Coupled Pacing and Coupled Pacing with Concealed Conduction

Report of a Case Describing a New Observation

By Lewis B. Sheiner, M.D., and Richard J. Stock, M.D.

SINCE their introduction by Lopez and co-workers, paired electrical stimulation and coupled pacing of the heart have been investigated intensively and have been shown to be useful in slowing the effective mechanical rate of the heart or in causing sustained potentiation of cardiac contraction or for both. A recent symposium on this subject provides an excellent review.2

The techniques, in essence, consist of electrically stimulating the heart shortly after the termination of the effective absolute refractory period of each previous spontaneously or electrically driven beat. These stimuli cause an artificial bigeminal rhythm, the second member of each pair being mechanically ineffective.

In paired stimulation (PS) both the mechanically effective beat and the coupled extrasystole are pacemaker induced, while in coupled pacing (CP) a spontaneous depolarization is permitted to occur and only the extrasystole, triggered by the preceding R wave, is artificially induced.

Each extrasystole produced by either of these methods possesses a refractory period of its own and thus causes a doubling of the myocardial refractory period to other stimuli. This lengthened refractory period can be utilized to control tachycardias.

In addition, the introduction of such extrasystoles causes postextrasystolic potentiation (PESP) of the next mechanically effective beat. By repetitive coupling of extrasystoles to each effective beat, a sustained potentiation of considerable magnitude is achieved.

Atrial PS involves stimulation of the atria. Although an atrial bigeminal rhythm is produced, the second of each pair of depolarizations often fails to traverse the refractory atrioventricular (A-V) node, and ventricular bigemini need not occur. Certain atrial tachycardias can be controlled by this technique, but atrial PS or CP is, in general, not useful in controlling tachycardias that originate in the A-V conduction system or the ventricles.

Ventricular CP or PS involves stimulation of the ventricles. Effective control of atrial conduction system, or ventricular tachycardias can be achieved, but such control is invariably accompanied by the production of mechanical extrasystoles which, ideally, are virtually ineffective.

In certain circumstances the coupled or paired stimulus cannot be made to produce a satisfactorily minimal mechanical contraction and the benefit of ventricular CP or PS is largely vitiated. In other circumstances, the extrasystole, even if mechanically ineffective, might still be undesirable (for example, in ischemic heart disease where the increased myocardial oxygen consumption attendant upon PESP from CP or PS might accentuate the disease).

Thus, a modification of ventricular CP or PS, which would control tachycardias but would eliminate the extrasystoles, might be desirable in some cases. For tachycardias originating in the atria or the A-V conduction system, PS or CP of the conduction system alone without subsequent ventricular myocardial depolarization would accomplish this objective. Such a

From the Department of Medicine, Columbia University, College of Physicians and Surgeons and the Presbyterian Hospital, New York, New York.

Work supported in part by Grant HE-05741-05 of the National Heart Institute, U. S. Public Health Service.
the technique would be dependent on direct stimulation of the conduction system with subsequent bidirectional block of the propagated action potential. This phenomenon has been proposed clinically to occur by Langendorf and Mehlman\textsuperscript{11, 12} in the form of A-V nodal premature systoles blocked in both directions leading to delay or block of the subsequent impulse but has never previously been observed with pacing stimuli, nor has a technique employing the repetitive production of such a phenomenon in a manner analogous to conventional CP or PS been utilized to control tachycardias.

It is the purpose of this paper to report a case in which such a phenomenon was observed and in which such a technique was employed. For reasons to be discussed, we suggest the term "coupled concealed pacing" (CCP) for this technique.

In addition, our patient underwent CP, PS, or CCP almost continuously for 28 days. This is the longest reported use of these techniques and because the long-term effects of their use are unknown, other aspects of the patient's course are also reported.

Report of Case\textsuperscript{*}

A 56-year-old Negro woman was first admitted to the medical service of the Presbyterian Hospital in 1945 at the age of 36 years because of severe anterior chest pain relieved by assuming the sitting position. Systolic and diastolic murmurs were heard at the apex, although there was no previous history to suggest acute rheumatic fever. The electrocardiogram was normal with sinus rhythm and a PR interval of 0.16 sec. Chest x-rays disclosed an increased transverse diameter of the heart and a cardiac configuration suggestive of left atrial enlargement. A diagnosis of rheumatic activity was made.

