Four-Year Experience with an Implanted Cardiac Pacemaker *

PAUL M. ZOLL, M.D., HOWARD A. FRANK, M.D., ARTHUR J. LINENTHAL, M.D.

From the Medical and Surgical Research Departments, Beth Israel Hospital, and the Departments of Medicine and Surgery, Harvard Medical School Boston, Massachusetts

LONG-TERM cardiac stimulation with implantable pacemakers and myocardial electrodes has become established, since the early reports by ourselves [25] and others,[5, 12] as a most effective means of preventing recurrent Stokes-Adams attacks and improving cardiac output in patients with heart block. The purpose of this paper is to summarize our experience with the 77 patients whom we have treated in this way since July 1960.

Pacemaker-Electrode System

Stimulus Threshold. Early attempts at direct stimulation of the heart by electrodes placed in the myocardium at thoracotomy failed within a few weeks because the threshold for stimulation rose progressively.[25] This difficulty resulted, not from polarization or other effects of the electric stimuli, but from tissue reaction to the foreign body, which in effect separates the electrode from excitable myocardium. Tissue reaction at the implantation site is minimized by the use of a nonreactive platinum electrode surface and by the meticulous avoidance of contamination of the electrode and the site of implantation with foreign particles of any kind.[25] In the nearly four years of the present study, we have not observed stimulus failure due to rise of threshold except in association with sepsis at the implantation site in 3 early cases. Tests in 5 patients during replacement of early pacemakers 1 to 3 years after implantation have shown thresholds of 1.5 to 4 volts and 1.3 to 6 milliamperes.

Electrode Wires. Implanted electrodes and wires are subjected several million times each month to mechanical stresses resulting from motion of heart, diaphragm, and thoracic and abdominal walls. Breakage of the electrodes or of the connecting wires is a significant possibility in every type of pacemaker system and poses a problem that is still under study. Wire breakage interrupts effective stimulation and carries the risk in these patients with Stokes-Adams disease of repeated seizures or sudden death. Initially, we used short segments of solid platinum wire as the active electrodes (Table 1). They were welded to connecting wires of 49 strands of stainless steel that were insulated with several coats of Teflon.[25] Breaks occurred in the platinum segment or in the adjacent wire (14 of 35 patients) and were attributed to the welding process or differing flexibility of the adjoining wires. Accordingly, the solid platinum electrode was discarded. Instead, the multistranded stainless steel wires were electroplated alternately with gold and platinum and were then insulated with Teflon, except for a 1-cm. bare segment to form the active electrode. When breaks occurred in these wires also (6 of 44 patients), heavier wires of 77 strands were introduced (Fig. 1); to date, no break has been observed in the 23 77-strand systems

Presented before the American Surgical Association, Hot Springs, Virginia, April 1, 1964.

Aided by grants from the United States Public Health Service, National Heart Institute (HE-02208, HE-05108, HE-06316, and HE-01984), the Mark and Anna Davidson Linenthal Fund, and the Edward Swartz Fund.

TABLE 1. *Electrical Failure and Sepsis*

Period of Implantation	Pacemaker Unit	Electrodes and Wires	Number of Patients in Each Phase*	Patients with Pacemaker Failure	Patients with Wire or Electrode Break	Patients with Sepsis
July 1960–May 1961	Early (metal-encased)	Platinum-solid	12	4	3	4
June 1961–March 1962			23	1	11	2
April 1962–September 1963	Present (epoxy-encased)	Platinum-plated 49-strand wires	44	0	6	0
September 1963–April 1964		Platinum-plated 77-strand wires	24	0	0	1

* 26 patients in more than one phase of the method.

that we have implanted since September, 1963. This period, however, is still too short to provide final evaluation of wire breakage in relation to the many years that patients may need reliable systems. On the basis of radiographic study of the movement of implanted wires, we have repeatedly revised the method of implantation to reduce points of fixation and flexion between the pacemaker unit and the heart. We know of no instance of electrode displacement in our series: the "in-line" electrode implanted in the myocardium provides a very stable arrangement.

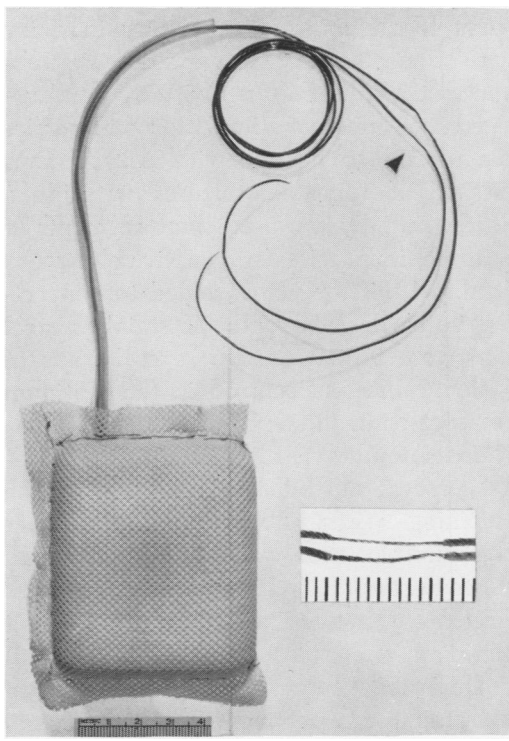

FIG. 1. The cardiac pacemaker-electrode system includes the pacemaker unit, the Teflon bag, 2 electrode wires, a length of Silastic tubing enclosing the proximal 6 inches of the wires, the bare electrode segments (*arrow* and *insert*), and needles at the ends of the wires.

