The introduction of electronic (artificial) pacemakers in the management of patients with transient and permanent complete heart block has met with outstanding success. Miniaturization has in turn given rise to small portable units and to smaller implantable ones. With the latter, the stimulus is standardized and in most types the rate (cycle) is preset and nonadjustable. As yet, there seems slight promise of developing, in the immediate future, a miniature implantable unit such that stimulation would occur only in the absence of AV conduction or such that ventricular excitation occurring from the normal mechanism could discharge the unit and modify its cycle.

When AV conduction and an electronic pacemaker function simultaneously, two pacemakers coexist and compete for ventricular control; the situation is akin to the interplay of two physiologic pacemakers within the heart. Usually, in the natural situation, the center in the ventricle does not drive the atrium (retrograde AV block), but it may be discharged or neutralized by excitation of the sinus beat. It is possible for the ventricular focus to be protected from premature discharge ("entrance block") and to show an "exit block," which may apparently be intermittent or have a 2:1 ratio of transmitted to blocked impulses. When two effective pacemakers are present, the phenomena regarded as "capture" and interference dissociation may occur. These have been studied extensively, and the terminology is under repeated review.1-3

There are advantages in drawing an analogy between the ventricular pacing by an electronic unit and that by a parasystolic focus. In the presence (resumption in some cases) of AV conduction, there will be interference dissociation phenomena and a possibility of marked arrhythmia. In this electronic paraventricular "focus," there is obviously no true exit block and there is always an entrance block. In the presence of sinus rhythm, the stimulus from the extrinsic pacemaker, thrown into the ventricle at the set cycle, may thus occur at any instant during the sinus cycle. As the stimulus gives a readily defined spike artifact in the record, the manifest refractory period of the ventricle for the specific stimulus can be mapped. The stimulus may occur during the relative refractory period, when it could theoretically give rise to partial excitation of the ventricle followed by fibrillation, but fortunately there is no known report of the latter having taken place. Although there is a theoretic danger of stimuli from artificial pacemakers operating in cases where AV conduction is present, experience has demonstrated repeatedly that there is no practical danger; and the theoretic one can be ignored as a factor in a decision involving the implantation of an artificial pacemaker.

In the presence of two pacemakers it is possible that the ventricle may be activated by both—with the timing of both being exactly right—and fusion beats occur (fig. 1). These may be recognized by parts of the ventricular complex resembling those of the conducted beat and parts those of the stimulated beat. With nearly identical rates of the intrinsic and extrinsic pacemakers, the possibility of synchronization (or isorhythmic dissociation)4,5 occurring merits continued study and will be commented on further in this communication.
In patients with a spontaneously active ventricular focus (ventricular parasystole) the mechanism may be regarded as a "standby ('rescue') pacemaker" that could prevent cardiac standstill. It is possible occasionally to demonstrate such a phenomenon by vagal inhibition of the sinus mechanism by carotid sinus pressure, when the unaffected ventricular focus continues operating to produce an effective rhythm (fig. 2a). A like phenomenon may be demonstrated with an artificial (extrinsic) pacemaker (fig. 2b).

Of the relatively large number of patients with artificial pacemakers under observation by Linenthal and Zoll, a significant number had restoration of normal mechanism. These authors noted, in the occurrence of interference dissociation, a phenomenon of timing that indicated the presence of a supernormal phase of excitability in the ventricle: subthreshold stimuli from the extrinsic pacemaker, occurring near the end of the T wave of the conducted beats, produced ventricular contractions. By varying the stimulus strength and studying many records, they clearly demonstrated in the human myocardium a supernormal period of excitability following the refractory period. An interesting phenomenon of a slightly varying stimulus-to-QRS latent period was observed, the duration of which was related to the preceding QRS-to-stimulus interval of such beats (that is, how prematurely the stimulus fell on the T wave). They pointed out that the observed phenomena would give support to the hypothesis that the coupling of ventricular premature contractions could be related to firing in the supernormal period of an ordinarily subliminal ventricular focus, in contradistinction to the "re-entry" hypothesis.

