azide, and moniodoacetate, all shortened the duration of the action potential and thus accelerated the return of excitability. The evidence that they also facilitated fibrillation gives strong support to the view

that the two actions are related, the effect on the action potential being the cause of the effect on fibrillation.

The view that energy is required to maintain a long action potential and thus to delay the return of excitability has been expressed by various observers. It would explain the action of adrenaline which in the atria increases the length of the action potential and prevents acetylcholine from facilitating fibrillation. Adrenaline may cause an increase in available energy. Why, then, does adrenaline have the opposite effect in the ventricle, where in the isolated perfused heart it facilitates fibrillation? One explanation of this is that in the ventricles of the rabbit heart under perfusion conditions the supply of energy is limited, and since adrenaline causes a great increase in rate and force of contraction there may be insufficient energy to maintain a long action potential. The ventricle may then fibrillate if any of its fibres get out of phase. There is, however, even in the ventricles some evidence of an effect like that in the atria, since Hoffman, Siebens, Cranefield, and Brooks (1955), studying the vulnerable period, found that adrenaline had two effects. While its immediate effect was to lower the minimum fibrillation threshold, its later effect was to make the heart less vulnerable than before. This period lasted from 10 to 30 minutes. It is probable that the general view that adrenaline facilitates fibrillation has its main basis in the effect of adrenaline in the presence of anaesthetics like chloroform, which probably interfere with the supply or availability of energy.

Summary

Three methods have been described of studying fibrillation experimentally. Atrial fibrillation has been produced in the dog heart-lung preparation by brief stimulation at a high rate during the infusion of acetylcholine. Atrial fibrillation has been produced in isolated rabbit atria by brief stimulation in the presence of acetylcholine and of a low concentration of potassium. Ventricular fibrillation has been produced by electrical stimulation in the isolated rabbit heart.

The observations which have been made are consistent with the view that fibrillation arises when individual fibres are out of phase. Excitation then spreads from one fibre which contracts to another which is resting. This excitation is effective only when the refractory period is for one reason or another abnormally short. Then the excitation causes the resting fibre to contract, and this in turn gives rise to spread of excitation and so on. The essential factor for fibrillation is thus a shortening of the refractory period (which is usually indicated by a shortening of the action potential).

As a rule it is also necessary to throw fibres out of phase. This occurs when rapid stimulation is applied electrically or when a stream of impulses is produced by an ectopic focus established by the use of aconitine. It seems likely that rapid stimulation acts by depressing the rate of conduction and that this depression is not uniform throughout the tissue. A single shock in the vulnerable period may act in the same way. In those cases where rapid stimulation alone produces fibrillation, it may do so by the double effect of shortening the refractory period and of depressing the rate of conduction.

The long refractory period (or the long action potential) of cardiac muscle as compared with that of

skeletal muscle protects the cardiac muscle from fibrillation. Energy is required to maintain its length, for when there is lack of oxygen or glucose, or in the presence of metabolic inhibitors, the action potential is shortened and fibrillation is facilitated.

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The International Atomic Energy Agency will send 20 nuclear experts in 1960 to Afghanistan, Austria, Brazil, Iran, Iraq, Korea, Philippines, Turkey, Venezuela, and Yugoslavia. One biochemist will work at the Austrian Cancer Research Institute in Vienna to advise on the use of radioisotopes in cancer research and on the establishment of a radioisotope laboratory. He will train Austrian scientists in the techniques of determining the distribution of labelled tumour cells in experimental animals. I.A.E.A. will also provide some nuclear equipment for this project. (International Atomic Energy Agency, Vienna.)

DISSECTING ANEURYSMS

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[WITH SPECIAL PLATE]

A dissecting aneurysm is a lesion produced by degeneration or disease of the tunica media of an artery. A split forms in the tunica intima and inner layers of the media with extravasation of blood within the tunica media of the vessel; the dissection produced by this extravasation extends in both centripetal and centrifugal directions from the original intimal split. The thoracic aorta is frequently involved, and death usually results from rupture of the aorta, cardiac tamponade, or ischaemia of essential organs.

Maunoir (1802) first described this lesion, and Laennec (1826) used the term "anévrisme disséquant." Pennock (1839) demonstrated that dissection occurred between the layers of the media, and Swaine *et al.* (1856) recorded the first clinical diagnosis. No attempt at surgical treatment was made until Gurin *et al.* (1935) operated on a patient who subsequently died of renal failure. Shennan (1934), in a comprehensive review of 297 cases of dissecting aneurysm of the aorta, concluded that the ascending aorta was the origin of the dissection in 69%, and death due to rupture occurred in 94.6%. Spontaneous cure by formation of a re-entry ostium and resultant double-barrelled aorta was described by Shekelton (1822). The frequency of this has been variously quoted as between 5% and 15%.

During the past few years an increasing number of successful surgical operations have been recorded. Creech *et al.* (1956) reported ten successful cases treated either by resection and grafting or by the formation of a re-entry ostium, Warren *et al.* (1956), four patients operated on with one survivor; and Shumacker and Harris (1956), one patient with recovery. More recently DeBakey (1958) has quoted a 27% mortality among 36 patients, and Beckwith *et al.* (1959) four successful results in 11 patients. In Great Britain, Martin and Muir (1958) and Birt (1959) have each reported a case with recovery.

We present our experience with seven patients who have undergone operation for dissecting aneurysms, with recovery in six.

Case Reports

Case 1

A railway porter aged 47 had been in good health until, three months before admission, he began to experience tiredness on exertion. He had previously had uncomplicated rheumatic fever at the age of 16. At 7.30 p.m. on the day of admission he experienced severe left upper abdominal pain, which radiated to the epigastrium and a few minutes later to the left leg, which became numb and white. Later the abdominal pain radiated to the right side of the chest posteriorly. Shortly before the onset of pain he had carried several heavy parcels without discomfort. On admission to hospital the patient, a heavily built, obese man, was rolling about in severe pain. There was no evidence of shock, pallor, or sweating. The pulse rate was 74 per minute and regular, the blood-pressure 160/95 mm. Hg, and the