Pacemaker Unit. Reliability is the primary consideration in the design of the pacemaker. For this reason we insist on a simple system with as few components as possible, a stimulus well above threshold, and no external components that might permit interruption of stimulation. The energy source of our pacemaker is 6 1.4-volt mercury batteries with an expected operating life span of 5 years. The output of the pacemaker is a 2-millisecond, 7.5-volt, 10 to 15-milliampere stimulus, which is delivered at a fixed rate, usually about 70 per minute. The electrical components are triply sealed in epoxy resin to prevent movement, short circuit, or fluid seepage. The external case, which measures 6.5 × 6.0 × 1.7 cm., is molded of an epoxy resin that is nonirritative and is tolerated well by human tissues. The pacemaker unit has

functioned perfectly in all but 1 of the 55 patients in whom it has been implanted since its revision to the present design in June 1961 (Table 1).* So far the longest period an individual pacemaker unit in our series has been functioning is 30 months. Some of the early units had an expected battery life of only 2 years and have been replaced. The methods for subcutaneous replacement of a pacemaker unit with attachment by crimp connectors to the original electrode wires have proved to be simple and effective.[25]

To avoid the need for surgical replacement of the unit when the batteries wear out it is possible to use batteries in the implanted pacemaker that can be recharged periodically from a radio receiver or secondary induction coil activated from an external power source. Such a pacemaker has been developed and used clinically.[21] The output of the instrument, however, was only 2 volts, and it failed in several cases. This approach, therefore, cannot be considered ready for clinical application.

Energy in the form of electric stimuli can also be transmitted across the skin by radio-frequency [11] or by induction [1] from external sources with easily replaceable batteries. Such approaches have the additional advantages of requiring relatively small implanted components and of permitting ready external variations in rate of stimulation. Furthermore, in some modifications the receiver has been fixed directly to the myocardium with the idea of eliminating possible breakage of wires between the myocardial electrodes and the receiver.[4, 23] Unfortunately, breakage of the stiff myocardial pin electrodes remains a problem. The energy requirements of all these systems are such that either the external source must be in close apposition to the subcutaneous unit or the external battery must be large. In either case, an ordinary bath or shower, for example, is difficult. Furthermore, preoccupation with the equipment creates a psychologic hindrance to normal activity.

The practical difficulty in maintaining uninterrupted stimulation appears to us to be the primary objection to systems with external components. There are many striking examples of the marked unpredictability and lethal potentiality of Stokes-Adams attacks when stimulation is interrupted even momentarily. Deliberate interruption of stimulation when atrioventricular conduction returns has even been recommended; [1] this is equally hazardous since complete heart block and ventricular standstill may supervene suddenly. Implantable pacemaker systems have been developed that permit variation of the rate of stimulation.[6, 12] The added complexity of the instruments and the requirement for subcutaneous or external manipulation seem both unnecessary and undesirable to us. Our patients with a fixed rate of 70 to 75 per minute can carry out normal activity, exercise, and other stresses without difficulty. Cardiac output is not altered significantly by change in pulse rate between 60 and 80 per minute.[2] Rates about 70 are also usually effective in preventing recurrent ventricular tachycardia and fibrillation; rates of 60 or less may not be reliable for this purpose.[29]

Several workers have suggested the desirability of driving the ventricles at the variable sino-atrial rate and with a normal atrioventricular sequence rather than at an arbitrary fixed rate with complete atrioventricular dissociation.[9, 18, 22] The ventricular rate would then vary in response to physiologic stimuli and would provide appropriate changes in cardiac output, as during sleep, exercise, and fever. Furthermore, the normal sequence and timing of atrio-

* Pacemaker system made by the Electrodyne Company, Norwood, Massachusetts; batteries made by the Mallory Battery Company, North Tarrytown, New York.

