The Role of Electropacing in Cardiac Diagnosis

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THE INTRODUCTION OF electrical stimulation of the heart in clinical cardiology has opened new ways to study several aspects of cardiac function directly in the unanesthetized patient. This is a selective review of the many papers which have appeared on this subject in recent years, together with comments based upon our own experience. It will be shown that several areas of diagnostic cardiology can profit from electropacing.

Technic

For diagnostic electropacing, electrode catheters and a stimulator are needed. The catheter, preferably a bipolar one, is inserted, usually by means of the Seldinger technic, into either a femoral or an antecubital vein. The tip of the catheter is positioned, under fluoroscopic control, at the desired intracardiac location and is connected with the stimulator. It is essential that the stimulator be safe[1, 2] and accurate and able to:

1. Pace the heart regularly at different frequencies.
2. Provide, during regular pacing, an extra stimulus at any desired interval and following any desired number of paced beats (the "single-test stimulus" method).
3. Make possible the insertion of a stimulus at any desired moment in the cardiac cycle during a spontaneous rhythm.

Stimulators capable of providing more than one premature stimulus during spontaneous and driven rhythms have been developed

Acta Int Med Vol 19 — 1974

from the "basic" stimulator described on the preceding page. There are four areas in which the use of diagnostic electropacing may be discussed: (1) disturbances in impulse formation and conduction, (2) atherosclerotic coronary artery disease, (3) miscellaneous diagnostic uses and (4) potential applications.

Disturbances in Impulse Formation and Conduction

As shown by Langendorf and Pick,[3] artificial pacing of the heart has contributed significantly to our understanding of arrhythmias and has confirmed earlier deductions from clinical electrocardiograms. These authors list 19 different disturbances of impulse formation and conduction that have been elucidated by artificial pacing. To stay within the scope of the present review, discussion has been limited to those conditions in which the method seems to be most valuable to the practicing clinician.

Atrioventricular conduction and block.—The use of atrial pacing with increasing driving rates and of the single-test stimulus with gradual decrease of the interval of prematurity of the test beat have increased greatly our knowledge of normal and abnormal patterns of atrioventricular conduction.[4-7] Especially in combination with recordings of the electrical activity of the bundle of His,[8] it is possible to localize the site of delay or block in the junctional and subjunctional conduction system. It has been shown that, in most patients with complete heart block, the conduction defect is located at the level of the bundle-branches and their divisions. These observations support the concept of Rosenbaum *et al.*,[9] who regard the atrioventricular conduction system as being trifascicular. Furthermore, these observations have increased our awareness of the fact that right bundle-branch block with left anterior or left posterior divisional block ("hemiblock") are frequent precursors of complete heart block. It is possible to stress conductive capability of the remaining fascicle in such patients by high rates of electropacing. If combinations of junctional and subjunctional conduction disturbances are present, the latter system can be tested by pacing the former. An excellent classification of the localization of atrioventricular conduction delay and block in relation to His bundle recordings has been given by Narula *et al.*[10] Although second-degree block of the Wenckebach type usually occurs in the AV node proper, it has been demonstrated to occur in the His bundle and in the bundle branches as well.[11-13]

Mobitz type-II block (sudden block in AV conduction without

gradual increase of the preceding P-R interval) has been found not only at the level of the bundle branches but also in the bundle of His and the AV node.[11, 14, 15] Pacing of the ventricle in patients with AV block has shown that, in the presence of total AV block, "normal" ventriculoatrial conduction may exist (unidirectional block).[5, 10] As the recent review by Damato and Lau[17] has shown, the effect of different drugs on atrioventricular and intraventricular conduction can be studied by atrial pacing combined with His bundle recordings.

The "sick sinus" syndrome.[18]—In recent years it has been recognized that, apart from conduction disturbances in the atrioventricular conduction system, syncope can result from abnormalities at the sinoatrial nodal level. Possible causes include: fibrosis, ischemia, increased vagotonus and drugs.

In patients with the "sick sinus" syndrome, two mechanisms of cardiac slowing may be observed:[19] (1) sinus bradycardia, with or without sinoatrial block, and (2) alternating periods of bradycardia and tachycardia (mostly atrial fibrillation and atrial flutter), with asystole and syncope usually occurring at the termination of the rapid rhythm.