As the supernormal phase of excitation has been observed under conditions of tissue injury and the clinical cases wherein AV conduction was facilitated or permitted in this presumed "supernormal" time zone have been ones where heart disease was present, the issue whether there is an actual or demonstrable supernormal phase of excitability following

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**Figure 1**

Electrocardiograms taken on patient with portable external pacemaker. Fusion beats are present at letters F. Interplay between sinus and external electronic pacemakers is evident. Established dominance of electric pacemaker (lower panel) occurred as rate was manually increased (note decreasing intervals between the stimulus artifacts—"S").
Figure 2

a. Leads (V₁ and V₅) recorded simultaneously on patient with ventricular parasystole (no artificial or electric pacemaker present). In upper panel aberrant beats have an exact relationship to one another but not to preceding sinus beat. In lower panel, carotid sinus pressure causes marked sinus slowing but parasystolic focus takes over, forestalling ventricular standstill. b. Electrocardiogram of patient with electronic pacemaker in operation showing effect of carotid sinus pressure in abolishing a chaotic rhythm related to atrial fibrillation, varying AV block, and interference or capture beats following stimuli from electronic pacemaker. With beats of supraventricular origin, QRS configurations indicate delay of left ventricular excitation presumably in left bundle. When beat is initiated by electronic pacemaker, QRS simulates a right bundle defect, which is consistent with stimulus originating at left ventricular electrodes. The QRS duration remains virtually the same (0.16 second). Different configurations of beats, marked (X), with QRS of 0.12 second raise question of whether these are fusion beats or "normalization" of a left bundle-branch conduction defect by carotid sinus stimulation. Data do not resolve problem, but former appears more plausible. Though seen more clearly on
refractoriness in normal myocardium, or in specialized tissue within the heart, cannot be settled by the artificial pacemaker with myocardial electrodes in place. The argument is sound that such a heart is not normal and there is injury from the electrodes. Nevertheless, under the conditions of the preparation with an adequate cardiac mechanism, such a supernormal phase is in operation.

Soloff and Fewell also have reported observations on ventricular excitation from a stimulating electrode with variations in current strength. In the presence of AV conduction and a sinus mechanism, they found that ventricular excitation occurred only if a stimulus fell 0.04 second after the peak of the T wave, the minimal effective current strength being 2.6 milliamperes. When current strength increased to 7 milliamperes, ventricular excitation occurred within 0.02 second after peak of the T wave as well as in the PR segment, the latter causing characteristic fusion beats. A change in the rate of the electric pacemaker from 40 to 120 did not alter the time interval between a spontaneous ventricular complex and one produced by the electric pacemaker. It was noted that not every subthreshold stimulus occurring during the demonstrated supernormal phase produced manifest electrical excitation.

The phenomenon of occasionally conducted sinus beats in what otherwise would be complete heart block has frequently engaged the interest of electrocardiographic investigators since Lewis and Master reported their careful study of the two cases in 1924 and attributed the temporally related permissiveness of the conducted beat to a supernormal phase of excitability. The conducted beats were coupled regularly to the preceding idioventricular beat, and it was assumed that atioventricular conduction occurred because the stimulus reached the area, usually blocked at the specific time, when it had just recovered from a retrograde excitation from the ventricular beat. Lewis and Master reasoned that the area involved was the junctional tissue. They also reported the first case wherein maintenance of AV conduction seemed dependent on a fairly rapid rate. Cases reported by others have illustrated these two mechanisms—namely, occasionally conducted sinus beats coupled with ventricular beats in otherwise complete heart block and heart block exactly related to slowing of the sinus mechanism wherein the explanation has been invoked that a supernormal period of excitability follows the refractory period.

It is of interest that in recent years when one occasionally observed heart block following surgical repair of ventricular septal defects, it was not uncommon to see interference dissociation phenomena, with conducted beats apparently facilitated by exact R-P time relationships, supporting the existence of a supernormal period in these hearts with trauma to the junctional tissue. The acute surgical injury thus produced a phenomenon similar to that sometimes associated with injury related to ischemia of coronary arterial disease.

The data forming the basis of this communication were garnered from a group of patients with implanted electrodes, but this report pertains primarily to studies of three patients.