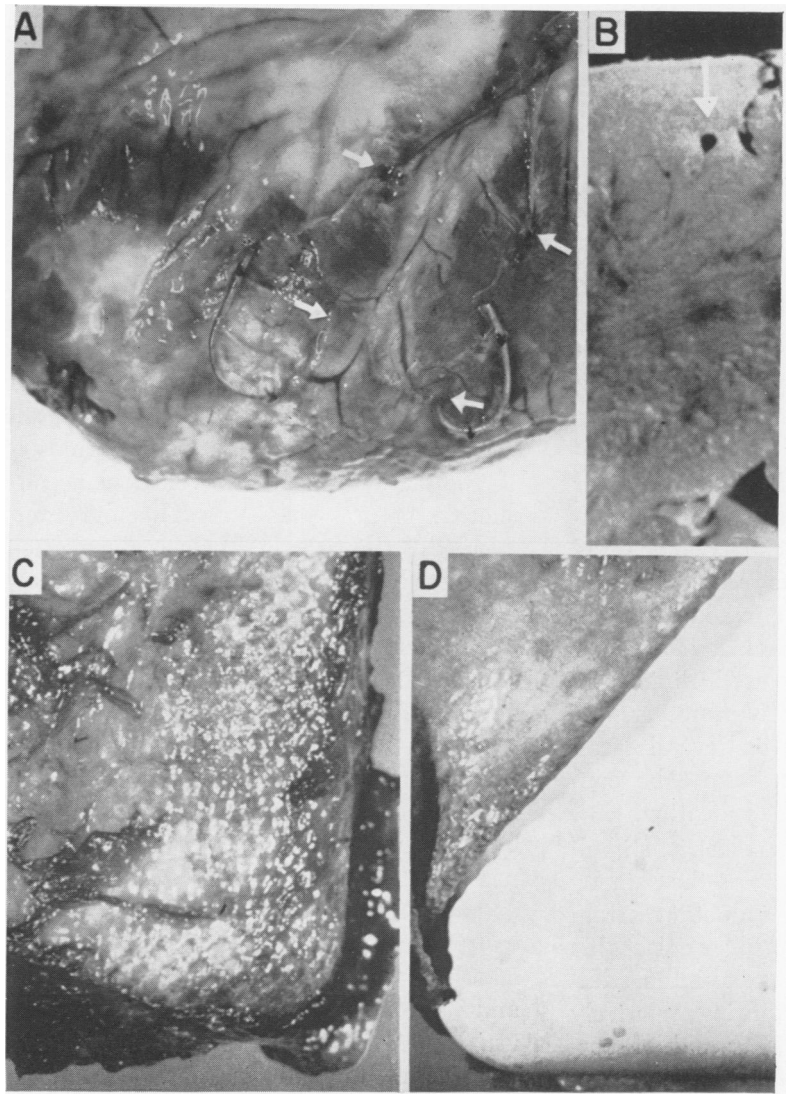

FIG. 2. Tissue sites one year after implantation. A. Surface of the left ventricle, showing minimal reaction at the site of electrode implantation (*arrows*). B. Section of left ventricular wall (enlarged), showing minimal reaction in the myocardial tunnel. C. External surface of pacemaker unit, showing loose ingrowth of fatty areolar tissue into the Teflon mesh. D. Internal surface of the Teflon bag, showing the smooth and glistening membrane apposed to the pacemaker.

ventricular excitation and contraction would restore the contribution of atrial systole to ventricular output. Ventricular output is said to increase 10 per cent or more due to increase in initial intraventricular tension and to normal closure of the atrioventricular valves. As demonstrated by Butterworth and Poindexter,[3] atrial impulses can be made by electronic means to stimulate the ventricle. These systems involve two sets of wires on the myocardium (atrial and ventricular) and many additional components in the unit. The disadvantages of increased complexity with consequent increased risk of component failure and of increased power requirement with consequent shorter life of the instrument must be balanced against the small and ordinarily inconsequential increase in cardiac output and refinement in physiologic function. It should be kept in mind that the primary purpose of artificial pacemakers is to provide completely reliable prevention of Stokes-Adams attacks; this basic objective should not be compromised for secondary gains.

Electrical Failure. Electrical difficulties in our pacemaker-electrode system may be manifested by variation in the rate of the pacemaker, which usually is constant within 5 per cent, as well as by ineffective stimulation. Depletion of the batteries does not accelerate the rate, which might be dangerous, but rather slows it and then produces intermittently or completely ineffective stimulation. Trouble in the timing circuit might lead to dangerous acceleration of the rate; stimulation should be interrupted promptly and the pacemaker replaced if the rate accelerates progressively beyond 10 per cent. Ineffective stimulation and rate changes may also result from breaks in the wires or in their insulation: increased electrical resistance, such as may be produced by a wire break, speeds up the rate; decreased resistance, which may be produced by loss of insulation, slows the rate.

Implantation Method

Control of Cardiac Action. Continuing experience reaffirms the need for constant control of cardiac action during all phases of surgical procedures in patients with heart block of any degree. Most of our patients have had ventricular standstill or fibrillation during the procedure. Adequate control requires continuous observation and readiness to stimulate, to countershock, to carry out cardiac massage, and to administer dilute solutions of isoproterenol or epinephrine intravenously.[25] The adequate management of the cardiac rhythm in these patients is especially difficult during surgery and requires undivided expert attention.

Stokes-Adams attacks are usually prevented pre-operatively by intravenous administration of dilute solutions of epinephrine or isoproterenol. In the operating room ability to stimulate the heart at all times is obtained first by precordial subcutaneous needle electrodes, and later by a pericardial wire.[25] An intracardiac catheter electrode may be used before and during surgery and may save some time at the outset of the operation.[10] It involves additional hazards, however, that we ordinarily prefer to avoid. We have used catheter electrodes in 13 patients to determine the usefulness of a pacemaker for the particular patient and its optimal rate, and to control cardiac action during necessary delays in surgery when drugs were unsatisfactory. Complications occurred in eight patients: perforation in 1; intermittently ineffective stimulation in three, one of whom died; staphylococcal septicemia in two; and clots on the catheter tips in two.