The major problem in these patients seems to be related not only to the bradycardia and supraventricular tachyarrhythmia but also to the failure of normal atrial, AV junctional or ventricular pacemakers to escape. Drug therapy is frequently unsatisfactory, and a pacemaker must be implanted. The identification of these patients is facilitated by recording the escape interval following pacing of the atrium at rates of 100–130/min. for a few minutes.[20, 21] Three points have to be mentioned:

1. In the patient in whom constant monitoring shows definite sinus node dysfunction, the escape interval following repeated atrial pacing at identical rates and duration may differ from each other by 2–11 seconds, with occasionally a completely "normal" escape interval following cessation of pacing.
2. These patients may display at times completely normal sinus rates.[21]
3. In addition to the "sick sinus node," abnormalities of atrioventricular conduction are frequently present.[22, 23]

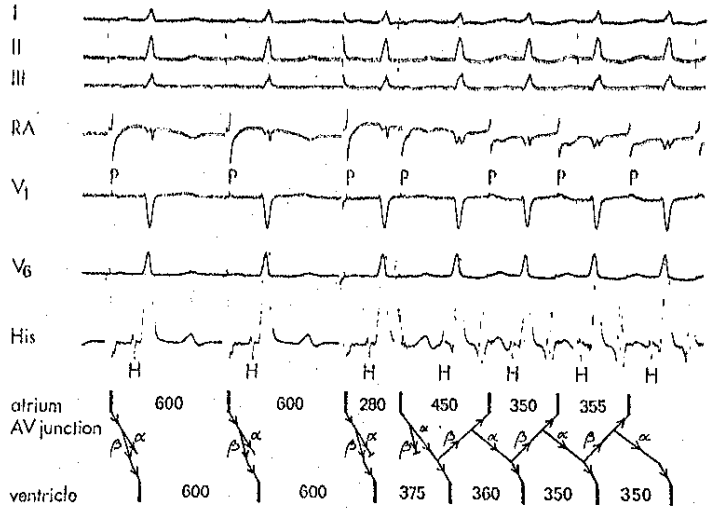
Although an atrial pacemaker for a deranged sinus node is hemodynamically preferable, in patients in the last category a ventricular pacer must be used. Furthermore, technical difficulties with permanent intravenous atrial pacing make ventricular pacing, in general, more feasible.

Re-entry and reciprocating tachycardia.—Moe and Men-

dez[24] observed in the canine heart that an early atrial or ventricular premature stimulus during atrial or ventricular pacing is frequently followed by a reciprocal beat or echo. The same phenomenon has been shown to occur in the human heart during continuous ventricular pacing at regular rates[25] and following the induction of a single atrial or ventricular premature beat.[26, 27] These findings fit the concept that at least two pathways, with functionally and spatially different properties, are present in the AV junction. This longitudinal dissociation enables a critically timed impulse arising in the atrium or ventricle to travel by one of the pathways within the AV junction and return to the atrium or ventricle by way of the other pathway. If such re-entrant activity in the AV junction continues, a junctional tachycardia results. This phenomenon—the induction of an AV junctional re-entrant tachycardia by an appropriately timed atrial or ventricular premature beat—has been described by several authors.[28-33]

As shown in Figure 1, an atrial premature beat, inserted after 280 msec during regular driving of the right atrium with a basic cycle length of 600 msec, is conducted with delay to the ventricle and followed by a tachycardia. In the ladder diagram, re-entry in the pres-

FIG. 1.—Initiation of an AV junctional tachycardia by way of an atrial premature beat. Three extremity leads (*I, II, III*), an intracavitary lead from the right atrium (*RA*), two precordial leads (V_1, V_6) and the His bundle electrocardiogram, recorded simultaneously, are shown. The mechanism of initiation of the tachycardia is shown in the ladder diagram (below). Longitudinal dissociation in the AV junction is thought to be responsible for the tachycardia.



ence of two pathways (α and β) in the AV junction is assumed to be the mechanism for this tachycardia.