Case 1. A woman, 63 years of age, had had an episode characteristic of myocardial infarction 4 years prior to admission to the hospital. From that attack of pain she made an uncomplicated recovery, and she had no effort angina. Two weeks prior to admission (April 12, 1962), she began to have orthostatic faintness and frequent episodes of syncope. The electrocardiogram showed persistent complete heart block with a ventricular rate averaging 24 per minute (fig. 3a). Her general health otherwise appeared excellent. After 10 days of observation, permanent electrodes were implanted in the left ventricle and an electronic pacemaker (Electrodyne) was implanted subcuta-

records taken at faster speed, stimulus-to-QRS delay may be noted at (Y), where stimulus occurs early on the descending slope of T wave, at boundary of refractory period. Amplitude of the deflection of stimulus artifact (not well reproduced) is in excess 70 mm, in precordial lead (V).
Figure 3

Case 1. a. Preoperative electrocardiogram shows complete block, slow ventricular rate, and QRS complexes of left bundle-branch-block configuration. b. Postoperative electrocardiograms show dissociation except for occasional conducted sinus beat which is interpolated and has right bundle-branch-block configuration. Subsequent electric pacemaker beat has different and somewhat varying configuration as compared to QRS regularly induced by electric pacemaker. There is probable facilitation of the conducted beat during a supernormal phase. c. Seventy days postoperatively, with ventricles paced by electric unit, lead II provides evidence of anterograde AV conduction once (1) and retrograde conduction three times (1). Retroconducted P wave (P2) falls 0.36 second (crest of P used in measurement) after artifact stimulus and there is constant relationship with a sinus P wave (P1) 0.36 second before stimulus.
neously by Dr. F. H. Ellis, Jr. Convalescence was uncomplicated.

Case 2. A man, 44 years of age, was admitted to the hospital May 9, 1962, because of frequent episodes of unconsciousness (in excess of 15 attacks a day) for 10 days. He had had mild angina and occasional syncope for effort for 8 months. An aortic systolic murmur was present. The electrocardiogram showed, the majority of the time, a sinus mechanism with right bundle-branch block and a PR interval of 0.22 second. Syncopeal episodes with complete heart block continued under a medical program; and, after 2 weeks of observation, "permanent" electrodes were placed in the left ventricle and an electric pacemaker (Medtronic) was implanted subcutaneously by Dr. F. H. Ellis, Jr. The patient had a systolic pressure gradient across the aortic valve of 20 mm. of mercury which was not believed to be of serious hemodynamic significance.

Case 3. A man, 74 years of age, was admitted to the hospital March 27, 1962, because of recurrent "blackouts." He remained free from any attacks while in the hospital and was dismissed on a medical program. Episodes of unconsciousness occurred and he was re-admitted to the hospital on May 21, 1962. A pacemaker system (Electrodyne) was installed by Dr. F. H. Ellis, Jr., on May 25. Recovery was uncomplicated.

The phenomenon of interpolated sinus beats, in a heart that was following regularly an implanted pacemaker (case 1), would appear to have novel interest in a number of respects. In the preoperative period there had been complete heart block (fig. 3a) and the mechanism, continuously monitored and frequently observed, never showed evidence of AV conduction. In the postoperative period, the phenomena of occasional conducted beats suggested the explanation of a supernormal phase of excitability. The permissive-time zone of conduction was very short.

In long electrocardiographic sequences, on three successive days, there were interpolated beats (for example, one every 30 to 200 beats), which study revealed always to be preceded by a P wave occurring just after the apex of a T wave (fig. 3b). All such beats had a P wave following in a time zone 0.36 to 0.40 second after the stimulus artifact, at the onset of the preceding QRS (fig. 4). As only the rounded apex of the P could be used in measurement and P was merged with the T wave, one lead (V1) was used in measurement and an error as large as 0.02 second is acknowledged as probable. The question of whether all P waves falling into this zone were conducted cannot be answered absolutely. The great majority were, but an occasional one at the limits (0.36 and 0.40 second) was not. There were no QRS complexes following P waves when they occurred in any other parts of the cycle.