Technical Considerations. The technic of implantation has not changed greatly since our previous description.[25] Pre-operatively, the skin is cleansed several times each day for several days and monitor electrodes on the chest are shifted frequently to reduce skin irritation. Despite its inconvenience we continue to use beta-propriolactone for sterilizing the pacemaker system because it is quick and effective at room temperature.[25]

The retropectoral site remains our first choice for pacemaker implantation. Our patients, male and female, have found this position comfortable for daily activity, heavy work, and sports. We enclose the pacemaker unit in Teflon mesh prior to implantation (Fig. 1) and coapt the tissues snugly about it without sewing the mesh. Pliable areolar tissue invades the mesh and forms a smooth mold that prevents migration of the unit and permits replacement without exciting new reaction (Fig. 2). Prophylactic antibiotic therapy has not usually been employed in either primary or secondary operations.

As the two wires emerge from the pacemaker unit, they are enclosed in Silastic tubing for mechanical stability and support. We have shortened the Silastic tube, however, so that it does not go through the

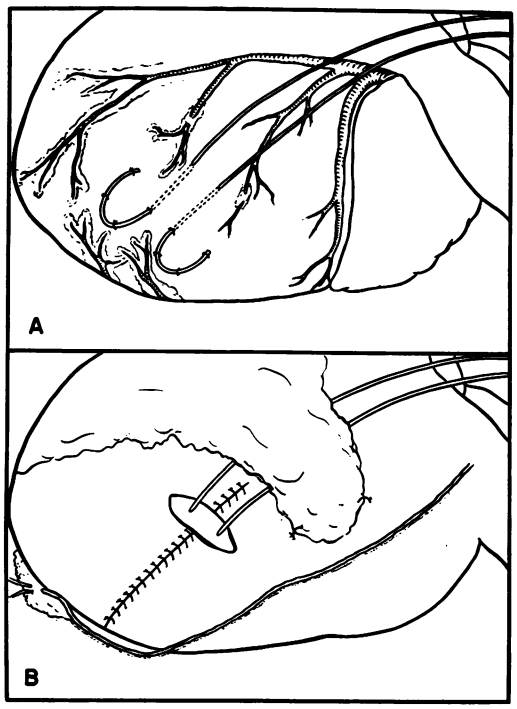

FIG. 3. Diagram of electrode implantation. A. The implantation tunnels are aligned toward the obtuse margin of the heart and the wires toward the base; the needles have been cut away and the distal wires turned back; all fixing sutures are distal to the tunnels. B. The pericardium is closed leaving an aperture about the wires; the wires are not sutured to the pericardium but are held in course by a flap of extrapericardial fat; the phrenic nerve has been displaced posteriorly.

chest wall and therefore can not act as a conduit for infection to the pericardium.

Broad exposure of the left ventricle is desirable to permit optimal placement of the electrodes. Their position is not critical for effective stimulation: the main considerations are the stability of the implantation, the avoidance of injury to coronary branches, and an alignment of the wires that minimizes flexion stresses. The implantation tunnels are aligned in parallel and somewhat obliquely downward and outward toward the lateral border of the ventricle, to minimize buckling of the wire as the ventricle contracts (Fig. 3A). The fixing sutures must avoid even small, hidden coronary branches. Local myocardial cyanosis should be looked for before each holding tie is completed. We have not observed evidence of surgical damage to coronary branches in our cases. We turn back the distal wires in J-shape (Fig. 3A), and hold them with several superficial sutures of fine silk before cutting off the needles and redundant wire. The wires are led from the implantation site along the long axis of the heart. The implantation site and distal wires are covered as the pericardium is closed, but we no longer fix the proximal wires to the pericardial edge. Instead, a cross-incision in the pericardium is left open around the wires (Fig. 3B) in order to avoid transmission of the small motion between myocardium and pericardium with each beat. From the heart, the two wires are led in a smooth curve upward along the mediastinum, anterior to the lung root but separated from the chest wall by the anterior margin of the lung, and then forward in the upper chest to the site of emergence in the second or third interspace anteriorly. In an abdominal wall implantation, the wires are also led upward from the ventricle to the base of the heart before being looped anteriorly and downward to the costophrenic sulcus. This course minimizes flexion with cardiac and diaphragmatic motion. The wires may be kept in their course by flaps of mediastinal pleura or fat, but they are not sutured so as to rub together or flex sharply. They are never grasped in a clamp or other bare instrument that may injure the strands or the insulation.

The phrenic nerve may be stimulated by conduction through myocardium and pericardium, and should therefore be mobilized if necessary, and placed well anterior or posterior to the implantation site.