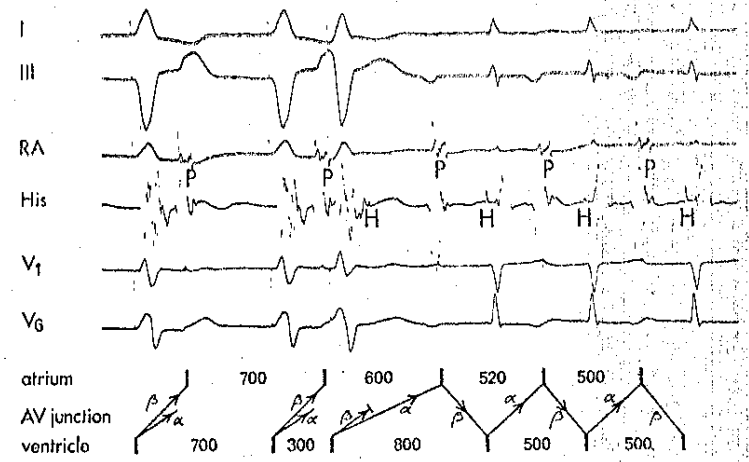
The initiation of a reciprocal AV junctional tachycardia by way of a ventricular premature beat during ventricular pacing is shown in Figure 2. Existence of a re-entrant mechanism can be demonstrated further by the fact that these tachycardias can be terminated by one or two atrial or ventricular premature beats.

As we have recently described,[34] ventricular tachycardias can also be based upon a reciprocal mechanism. Both the initiation (Fig. 3) and the termination of a ventricular tachycardia by a single ventricular premature beat and the influence of ventricular premature beats upon the time relations of the tachycardia fit into this concept.

Contrary to the traditional concept of atrial flutter,[35] we could not find, by means of atrial stimulation, that a circus movement involving a large area of the atria is present.[33]

The finding that AV junctional tachycardias and ventricular tachycardias can be terminated by a single well-timed stimulus has therapeutic implications. Termination of a tachycardia by an induced premature beat will depend on: (1) the distance between the site of stimulation and the tachycardia pathway; (2) the conduction properties of the tissue between the site of stimulation and the tachycardia pathway; (3) the frequency of the tachycardia and its resulting refrac-

FIG. 2.—Initiation of an AV junctional tachycardia by way of a ventricular premature beat. As shown in the His bundle lead, the retrograde conduction time of the ventricular premature beat through the AV junction is long. This is essential for initiation of reentry in the AV junction.



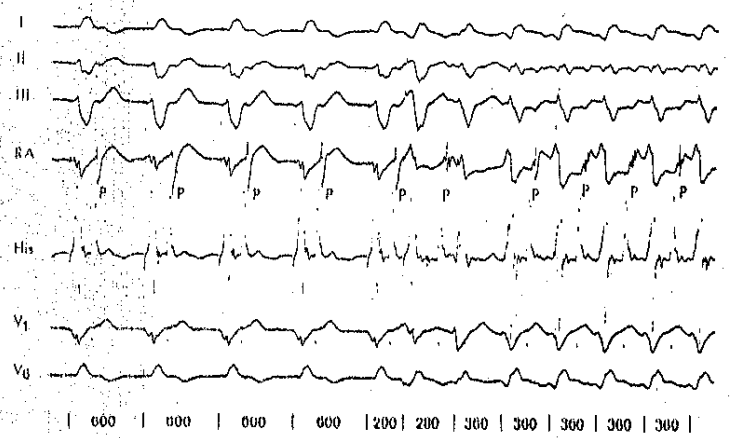


FIG. 3.—Initiation of a ventricular tachycardia. A ventricular premature beat, given after 200 msec during regular pacing of the ventricle with basic cycle length of 600 msec, initiates a tachycardia. As shown in the His bundle lead, the absence of His bundle activation preceding the QRS complex indicates a ventricular origin of the tachycardia. The intracavitary lead from the right atrium (*RA*) shows that the first ventricular complex of the tachycardia is not followed by retrograde activation of the atrium. Thereafter, every QRS complex of the tachycardia is followed by retrograde conduction to the atrium.

tory period; and (4) the spatial dimensions of the tachycardia pathway.