On June 30, 70 days after operation, the patient’s tracings sent by the home physician showed only occasional (two) conducted sinus beats with 0.42 second elapsing between the stimulus and the conducted P wave. It is again proposed that a supernormal period facilitated the conduction (PR interval 0.20 second). The sequential artificial stimulus fell on the first half of the T wave in a refractory state. In this record the electric pacemaker cycle (0.83 second) had a rate of 72, and the sinus cycle (0.72 to 0.80 second) had an average rate of approximately 77 (at no time did the sinus rate drop below the pacemaker rate to create a situation where synchronization, accrochage, might be expected as a possibility). The tracings on this date, composed

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**Figure 4**

This shows site of P wave in electric pacemaker cycle, which resulted in conducted (and interpolated) beat. QRS of conducted impulse has right bundle-branch-block configuration. St. = stimulus artifact.
Case 2. a. Electrocardiograms second postoperative day show sinus mechanism and electric pacemaker capture. Former has much more rapid rate, 100 as compared to 60. Short refractory periods with markedly aberrant QRS beats are present at A, B, and C, which demonstrate that the earlier the impulse the longer the slight latent period before a ventricular QRS is recorded. P = sinus P waves. St. = stimulus artifact. b. Simultaneous leads I, II, III, and V₂ illustrate interplay of three pacemakers: sinus, node, and ventricular electrodes. Stimulus artifact, clear in all leads in original, has been retouched.
entirely of 200 cm. of lead II revealed five QRS complexes followed by a sharply inverted P wave and in each instance the prior sinus P preceded these QRS complexes by exactly 0.36 second (fig. 3c) (measurement was made from the top of P wave to the stimulus artifact). It is suggested that a sinus impulse conducted to the blocked area allowed retrograde conduction during a supernormal phase of recovery.

Sometime in September a sinus mechanism with normal atrioventricular conduction was reestablished, and the heart did not follow the artificial pacemaker stimulus regularly even when its cycle was more rapid than the sinus cycle. Three electrocardiographic studies, about a week apart, showed a normal PR interval, right bundle-branch block, and occasional premature ventricular beats initiated by artificial pacemaker stimuli. These premature (interference or capture) beats occurred only when the stimulus of the electrodes fell between 0.38 and 0.54 second after the onset of the R wave of a sinus beat; all other artificial stimuli were ineffective. The early boundary was observed more often and could be defined with greater exactitude than the later one. Prudent carotid sinus pressure slowed the heart rate but had no effect on the PR interval or the effectiveness of the external pacemaker. There was thus demonstrated a facilitation of a propagated impulse from the artificial pacemaker stimulus in a select interval of time after the manifest refractory period. The question arose whether to replace the artificial pacemaker and electrodes, which were now malfunctioning. But, as the patient was asymptomatic, such action was deferred.

The other two patients with implanted pacemakers with fixed rates also demonstrated interference phenomena; in one the arrhythmia was at first quite chaotic, and in each there were peculiarly aberrant beats when the stimulus fell in a narrow interval at the end of the absolute refractory period. Measurements of the refractory period made from tracings taken at speeds of either 25 or 50 mm. per second lacked precision because of our inability to measure closer than 0.01 second at best.

In the patient (case 2) with the greater irregularity (fig. 5a), the pacemaker rate was relatively slow (60 per minute). In an effort to slow the sinus rate, reserpine (0.25 mg. four times daily) was given. The sinus rate slowed and the refractory period lengthened greatly; however, when reserpine had been stopped for 1 week, no significant reduction of the refractory period occurred (table 1).

On July 6, 44 days after operation, this patient showed an interplay between three pacemakers: the sinus, the AV node, and the extrinsic electric one. With the patient at rest, the predominant rhythm was nodal with an RP period of 0.20 second. Occasional capture by the electric pacemaker occurred when the stimulus had "drifted through" the QRS-T period to an adequate degree. The nodal rate barely exceeded the electric-pacemaker rate, allowing long sequences of nodal beats to be followed, after the interference or capture beat, by long sequences of electric-pacemaker beats. When the latter occurred, the QRS complex changed from that of right bundle-branch block to one simulating that of left bundle-branch block. The ventricular beats paced by the electric pacemaker were regularly followed by atrial beats with an RP period of 0.32 second. The first capture (or

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for clarity in lead III. At the beginning there is sinus rhythm which phases into nodal rhythm with transient AV dissociation, then the ventricular pacemaker takes over at A, the ventricular refractory period being manifest at 0.36 second as the stimulus artifact has "drifted through" previous T waves. There is apparent retrograde conduction to atrium. In middle of lower panel a fusion beat is suggested, then QRS complexes are same as when there was a sinus rhythm, thus a nodal rhythm of RP type, and stimulus artifact begins again to drift through refractory QRS and early T period. There is near identity of three rates, electric pacemaker at 100, sinus averaging 96, and node 102. The RP period changes from 0.28 to 0.12 as complexes change from those of electric pacemaker to nodal.