Secondary operations may be required for specific problems. When a wire is broken within its insulation, stimulation may be intermittently or completely ineffective. A single electrode in the myo-

cardium with a distant indifferent one is satisfactory and, indeed, is used in some systems;[8, 20] we do prefer two myocardial electrodes, however, to provide a factor of safety in case of a broken wire or a high threshold. Consequently, the electrical circuit may be re-established and effective stimulation restored by baring a proximal segment of this wire and fixing it in contact with the soft tissue of the chest wall. Muscle twitch from local stimulation may become painful and may be corrected by relocation of the bared wire. Both wires may need to be bared before the broken one is identified; the unbroken one must be carefully re-insulated by silicone adhesive * within a crimp connection or a Silastic tube. This simple procedure, carried out under local anesthesia, should always be considered before a complete pacemaker system is replaced because of a wire break. Two of our patients have been satisfactorily controlled in this way for more than a year. If stimulation is not restored by contact of either wire with tissue, they should be cut; then the threshold for stimulation and the output of the pacemaker may be determined. The former is done by connecting an external pacemaker to the distal wire and to a temporary indifferent electrode. For the latter, the proximal wires are connected to a calibrated oscilloscope. If the thresholds are high or if there is any question about the integrity of the myocardial electrodes, a new system is needed. The pacemaker alone must be replaced if its output is low; the new one can be slipped into the old Teflon envelope and connected to the myocardial wires by crimp connectors.[25]

When the primary sites are infected, extreme care must be taken to avoid contamination of the secondary field. Skin sterilization is carried out over the entire trunk for two or three weeks prior to operation. The new surgical field is carefully separated from the old. If the initial incision has been anterior or anterolateral, the secondary incision is kept posterolateral and lower. The course of the initial wires is avoided, and the second electrodes are placed in the posterior rather than the anterior aspect of the ventricle. The pacemaker unit is then usually placed in the abdominal wall, anteriorly or in the flank. With these precautions, we have obtained clean healing of all secondary implantations and have then in subsequent procedures successfully removed the infected systems.

* Medical Adhesive type A, Dow Corning Corp., Midland, Mich.

Clinical Experience

Our series consists of 77 patients. There is a 2-to-1 sex ratio, with 52 men and 25 women. One third (24) was under 60 years of age and one sixth (13) was 75 to 89 years old. Many were desperately ill, some almost moribund; many were worn out by repeated, harrowing Stokes-Adams attacks, others by refractory congestive heart failure. Serious illnesses in addition to the heart block itself were frequent; they included coronary heart disease, aortic and mitral valvular disease, chronic pulmonary disease, cerebral and peripheral vascular disease, obstructive uropathy and chronic renal disease, lupus erythematosus, sarcoidosis, diabetes mellitus, and severe arthritis. The primary indication for surgery in most of the patients was Stokes-Adams disease, in 5 it was congestive heart failure, and in one it was angina pectoris. Many of the patients had multiple indications for operation; and several had inadequate cerebral or renal function as manifestations of reduced cardiac output without obvious congestive failure.

All but one of our patients had atrioventricular block: in most the block was complete and fixed, but in 32 patients A-V conduction of some degree, even completely normal, was observed at least in-

TABLE 2. *Duration of Treatment with Implanted Pacemakers*

Treatment Period	Number of Patients	
	Alive	Dead
(months)		
0–11	25	12
12–23	23	2
24–40	12	3
Total	60	17

termittently. In none of our patients was the heart block of a transient nature, resulting from a reversible cause such as acute myocardial infarction or digitalis toxicity. One patient suffered repeated episodes of ventricular standstill due to sino-atrial arrest; since he never showed A-V block of any degree, strictly speaking he is classified as having cardiac syncope but not Stokes-Adams disease.[19, 28]

The etiology of the heart disease in these patients was varied; in most cases it was unknown. In some, coronary artery disease, hypertensive heart disease, or valvular disease, mitral or aortic, was clearly present. Congenital A-V block was present in 1 patient, aged 26 at operation; sarcoid in another, aged 72 at operation; and disseminated lupus erythematosus in a third.

In several patients additional unrelated procedures were carried out during the primary thoracotomy: reduction of a large incarcerated diaphragmatic hernia, segmental resection of lung, lung biopsy, and mediastinal lymph node biopsy. These procedures were all tolerated well.

Twenty-nine of the 77 patients required more than one operation. The entire system was replaced 22 times in 17 patients; 56 other secondary procedures were necessitated by pacemaker failure, wire break, or sepsis, nearly all in the early phase of the program (Table 1). The longest period of treatment with implanted pacemakers is 40 months (Table 2). The cardiac status in all these patients has been recently confirmed by us.

Mortality. There was one early postoperative death in the 155 surgical procedures performed; this was due to respiratory insufficiency in an obese woman with severe thoracic spondylitis.

There were 16 late deaths, months to years after initial implantation. Eight patients died of obvious causes other than Stokes-Adams attacks. They were congestive heart failure from severe aortic regurgitation and from severe cor pulmonale; sepsis due to exteriorized wires early in our series; unexplained hypotension; acute myocardial infarction; renal failure associated with lupus erythematosus; pneumonia; and brain tumor.

The remaining eight patients died suddenly. In one, a broken wire was found which presumably caused death from a Stokes-Adams attack when stimulation became ineffective. In three, all with severe coronary artery disease, ventricular fibrillation appeared to be the cause of death. Fibrillation was observed as the terminal mechanism in one of these patients; he had shown no recent A-V conduction or spontaneous ventricular activity and the electric pacemaker was functioning well just before the sudden arrhythmia and at postmortem. The other two patients had frequent, multifocal ventricular beats, singly or in short runs, despite stimulation about 70 per minute and administration of quinidine; although these patients showed A-V conduction, the ectopic activity was never initiated by an effective stimulus in the vulnerable period.