THE PRE-EXCITATION SYNDROME.—In the area of anomalous atrioventricular conduction, the introduction of electrical stimulation of the heart,[36] combined with the recording of His bundle activity[37] and epicardial excitation mapping,[38-41] have led to fascinating new developments.[42] Theories advanced in the past, based upon the careful analysis of clinical electrocardiograms, have been proved correct. Epicardial excitation mappings[38-41] and His bundle recordings[37] clearly demonstrate that the whole or some part of the ventricular muscle is activated earlier by an impulse from the atrium than would be expected when the impulse reaches the ventricles by way of the normal specific conduction system only. A circus movement, using the normal AV conduction system and an anomalous AV bypass, has been shown to exist during tachycardias in patients with pre-excitation.[36, 39, 43]

These observations have led to successful surgical interventions.[40, 44] The tachycardia pathway has been interrupted either by dissection of the anomalous connection[40] or of the AV node.[44] The negative outcome of surgical procedures in some patients[39, 45, 46] have further contributed to our understanding of the complexity of atrioventricular conduction in the Wolff-Parkinson-White syndrome. Surgical procedures have also confirmed that identical electrocardiograms can result from different types and combinations of anomalous pathways.

What is the diagnostic value of cardiac pacing in the pre-excitation syndrome?

1. The normal AV conduction system shows a lengthening of transmission time during atrial pacing at increasing rates and following atrial premature beats, with progressive degrees of prematurity. The absence of this phenomenon in the anomalous pathway leads to an increase in and clearer localization of the pre-excited area during these two modes of testing.

2. Stimulation at different sites in the right and left atrium help in localizing the atrial end of the anomalous bypass, because atrial stimulation close to the bypass will result in a greater area of pre-excitation.

3. When combined with His bundle recordings using the single-test stimulus method, it is frequently possible to decide between a complete AV bypass (a so-called Kent bundle) or bypasses between parts of the conduction system and the atrium or ventricle (James and Mahaim fibers). In the presence of a Kent bundle, atrial premature beats produced with increasing prematurity will show no change in the P-delta interval, but the QRS complex will show a gradual increase in pre-excitation, with the His bundle electrogram occurring progressively later after the beginning of the delta wave.

When the accessory pathway takes off from the AV node or His bundle (Mahaim fiber), the His bundle potential will usually be located before the beginning of the delta wave, but more important is the observation that increasing prematurity of the testing stimulus will produce lengthening of the P-delta interval. The lower the origin of the Mahaim fiber from the AV node-His pathway, the less the changes in pre-excitation following test pulses of increasing prematurity.

In the case of a James fiber inserted into the His bundle that short-circuits the AV node, no change in the interval between atrial activation and His bundle activation will be seen on increasing the prematurity of the testing stimulus.

4. The mechanism of the tachycardia can be studied by initiation (Fig. 4) and termination of the tachycardia. This is necessary if the use of electrical stimulation to terminate and prevent tachycardias on a long-term basis is to be considered.