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interference) beat from the electric pacemaker had an RP period of 0.40 second. The RP periods were measured in a nontraditional way, from the onset of the QRS to the peak of the P wave, as the onset of the P wave could not be identified within the T wave. As control of the ventricle was about to pass from the electric pacemaker to the nodal, the RP period decreased to 0.22 second (fig. 5b) before there was any change in the QRS configuration, indicating that the node and atria were not following or dominated by the electric pacemaker but, perhaps only for a short time, were "pulled in" to an identical oscillation (acerochage). The domination of the ventricle by the nodal center was observed during the phase when it replaced the sinus mechanism; when there was a spurious shortening of the PR interval for a few beats when the atria followed the sinus rhythm and the ventricles (dissociated) followed the nodal (left upper panel fig. 5b).

The records from case 3 on the second and third postoperative days (fig. 6) showed the interplay of two pacemakers: the normal sinus and the artificial electric ones. The manifest refractory period was 0.28 second and the period of relative refractoriness, as defined, between 0.28 and 0.32 second. In this patient digitalis administration was apparently effective in improving the rhythm.

Records on this patient (case 3) 4 to 5 weeks later showed a regular ventricular rate following the electric pacemaker. On the first of these occasions, P waves were not identified; and, on the second, there clearly appeared to be P waves in the ST periods. Whether this represented synchronization is uncertain; while it is certainly suggested, simple retrograde propagation seems more likely.

In this patient (case 3) atrial and ventricular (electrically driven) rates in the early records were so nearly identical that an environment favorable to synchronization was present as soon as the sinus rate dropped below the rate of the ventricular pacing. At this early time, the slower sinus rate was not observed to pick up or "pull in" and synchronize (phénomène d'acerochage).

In two patients (cases 2 and 3), delay between the stimulus artifact and the first recognizable potential of the earliest conducted, more grossly aberrant, QRS complex is particularly noteworthy. The earlier the stimulus in this presumed semirefractory period, the longer was the stimulus artifact-QRS interval (fig. 6).

**Discussion**

The apparent emergence of a supernormal phase permissive of AV conduction and the narrow time band of such permissiveness in

### Table 1

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*Cyc...
ELECTRONIC PACEMAKER AND VENTRICULAR PARASYSTOLE

Figure 6
Case 3. Electrocardiograms second postoperative day showing interplay of two rhythm centers of nearly same frequency. At top, coding represents sinus mechanism when letters “P” are connected and pacemaker dominance when letters “St.” are connected. Short refractory period of ventricles with almost stereotyped early aberrant QRS and short latency before response is to be noted above arrows. When electric pacemaker is dominant at right-hand side of each panel it might be conjectural whether the atria were transiently synchronized but this is not supported in strength in other parts of the tracings.

Case 1 would seem related to the preceding artificially stimulated beat, but the method of its operation is conjectural. In previous spontaneous cases of interference with block, one did not know the site of the ventricular focus; in the present instance it is known. It is also known that the left bundle branch was utilized in the conducted beat. If the case were one of bilateral bundle-branch block (and the very slow spontaneous ventricular rates are in accord), it would be possible that conduction facilitation was over the left branch (the conducted beats showing a QRS consistent with right bundle-branch block).

There are disadvantages of any “entrance” of interpolated sinus beats, namely, the inadequacy of ventricular filling for the sequential beat and the possibility of the artificial stimulus occurring at a time of vulner-
if the first from R to P (conducted) equals approximately 0.36 second and the second from P to R (conducted beat) equals approximately 0.20 second, then the third part, R (conducted) to stimulus, would be approximately 0.19 second allowing such a stimulus to fall in the period usually regarded as the vulnerable one (fig. 4). In this situation it is evident that the PR of the conducted interpolated beat would be a critical determinant of where the conducted QRS would occur between the pacemaker stimuli and, as a corollary, where the artificial stimulus would fall on the Q-TU period of the conducted beat.