Important in this regard are three additional patients who had sudden ventricular tachycardia despite effective stimulation but who survived; they all had significant clinical coronary disease. One of these patients had frequent interpolated ectopic ventricular beats which were not controlled by quinidine or procaine amide, or by rapid stimulation up to 110 per minute by means

of a temporarily substituted variable rate pacemaker. It seems, therefore, that effective stimulation, even at rates of 70 per minute or higher, does not completely prevent ventricular irritability especially in patients with severe coronary artery disease. Consequently, they may suffer ventricular fibrillation with syncope or sudden death just as they may even if they do not have A-V block.

In the remaining four patients who died suddenly the cause of death is not known. The pacemaker-electrode systems were found to be functioning properly in the two in whom autopsies were done: one had congenital aortic stenosis, which may account for his sudden death. The other two patients were well with pacemakers that were observed to be functioning normally a few hours before death.

Risk of Ventricular Fibrillation from Competition. The fear is often expressed that electric stimuli may produce repetitive responses and ventricular fibrillation when they fall in the vulnerable period after conducted beats or ectopic ventricular beats. As a result, A-V conduction of any degree has even been suggested to be a contraindication to implantation. More than half of our patients have had such competition between the electric pacemaker and intrinsic pacemakers, either from conducted beats (32 patients) or ectopic ventricular beats. In the intensive studies that we have carried out in these patients, we have never observed repetitive responses or ventricular fibrillation from a stimulus in the vulnerable period even though we have examined thousands of such stimuli. Furthermore, ventricular fibrillation from stimulation in the vulnerable period can not explain most of the sudden deaths in our series. Of eight patients who died suddenly only three had had competition in the months before death.

Three cases are reported, however, in which repetitive responses to stimuli in the vulnerable period did occur.[7, 8, 24] Some features of the stimulation may explain these untoward experiences. The stimuli were long in one case (5 milliseconds), they were of spike form in two, and the intervals between beats were prolonged (0.9 to 1.8 seconds) in all three. All these features may increase the likelihood of repetitive responses.[14, 26]

It must be recognized, nevertheless, that the threshold for repetitive responses may at times be lowered by factors such as local myocardial ischemia, so that this hazard may not be entirely avoidable. Such arrhythmias should be most infrequent with stimuli of short duration (2 milliseconds), at rates that usually suppress ectopic ventricular activity (70 per minute or more), and by careful placement of electrodes to minimize myocardial damage.

Postoperative Morbidity. Postoperative morbidity has in general been mild, and most patients were discharged by the tenth postoperative day. Eight patients had clinically significant bronchitis, atelectasis, or pneumonitis, one with transient septicemia. One patient showed extensive cerebral damage postoperatively with subsequent slow recovery even though there had been no fall in blood pressure or pulse rate during surgery. Another had a cerebral vascular accident with full recovery. An acute transient fibrinolytic reaction occurred during one secondary thoracotomy. There has been no recognized instance of myocardial infarction or pulmonary embolization during or immediately after surgery.

Four patients developed fever, chest pain, and pericarditis or pleuritis with effusion, ten to 14 days after operation. No evidence of sepsis was found, and the diagnosis of post-pericardiotomy syndrome was made. All manifestations subsided promptly with steroid administration but relapses occurred when the drug doses were reduced too quickly.

Sepsis. Primary infection around the pacemaker occurred in 3 of the early patients in whom corrosion of the metal case led to severe local inflammation. Three other in-

fections resulted from the multiplicity of the secondary operations needed to correct electrical failure of early pacemakers or electrodes. Sepsis extending to the myocardial implantation site led to the loss of effective cardiac stimulation in several of these patients. Since the introduction of the present pacemakers embedded in epoxy resin in June 1961, there has been only one instance of infection (Table 1).

The surface materials now in use (Teflon, epoxy resin, Silastic, platinum) have proved remarkably nonirritating. Re-operations in uninfected cases have disclosed no inflammation, fluid accumulation, or significant scarring about electrodes, wires, or pacemaker unit (Fig. 2). When sepsis has occurred, however, it has with few exceptions persisted in spite of chemotherapy and drainage, until the foreign bodies were removed. Consequently, although sepsis has been infrequent, each instance has led to prolonged morbidity and multiple operations. Since cardiac stimulation cannot be interrupted safely in these patients, it is necessary to implant a complete new system before the old system is removed.

Late Complications. Some months after operation, two patients developed a diaphragmatic twitch, synchronous with cardiac stimulation. This has not required correction in these patients, but we now displace the phrenic nerve routinely at the time of implantation, even though no phrenic stimulation is observed.

Six months after implantation one patient noted the onset of a severe pectoral muscle twitch due to a wire break; this was corrected by connecting the broken wire from the pacemaker to a long bare wire which was placed subcutaneously well away from muscle.