In 1952, the patient first noticed swelling of the ankles, for which treatment with digitalis was begun and she improved. Atrial fibrillation also began in 1952. An attempt at conversion to sinus rhythm with quinidine was unsuccessful. In 1956, a closed mitral commissurotomy was performed because of increasing right heart failure. At operation the mitral valve admitted only the tip of the index finger. A small regurgitant jet was felt. No improvement followed surgery. Her congestive failure was managed without further admissions over the next 7 years with digitalis, diuretics, and a low-salt diet.

On August 31, 1964, she was admitted to the hospital because of severe right and left heart failure and was found to be in atrial fibrillation with a ventricular rate of 165 per minute. The ventricular rate slowed to 80 per minute with supplemental use of digitalis. Left and right heart catheterization suggested severe mitral stenosis and mild tricuspid insufficiency with left and right heart failure. Open heart surgery was advised, but the patient refused. Ankle edema reappeared and slowly increased over the ensuing months.

On March 1, 1965, she was readmitted with severe left and right heart failure. Orthopnea, peripheral edema, gallop rhythm, a pulsating liver enlarged 9 cm below the right costal margin, engorged neck veins, and hepatojugular reflux were present. Chest x-rays disclosed aneurysmal dilatation of the left atrium, dilated pulmonary arteries, bilateral pleural effusions, and interstitial pulmonary edema. The patient stated that she had consistently taken 0.5 mg of digoxin daily prior to admission. The electrocardiogram revealed atrial fibrillation with a ventricular response ranging from 140 to 180 per minute. She was given an additional 1.5 mg of digoxin orally in divided doses during the first 24 hours of hospitalization. This was followed by the appearance of ventricular premature beats but no slowing of her rapid ventricular rate, which was then about 180 per minute. At the end of the second hospital day she was transferred to a cardiac monitoring and intensive care unit. Digoxin, 0.125 mg, was administered intravenously on both the third and fourth hospital days. Three hours following each dose ventricular premature beats increased in frequency with many runs of repetitive ventricular firing of two beats in duration, without slowing of the rapid ventricular response.

Thyroid function tests were within normal limits.

Attempts to achieve a diuresis with meralluride, chlorothiazide, spironolactone, and ethacrynic acid were ineffective. Cardioversion was attempted with three direct current precordial countershocks of 350, 400, and 400 joules. They failed to change the cardiac rhythm.

By the fifth hospital day (March 6, 1965) the patient was moribund and semicomatose with a ventricular rate of approximately 180 per minute. The decision to undertake coupled pacing was made (see "Observations"). After beginning coupled concealed pacing (CCP), with the reduction in ventricular rate from 180 to 85, the pa-

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\textsuperscript{*}A preliminary report of this case has been published previously as Case 6 in Cranesfield, P. F.: Paired pulse stimulation and postextrasystolic potentiation in the heart. Progr Cardiovase Dis 8: 446, 1966.
tient's sensorium cleared and the blood pressure rose from 90/50 to 120/60 mm Hg. Digitalis was canceled. Responsiveness to diuretics returned and the patient lost 16 pounds during the first 6 days of CCP. The peripheral edema and pleural effusions decreased. The ventricular rate remained in the range of 80 to 90 per minute without digitalis.

On the eighth day of CCP the patient suddenly went into ventricular fibrillation, which was presumably pacemaker-induced. Immediate defibrillation with one counter shock of 200 joules caused reversion to atrial fibrillation. CCP was discontinued. Her ventricular rate returned to 180 per minute and her clinical condition once again seriously deteriorated. Twelve hours after cardiac arrest, CP (CCP was no longer possible) was re-instituted and carried on continuously for the next 17 days. With the reduction in the effective mechanical rate of the ventricles from 180 to 72, the blood pressure which was at a level of 90/50 with pressor amines rose to 130/70 with the pressor amines discontinued. She experienced an additional 9 pound diuresis over the next 16 days, and her condition improved to the point that open heart surgery was again contemplated.

After 17 days of conventional CP, the patient was changed to PS to free coupled pacing equipment for emergency use elsewhere. The patient initially appeared to respond equally well to the paired stimulation technique, but over the next 4 days she became progressively hypotensive and developed uremia. She died April 4, 1965.

At postmortem examination, the heart weighed 580 g and was described as flabby. The mitral valve was stenotic, calcified, and measured 6.5 cm in circumference. The mitral leaflets were virtually immobile. The tricuspid ring was dilated and measured 14.0 cm in circumference. Both atria were massively dilated, and the right ventricle was hypertrophied. Examination of the kidneys revealed congestion of the corticomedullary vessels and early degenerative changes in the proximal tubules.