5. The induction of atrial premature beats during atrial pacing (by

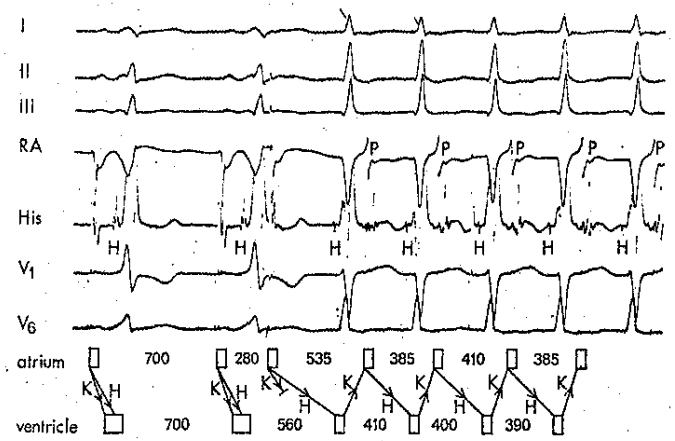


FIG. 4.—Initiation of a circus movement tachycardia in Wolff-Parkinson-White syndrome. During regular pacing of the atrium with a basic cycle length of 700 msec, an atrial premature beat after 280 msec is conducted to the ventricle by way of the AV node-His pathway (*H*) only. This is followed by retrograde conduction from the ventricle toward the atrium by way of the anomalous connection (*K*). This mechanism is continued, resulting in tachycardia. As shown on the left, during basic rhythm the His bundle lead indicates that ventricular activation starts before the His bundle is activated. This is diagnostic for pre-excitation.

way of the single-test stimulus) and atrial pacing with increasing frequencies make it possible to measure the refractory period of the anomalous pathway. In this way the pathways which have a short refractory period can be identified. It is obvious that, as far as the ventricular rate is concerned, these patients do not have the protective effect of the AV node if rapid atrial rhythms like atrial flutter or atrial fibrillation supervene. Sudden death might follow the onset of such an arrhythmia.

6. The effect of drugs on conduction in the anomalous pathway can be studied.

If surgical transection of the anomalous connection is necessary, accurate localization of the anomalous bypass is mandatory. In this situation, the combined use of pacing and epicardial excitation mapping is essential. The atrial end of the bypass can be localized by recording epicardial atrial excitation during ventricular pacing, and the ventricular end can be localized by recording epicardial ventricular excitation during atrial pacing. From the preoperative stimulation study, the site and pattern of stimulation which gave the greatest amount of information (see above) should be known and used during operation.

ATHEROSCLEROTIC CORONARY ARTERY DISEASE

In 1967, Sowton *et al*[47] described the use of atrial pacing for measuring the angina threshold in patients with angina pectoris. The thought behind the test was that an increase in heart rate will precipitate anginal pain by raising cardiac work and oxygen consumption in patients who cannot enhance their coronary flow because of coronary artery disease. As outlined by Linhart,[48] electrocardiographic,[49] hemodynamic[50, 51] and metabolic changes,[52-54] coronary blood flow,[53-55] ventricular function[56-58] and ventricular motion[59, 60] can be studied during atrial pacing. The fact that, contrary to exercise stress, systemic changes during atrial pacing are usually absent favors reproducibility of results. Another advantage over exercise is that atrial pacing can be controlled precisely and discontinued rapidly; thus, it can be used even in patients with preinfarction angina.[61]

During the pacing stress test, the atrial rate is gradually increased until angina occurs or the development of incomplete AV block prevents a further increase in heart rate. The left ventricular end diastolic pressure (LVEDP) is measured prior to, during and following atrial pacing. Although the LVEDP may become lower or stay the same during pacing-induced angina, it is usually found to be above control value. Following sudden cessation of pacing in patients with angina, the LVEDP may rise considerably as compared to the LVEDP during the pacing and to the resting control values. An increase in LVEDP during pacing or a marked overshoot following pacing usually indicates abnormal myocardial function.

In addition to the determination of the LVEDP, other measurements of ventricular function[50-58] and of pressure-volume relationships[59] can be made. In this way, it is possible to study both muscle function and pump function in patients with atherosclerotic coronary artery disease. The value of these observations for the selection of suitable candidates for coronary by-pass surgery remains to be demonstrated. Preferably this should be done by comparing the results of atrial pacing pre- and postoperatively. Pasternac *et al*,[60] have shown that abnormalities of ventricular motion can be provoked or augmented by atrial pacing.

Pacing stress can also be used to study the effect of drugs like nitroglycerin[62, 63] and of oxygen[64] on the angina threshold and on myocardial function.