Results

The implanted pacemaker has been a most effective means of preventing recurrent Stokes-Adams attacks. Except for instances of malfunction due to wire breakage, which are becoming more and more infrequent, attacks due to ventricular standstill have been eliminated. Seizures due to ventricular tachycardia or fibrillation have also largely been prevented; these arrhythmias were observed, however, despite effective stimulation in 6 patients with severe coronary artery disease.

The artificial pacemaker has also been very valuable in improving congestive heart failure. Other manifestations of diminished cardiac output were also significantly ameliorated. In several patients improvements in cerebral function have been particularly striking: mental acuity and memory were greatly improved; headache and confusion to the point of dementia were relieved. Objective measures of improved cardiac output were also obtained in many patients: significant reductions were measured in blood volume, heart size, and systolic or pulse pressure.

In view of the recent discussions of the advantages of variable-rate or P-wave synchronized pacemakers,[18] we have made a careful clinical analysis of the functional status of our patients after surgery. In particular, we wished to determine how many patients had significant limitation of function that might possibly have been improved by a variable rate. Most of the patients have been well and able to function without cardiac symptoms at levels of activity compatible with their general physical condition. Unless prevented by other infirmity they have returned to work, household activity, and sports (golf, water skiing, swimming, hunting) without limitations. Only five patients had some congestive failure or weakness after recovery from surgery. In two, severe sepsis and anemia were adequate explanations for the symptoms; indeed, the congestive failure cleared when the sepsis was controlled. In the other three patients extensive myocardial infarction, marked cardiac hypertrophy, and pulmo-

nary emphysema accounted for the congestive failure and weakness. Many of the patients underwent severe stresses with remarkably little circulatory difficulty: 11 had serious infectious processes, 15 had major surgery, four suffered the post-pericardiotomy syndrome, one suffered peripheral vascular collapse from massive gastro-intestinal hemorrhage, and one enjoyed a normal pregnancy and delivery without difficulty.

Electric stimulation of the heart, both external and direct, has provided opportunities for physiologic and pharmacologic studies, many of which have previously not been possible in man, and has led to revived interest in heart block and Stokes-Adams disease in the last decade. Such studies have included the relation of heart rate to cardiac output,[2] effects of sympathomimetic amines on ventricular rhythmicity and atrioventricular conduction,[27] depression of idioventricular pacemakers by rapid stimulation,[16] delineation of refractory and supernormal periods of ventricular excitability,[13] features of antegrade and retrograde atrioventricular conduction,[17] and an analysis of fusion beats.[15] Advances in our knowledge of cardiac physiology, particularly in relation to arrhythmias, must surely come from such observations, which have their origin in this electrical approach to the treatment of this long-recognized, somewhat uncommon, and still poorly understood disease.

Summary

This report presents our experiences with long-term electric stimulation of the heart in 77 patients during the last four years. Our implanted, fixed-rate pacemaker has eliminated Stokes-Adams attacks due to ventricular standstill and has also largely prevented seizures due to ventricular tachycardia or fibrillation. In addition, the artificial pacemaker has been very valuable in improving congestive heart failure and other manifestations of diminished cardiac output in patients with heart block and slow ventricular rates.

Stokes-Adams attacks, unless due to a transient or reversible condition, are a compelling indication for implantation of a pacemaker. In view of the unpredictability and lethal potentiality of the attacks and their uncertain prevention by drugs, even a single, mild episode calls for the assured prevention of further seizures by a reliable electric pacemaker. The low operative mortality and morbidity in our series, even with elderly and desperately ill patients, indicate that there are few if any patients with Stokes-Adams disease to whom this treatment should not be offered. Congestive heart failure and other manifestations of diminished cardiac output in patients with slow ventricular rates constitute an additional indication for surgery. We do not consider heart block alone in an asymptomatic patient to be an indication for treatment.

Acknowledgments

We wish to acknowledge the assistance of Dr. L. R. N. Zarsky and Alan H. Belgard.

References

1. Abrams, L. D., W. A. Hudson and R. Lightwood: A Surgical Approach to the Management of Heart-block Using an Inductive Coupled Artificial Cardiac Pacemaker. Lancet, 1:1372, 1960.
2. Benchimol, A., Y-B Li and E. G. Dimond: Cardiovascular Dynamics in Complete Heart Block at Various Heart Rates. Effect of Exercise at a Fixed Heart Rate. Circulation. In press.
3. Butterworth, J. S. and C. A. Poindexter: Fusion Beats and Their Relation to the Syndrome of Short P-R Interval Associated with a Prolonged QRS Complex. Am. Heart J., 28:149, 1944.
4. Cammilli, L., R. Pozzi and G. Drago: Remote Heart Stimulation by Radio Frequency for Permanent Rhythm Control in the Morgagni-Adams-Stokes Syndrome. Surgery, 52:765, 1962.