**Observations**

The pacing equipment* employed permitted introduction of a stimulus, 2.5 msec in duration and from 0 to 25 volts in strength after a delay of 0 to 1,000 msec (adjustable in 1-msec units) from the preceding R wave of the electrocardiogram. The pacing stimulus was delivered through a no. 6 bipolar catheter pacemaker, inserted into the right ventricle under fluoroscopic control through a right jugular vein cutdown. Measurement of the latency between stimulus and the following ventricular depolarization was made from a conventional direct-writing electrocardiogram, operating at a paper speed of 25 mm per second and must be considered approximate. Measurement of the R wave-to-stimulus coupling interval was taken directly from the gauge setting of the pacing equipment. Stimulus strength was read directly from the amplitude dial of the pacemaker, which was calibrated in 1-volt increments.

The following observations characterized the initial attempts at coupled pacing and are summarized in Table 1. Mid-diastolic pacing

<table>
<thead>
<tr>
<th>Line*</th>
<th>Stimulus strength (volts)</th>
<th>Coupling interval (msec)</th>
<th>Pacemaker-induced depolarization</th>
<th>Latency (msec)</th>
<th>QRS rate per min</th>
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<tr>
<td>(a)</td>
<td>7.5-25</td>
<td>140-200</td>
<td>Yes</td>
<td>80</td>
<td>180</td>
</tr>
<tr>
<td>(b)</td>
<td>7.5</td>
<td>60-138</td>
<td>None</td>
<td>None</td>
<td>180</td>
</tr>
<tr>
<td>(c)</td>
<td>25</td>
<td>138</td>
<td>Concealed</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>(d)</td>
<td>25</td>
<td>60</td>
<td>Concealed</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>(e)</td>
<td>25</td>
<td>138</td>
<td>Yes</td>
<td>160-230</td>
<td>160</td>
</tr>
</tbody>
</table>

*(a) Coupled pacing during both diastole and the relative refractory period with threshold and suprathreshold stimuli. There is a short latency, and the coupled beat produces a significant myocardial contraction. (b) Coupled pacing during the effective ventricular refractory period with threshold stimuli. There is no effect on the cardiac mechanism. (c) Coupled concealed pacing during the effective refractory period with suprathreshold stimuli, causing rate slowing. (d) The same as (c) with more premature stimuli producing less rate slowing. (e) The same as (c) with conduction of the stimulus to the ventricle, a prolonged latency, and a significant myocardial contraction.

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*Supplied through the generosity of the American Optical Company, Buffalo, New York.

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*Table 1: Effect of Stimulus Strength and Coupling Interval on QRS Rate*
threshold varied from 2.5 to 5 volts. At stimulus strengths varying from 7.5 to 25 volts a pacemaker-induced ventricular depolarization was produced when the R wave-to-stimulus coupling interval was 140 msec or more. The stimulus to depolarization latency was approximately 80 msec (line a, table 1).

When such stimuli were introduced repetitively after each spontaneously occurring beat, conventional CP was taking place although the overall clinical effect resembled a naturally occurring bigeminal rhythm because the coupled extrasystoles were not mechanically ineffective. With stimulus strength limited to 7.5 v, more premature stimuli (coupling intervals less than 140 msec) failed to produce any noticeable effect on the underlying electrocardiographic events (line b, table 1).

When the stimulus strength was increased to 25 v, stimuli at coupling intervals of 138 msec or less still failed to produce a ventricular depolarization but caused a significant delay of the next spontaneously conducted depolarization and thus a significant prolongation of the cardiac cycle (fig. 1). When such stimuli were repetitively introduced after each spontaneous depolarization in a manner analogous to that of CP, a reduction in ventricular rate resulted without accompanying coupled extrasystolic ventricular depolarizations. This technique we have called "coupled concealed pacing" (see "Discussion").

A graded and direct relationship existed between the length of the coupling interval and the length of the ensuing R-R interval (fig. 2). Thus, the average ventricular rate was slowest (longest cardiac cycles) when the coupling interval was the longest one capable of eliciting this type of response (138 msec; line c, table 1).