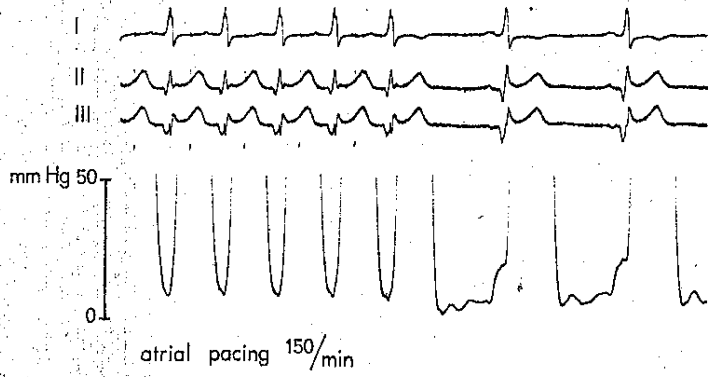
Miscellaneous Diagnostic Uses

Both Benchimol and Goldstein[65] and Linhart[66-68] have called attention to the use of atrial pacing in the evaluation of myocardial function in heart disease other than coronary artery disease. In patients with valvular heart disease, it should be possible to decide what part of impaired cardiac function is the result of dynamic abnormalities of the valve and what part results from disturbances in muscle contractility.

Linhart[67] showed that in valvular aortic stenosis the LVEDP may show a postpacing overshoot, which he attributed to a decrease in myocardial compliance. We have observed the same phenomenon in patients with cardiomyopathy (Fig. 5). By shortening the period of flow over the mitral valve by atrial pacing with increasing rates, the severity of mitral stenosis can be demonstrated.[69]

In patients with severe aortic insufficiency, a reversed gradient may exist, during the latter part of diastole, between left atrium and left ventricle.[70, 71] This can be nicely demonstrated by observing the simultaneously recorded left atrial and left ventricular pressure in the pause following an induced atrial premature beat (Fig. 6). If severe aortic insufficiency and mitral stenosis are present in the same patient, mitral stenosis can be demonstrated by pacing the atrium at increasing rates. This will result in a decrease in left ventricular diastolic pressure[72] and an increase in left atrial pressure following abbreviation of the period of forward diastolic flow over the mitral valve.

FIG. 5.—Atrial pacing in a 27-year-old male with cardiomyopathy. Angiography showed normal coronary arteries. No outflow tract obstruction was present. The LVEDP rises from 10 mm Hg during pacing to 20 mm Hg following sudden cessation of pacing.



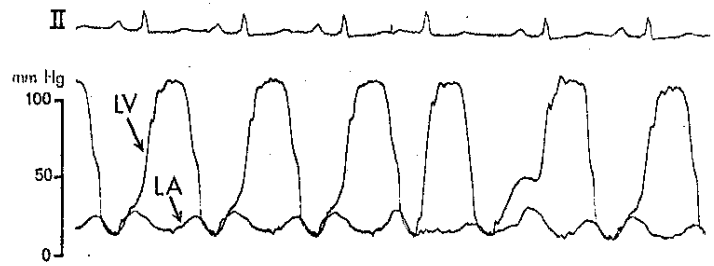


FIG. 6.—Reversed diastolic gradient over the mitral valve in a patient with severe aortic insufficiency. Following the atrial premature beat, the late diastolic pressure difference between left ventricle (*LV*) and left atrium (*LA*) rises to 20 mm Hg.

In patients with constrictive pericarditis or restrictive myocardiopathy, the diagnostic dip-plateau curve can be more easily demonstrated if one registers the ventricular pressure tracing following an induced premature beat.

Brockenbrough *et al.*[73] have pointed out the value of extrasystoles for the diagnosis of idiopathic hypertrophic subaortic stenosis (IHSS). In patients with a fixed form of aortic stenosis, a postextrasystolic beat shows a rise in left ventricular systolic pressure, due to the combined effects of postextrasystolic potentiation[74, 75] and increased ventricular filling, and an increase in pulse pressure in the arteries. In patients with IHSS, however, no change or a decrease of the arterial pulse pressure is seen in the postextrasystolic beat. It has been postulated that in patients with IHSS a more forceful postextrasystolic contraction results in stronger contraction of the obstructing muscle mass and increased narrowing of the left outflow tract, resulting in a decrease in stroke volume. However, this phenomenon may be absent in typical cases of IHSS.[76, 77] Recently, Beck *et al.*[78] have shown that in the "normal" left ventricle no postextrasystolic rise in systolic pressure occurs. If it was present, abnormalities of the left ventricle were found. This rather surprising finding requires further investigation by the induction of timed atrial and ventricular premature beats during atrial pacing at regular rates in normal subjects.