5. Chardack, W. M., A. A. Gage and W. Greatbatch: Correction of Complete Heart Block by a Self-contained and Subcutaneously Implanted Pacemaker. Clinical Experience with 15 Patients. J. Thoracic and Cardiovas. Surg., **42**:814, 1961.
6. Chardack, W. M., A. A. Gage, G. Schimert, N. B. Thomas, C. E. Sanford and W. Greatbatch: Two Years' Clinical Experience with the Implantable Pacemaker for Complete Heart Block. Dis. Chest, **43**:225, 1963.
7. Dittmar, H. A., G. Friese and E. Holder: Erfahrungen über die langfrigstige Elektrische Reizung des menschlichen Herzens. Z. f. Kreislaufforsch., **51**:66, 1962.
8. Elmquist, R., J. Landegren, S. O. Pettersson, A. Senning and G. William-Olsson: Artificial Pacemaker for Treatment of Adams-Stokes Syndrome and Slow Heart Rate. Am. Heart J., **65**:731, 1963.
9. Folkman, M. J. and E. Watkins: Artificial Conduction System for Management of Experimental Complete Heart Block. Surg. Forum, **8**:331, 1958.
10. Furman, S., J. B. Schwedel, G. Robinson and E. S. Hurwitt: Use of an Intracardiac Pacemaker in the Control of Heart Block. Surgery, **49**:98, 1961.
11. Glenn, W. W. L., A. Mauro, E. Longo, P. H. Lavietes and F. J. MacKay: Remote Stimulation of the Heart by Radio Frequency Transmission. Clinical Application to a Patient with Stokes-Adams Syndrome. New England J. Med., **261**:948, 1959.
12. Kantrowitz, A., R. Cohen, H. Raillard, J. Schmidt and D. S. Feldman: The Treatment of Complete Heart Block with an Implanted, Controllable Pacemaker. Surg., Gynec. and Obst., **115**:415, 1962.
13. Linenthal, A. J. and P. M. Zoll: Quantitative Studies of Ventricular Refractory and Supernormal Periods in Man. Tr. A. A. Physicians, **75**:285, 1962.
14. Linenthal, A. J. and P. M. Zoll: Prevention of Ventricular Irritability in Stokes-Adams Disease by Intravenous Sympathomimetic Amines. Circulation, **27**:5, 1963.
15. Linenthal, A. J. and P. M. Zoll: Ventricular Fusion Beats and Myocardial Conduction Time in Man; Their Significance for Anomalous A-V Excitation. Tr. A. A. Physicians, **76**:272, 1963.
16. Linenthal, A. J., P. M. Zoll, G. H. Garabedian and K. Hubert: Ventricular Slowing and Standstill after Spontaneous or Electrically Stimulated Runs of Rapid Ventricular Beats in Atrioventricular Block. Abstract, Circulation, **22**:781, 1960.
17. Linenthal, A. J., P. M. Zoll, G. H. Garabedian and K. Hubert: Retrograde Conduction to the Atria from Electric Stimulation of the Ventricles in Man. Abstract, Circulation, **26**: 752, 1962.
18. Nathan, D. A., S. Center, C-Y Wu and W. Keller: An Implantable, Synchronous Pacemaker for the Long-term Correction of Complete Heart Block. Circulation, **27**:682, 1963.
19. Parkinson, J., C. Papp and W. Evans: The Electrocardiogram of the Stokes-Adams Attack. Brit. Heart J., **3**:171, 1941.
20. Siddons, A. H. M.: Long-term Artificial Cardiac Pacing: Experience in Adults with Heart Block. Annals Royal Coll. Surg., **32**:22, 1963.
21. Siddons, A. H. M. and O'N. Humphries: Complete Heart Block and Stokes-Adams Attacks Treated by Indwelling Pacemaker. Proc. Royal Soc. Med., **54**:237, 1961.
22. Stephenson, S. E., Jr., W. H. Edwards, P. C. Jolly and H. W. Scott, Jr.: Physiologic P-wave Cardiac Stimulator. J. Thoracic & Cardiovasc. Surg., **38**:604, 1959.
23. Stoeckle, H. and J. C. Schuder: Experimental Experience with a Micromodule Pacemaker Receiver Sutured Directly to the Left Ventricle. Circulation, **27**:676, 1963.
24. Tavel, M. E. and C. Fisch: Repetitive Ventricular Arrhythmia Resulting from Artificial Internal Pacemaker Stimulation. Circulation. In press.
25. Zoll, P. M., H. A. Frank, L. R. N. Zarsky, A. J. Linenthal and A. H. Belgard: Long-term Electric Stimulation of the Heart for Stokes-Adams Disease. Ann. Surg., **154**:330, 1961.
26. Zoll, P. M. and A. J. Linenthal: External Electric Stimulation of the Heart. N. Y. Acad. Sci., **111**:932, 1964.
27. Zoll, P. M., A. J. Linenthal, W. Gibson, M. H. Paul and L. R. Norman: Intravenous Drug Therapy of Stokes-Adams Disease. Effects of Sympathomimetic Amines on Ventricular Rhythmicity and Atrioventricular Conduction. Circulation, **17**:325, 1958.
28. Zoll, P. M., A. J. Linenthal, L. R. Norman, M. H. Paul and W. Gibson: External Electric Stimulation of the Heart in Cardiac Arrest: Stokes-Adams Disease, Reflex Vagal Standpected Circulatory Arrest. Arch. Int. Med., **96**:639, 1955.
29. Zoll, P. M., A. J. Linenthal and L. R. N. Zarsky: Ventricular Fibrillation: Treatment and Prevention by External Electric Currents. New England J. Med., **262**:105, 1960.