Not all 25 v stimuli at coupling intervals of 138 msec or less failed to produce a ventricular response. This effect could be elicited approximately 90% of the time. Ten per cent of the stimuli were conducted to the ventricles and produced a markedly aberrant ventricular complex characterized by a prolonged latency which varied from 160 to 230 msec (fig. 3). These conducted beats were associated with a cardiac contraction detected by palpation and auscultation of the precordium (line e, table 1).

Catheter position was checked frequently while the patient was undergoing CCP, and it can be stated that CCP was possible whenever the catheter tip was within the right ventricle and was not possible whenever the catheter tip was known to be within the right atrium.

At a time when CCP was possible, a single unipolar electrocardiogram taken from each of the pacemaker wires revealed one electrode to be lying against the ventricular myocardium and the other to be free in the right ventricular cavity.

Discussion

This patient underwent 7 days of CCP, 17 days of conventional CP, and 4 days of PS. This total of 28 days represents the longest period of continuous CP or PS reported to

**Figure 1**

Electrocardiogram, lead II. Coupled concealed pacing with a stimulus of 25 v at a coupling interval of 138 msec. The first four QRS complexes were followed by a pacing stimulus, which was then turned off. The ventricular rate rose from 85 to 180 per minute. When pacing was resumed 4 sec later, the ventricular rate again fell to 85 per minute. With the resumption of pacing, the second pacemaker artifact was followed by a conducted extrasystole.
COUPLED PACING

Figure 2
Electrocardiogram, lead II. (Top strip) Atrial fibrillation with a ventricular rate of 170 per minute. (Middle strip) Coupled concealed pacing at 60-msec coupling interval producing ventricular rate slowing to 110 per minute. (Bottom strip) On increasing the coupling interval to 138 msec the ventricular rate slowed to 85 per minute.

date. Although measurements of cardiac output, venous pressure, or direct arterial pressure were not undertaken, it was clear that the patient derived a great deal of benefit from its use, as detailed in the case report.

The primary purpose of this paper, however, is to report the electrophysiological phenomenon which is the basis for the technique which we have termed "coupled concealed pacing." The technique produced a marked slowing of the ventricular rate in atrial fibrillation in response to repetitive intracavitary ventricular pacing stimuli, each coupled to the preceding R wave and occurring during the effective ventricular refractory period. These stimuli elicited neither a mechanical nor a propagated electrical ventricular response (fig. 1).

The observation of cardiac cycle prolongation (and, therefore, of production of a prolonged refractory period in some portion of the conduction system) without electrocardiographically discernible depolarization suggests that concealed conduction was occurring.

The concept of concealed conduction was introduced by Langendorf\(^13\) to describe a local conduction delay or complete failure of propagation of an electrical impulse in the A-V node caused by a preceding atrial impulse which failed to propagate to the ventricles or a ventricular impulse which failed to propagate to the atria. A number of effects in-
cluding some of the mechanisms responsible for the rate reduction obtained with atrial CP or PS can be attributed to concealed A-V nodal conduction; they are discussed and demonstrated in human electrocardiograms in a recent paper by Langendorf and associates.14
In addition, studies on single cardiac fibers have shown that concealed conduction can take place wherever there is a junction of two fibers whose action potentials differ in duration. Such differences do exist at the junction of A-V nodal and bundle of His fibers, bundle of His and bundle-branch fibers, bundle-branch and peripheral Purkinje fibers, and Purkinje fibers and papillary muscle.15, 16 In the dog heart, the duration of refractoriness (action potential) increases progressively at these respective junctions, and in the in situ dog and rabbit heart, Hoffman and associates17 have shown that concealed conduction with failure of propagation of premature impulses can, in fact, occur at such junctions.

We propose, in our patient, that (1) the primary locus of excitation of the coupled stimulus was the bundle of His or a bundle branch; (2) antegrade concealed conduction was occurring with block in the peripheral conduction system (to account for the lack of an observable depolarization); and (3) retrograde concealed conduction was occurring in the A-V node (as evidenced by the cardiac cycle prolongation). These conclusions are supported by the following considerations:

If it is assumed that in this patient conduction time between the bundle of His or bundle branch and the ventricular musculature was somewhat prolonged18, 19 so that the coupled stimulus found the bundle of His or bundle branch excitable, but not the ventricular muscle, the coupled stimulus could have caused a depolarization of the infranodal conduction system with subsequent concealed conduction and block at a more distal site. The presence of occasional conduction of the depolarization to the ventricles (fig. 3) with greatly prolonged latency supports the interpretation that the ventricular myocardium could not be stimulated directly at this time, but only via the conduction system after a delay.