In the right ventricle, Beck and co-workers[78] reported, there was a rise in postextrasystolic pressures both in normal and in abnormal subjects. Exceptions were found in patients with constrictive pericarditis and patients with congenital defects in which the right ventricle ejects against the aortic impedance, as in Fallot's tetralogy. The latter phenomenon has also been observed by Hoffman *et al.*[79] and Childers.[80] They indicated that it can be helpful in differentiating between

pulmonic stenosis, with pressures at systemic level and intact ventricular septum, and Fallot's tetralogy.

In patients with muscular ventricular septal defects[81] and in patients with late systolic mitral insufficiency,[82, 83] the systolic murmur can disappear in the postextrasystolic beat. It seems likely that, in muscular septal defects, postextrasystolic potentiation results in abbreviation or disappearance of the early systolic murmur. In patients with papillary muscle dysfunction, postextrasystolic potentiation might be responsible for better contraction of the papillary muscle and competence of the AV valve. It has also been reported[83] that in patients with late systolic murmurs the murmur may become holosystolic in the postpremature beat. Apparently not only postextrasystolic potentiation, but also volume changes which might result in mitral annular dilatation and insufficiency, play a role. These observations require further investigations by combining electrical stimulation of the heart with the new methods for determining muscle contractility and pump function of the heart.

In patients with recurrent tachycardias, such as atrial tachycardia, atrial flutter and ventricular tachycardia, the hemodynamic effects of the tachycardia, even when not present, can be studied by pacing the heart at identical rates in the cardiac chamber where the tachycardia originates. Atrioventricular tachycardias can be simulated by pacing both the atrium and the ventricle, with an interval between atrial and ventricular pacing as present during the tachycardia. In normal hearts, rapid pacing from right atrium, right ventricle and left ventricle does not seem to influence cardiac dynamics significantly.[84-86] In diseased hearts, however, and following surgical correction of diseased valves, cardiac output may be augmented by pacing the atrium above normal heart rates.[86, 87]

Lown[88] reported on the use of a unipolar single electrical stimulus, given at the junction of the downslope of the T wave with the isoelectric base line, to estimate the degree of digitalization. With advancing degrees of digitalization, trains of extrasystoles and paroxysms of ventricular tachycardia ensued. When concentrations were close to toxic levels, the zone for electrically induced repetitive ventricular responses extended throughout two thirds of the diastolic interval.

As previously outlined, during atrial pacing the effect of drugs on atrioventricular conduction, both by the normal AV conduction system[17] and by anomalous AV bypasses, can be studied. It is also possible to investigate the influence of drugs on intraventricular conduction and their effect on the stimulation threshold and the refractory period of atrial and ventricular muscle.

Potential Applications

The electrocardiographic diagnosis of myocardial infarction can be hampered or made impossible by block in one of the fascicles of the left bundle or complete left bundle branch block. Theoretically, by appropriate stimulation of the left ventricle a normal sequence of activation can be restored, and criteria for electrocardiographic diagnosis without block can be applied. In patients with myocardial infarction of the interventricular septum, it should be possible to outline the area of infarction by stimulating the ventricular septum at different parts and registering intracavitary and precordial electrocardiograms.

The influence of the site of origin of ventricular excitation and the timing of atrial contraction on closure of the AV valves can be studied. Data from patients with pre-excitation[89] and clinical observations on patients with mitral insufficiency suggest that these factors play an important role in the competence of the AV valves.

To get a better idea about the relation between the configuration of the QRS complex and the site of origin of the impulse in the ventricle,[90-92] electrical stimulation at different sites of the heart could be performed. Also, in view of possible surgical intervention in patients with medically refractory ventricular tachycardias, the size of the ventricular area where impulse formation results in identical forms of QRS in 12-lead electrocardiograms should be investigated.

Summary

Electropacing of the heart has not only established its value as a therapeutic measure but has become an important diagnostic tool in cardiology. Present trends suggest that several new clinical applications will be developed in the future.

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