Two other possible sites for the depolarization by the coupled stimulus should be considered, but seem far less likely. It is possible that despite the presence of atrial fibrillation

Figure 3

Electrocardiogram, lead II. Coupled pacing with a stimulus of 25 v at a coupling interval of 138 msec. (Top strip) Coupled concealed pacing and a ventricular rate of 90 per minute. (Bottom strip) the pacing stimulus was conducted to the ventricles with a latency of 200 msec. The coupled beat produced a significant mechanical contraction, and the ventricular rate rose to 130 per minute.
there existed about the atrial margin of the node a sufficient number of adequately repolarized atrial fibers so that the stimulus could have caused depolarization there. The impulse could then have propagated into the node, undergone concealed conduction and block, and could have caused a prolonged A-V nodal refractory period. Because of the chaotic state of the atria in atrial fibrillation, however, one would not expect that a sufficient number of atrial fibers about the node would be available for depolarization at any given instant as predictably as the phenomenon itself was observed.

It is unlikely that the coupled stimulus excited the A-V node directly causing concealed conduction, since A-V nodal depolarization cannot be produced in the experimental animal by direct stimulation under conditions similar to those in our patient. (Personal communication, B. F. Hoffman.)

The depolarization induced in the bundle of His or a bundle branch by the coupled stimulus would be expected to propagate in a retrograde fashion as well as in an antegrade one, and to undergo concealed conduction and block in the A-V node. The next spontaneous ventricular beat would then be delayed and the observable cardiac cycle prolonged because the next supraventricular impulse which would normally have traversed the A-V node would be blocked as a result of refractoriness in the lower part of the node occasioned by this retrograde concealed conduction. The depth of retrograde penetration of the A-V node by the coupled depolarization would vary directly with the length of the coupling interval and would thus account for the observed graded relationship between the length of the R-R interval and the coupling interval.14

Although the electrophysiological phenomenon which underlies CCP appears to depend upon the fundamental electrical properties of the cardiac conduction system, it is possible that the particular combination of refractory periods and conduction times necessary for simultaneous retrograde and antegrade concealed conduction would be met in only a few patients.

CCP as used in this patient carries a greater theoretical risk of ventricular fibrillation than does conventional CP or PS. To achieve maximum reduction of rate by the coupled stimulus, it is caused to fall in or near the vulnerable period for ventricular fibrillation in the cardiac cycle. Since the risk of fibrillation is greater with stronger stimuli, it has been suggested20 that stimulus strength not exceed twice diastolic threshold. The stimulus necessary to produce coupled concealed pacing in our patient was five to 10 times diastolic threshold. In addition, a coupled pacing type of technique as used in this patient, rather than a paired-stimulation one, is particularly hazardous in atrial fibrillation.21

Perhaps because of these increased risks, ventricular fibrillation occurred once in our patient, after 1 week of continuous CCP. It is presumed, however, that the risk of ventricular fibrillation in CCP can be virtually abolished by employing shorter coupling intervals, although the reduction in ventricular rate will be less marked.

**Summary**

In the case reported coupled pacing via an intracardiac catheter electrode was undertaken and continued for 28 days in order to slow the rapid ventricular response in atrial fibrillation, refractory to drug management and cardioversion.

A new phenomenon was observed in which the coupled stimulus caused cardiac cycle prolongation but elicited neither a mechanical nor a propagated electrical ventricular response. Possible mechanisms of this phenomenon are discussed. Stimulation of the bundle of His or a bundle branch with retrograde, concealed conduction in the A-V node and simultaneous antegrade concealed conduction and block are suggested as the most likely.

When this phenomenon was produced after each consecutive spontaneous depolarization, a reduction in ventricular rate resulted without the production of coupled extrasystolic
ventricular depolarizations. This constituted a new coupled pacing technique, termed “coupled concealed pacing.”

The long-term effects of this technique and of conventional coupled pacing and paired stimulation in this patient are also reported.

**Acknowledgment**

The authors are indebted to Drs. Paul Cranefield and Brian Hoffman for their invaluable assistance in the preparation of this manuscript.

**References**

Coupled Pacing and Coupled Pacing with Concealed Conduction: Report of a Case Describing a New Observation

LEWIS B. SHEINER and RICHARD J. STOCK

Circulation. 1966;34:759-766
doi: 10.1161/01.CIR.34.5.759

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