Eight weeks postoperatively, one patient (case 2) showed rather frequent interpolated nodal (RP-type) beats occurring at various periods after the T wave of the regular electrically driven beat.

Surmises arising from assumed refractory periods have been pointed out by Hoffman and Cranefield\(^{11}\) to be rather meaningless as the junctional or specialized tissues have refractory periods which are markedly rate dependent. It is noteworthy how constant was the manifest refractory period, from day to day, after the initial few days (table 1).

The prolongation of the refractory period concomitant with reserpine administration suggests that there was a causal relationship consequent to depletion of sympathomimetic amines from the myocardium. Such a possibility would gain some credence from the report of Innes and co-workers,\(^{12}\) who demonstrated an increase in the functional refractory period of atrioventricular conduction in the heart-lung preparation of the dog by some of the rauwolfia alkaloids. Whether this would be the same with direct ventricular stimulation is unknown. After the patient had been off reserpine for a week, no shortening of the refractory period occurred, and the drug when repeated at a dose of 1 mg. daily for 4 days did not appreciably lengthen it. Thus, with the doses used, the data do not establish a specific reserpine effect on the refractory period in the specific situation studied.

Retrograde conduction to the atrium from the paced ventricle was observed in cases 2 and 3. As such is not an infrequent occurrence with ventricular premature contractions, when the AV conduction pathway is open, it might have been expected. The question is conjectural whether there is true conduction over a normal pathway retrograde to the atrium or the nodal cycle becomes synchronized with the ventricle by an even more complex association (as theorized by analogy to coupled oscillators by Grant).\(^{15}\)

An occasional patient is seen with bradycardia related to permanent sinus arrest, or destruction, and a slow nodal mechanism of an RP type. There being no evidence of AV block, such a case would have interest for two reasons at least—(1) one could expect good results from implantation of electrodes in the atria, and (2) if the electrodes were implanted in the ventricle, one would have a “natural preparation” akin to that made by Rosenblueth\(^{14}\) and by Moe and associates\(^{15}\) to study the refractory period of cardiac tissues, wherein by increasing the rate of the stimulus there were obtained reciprocal or echo beats.

**Summary**

The artificial pacemaker has been compared to a physiologic ventricular parasystolic focus. In hearts being driven by a pacemaker, in the absence of atrioventricular (AV) block, capture (interference) phenomena are constantly seen. While variations in QRS complexes have been observed when the external pacemaker stimulus occurs early in the T-wave period of a sinus conducted beat, no sequence of aberrant beats has been observed. One patient showed occasional sinus beats interpolated between ventricular beats arising from the artificial pacemaker, and these occurred at a very narrow time band suggesting that AV conduction was permitted by phenomenon of a supernormal phase. At a later date this patient showed also retrograde conduction believed related to a supernormal phase during recovery of junctional tissue penetrated by an impulse entering from above, though the impulse itself was blocked.
Records of two patients are used to illustrate grossly aberrant QRS complexes produced by the stimulus of the electric pacemaker when this fell in the semirefractory period. Noteworthy was the presence of a latent period before potentials of the propagated impulse were recorded, there being evident stimulus-to-QRS delays. The situation wherein the rhythm is most chaotic is that where AV block is absent, the sinus rate is fast, and the electric pacemaker rate is relatively slow. In two patients, retrograde activation of the atria occurred as a stable mechanism. In one patient, nodal rhythm of the RP type occurred, and sequences of the records suggested that the AV node might have become synchronized with the extrinsic pacemaker cycle. In this last instance three independent centers of effective impulse formation coexisted, the sinus node, AV node, and stimulating electrodes of the electronic pacemaker.

A marked increase in the refractory period of the ventricle, as measured by its response to the set stimulus of the electric pacemaker delivered at varying instants with respect to the sinus mechanism, occurred in one case within a few days. The possibility that serpentine therapy contributed to this change is possible but has not been established, for the effective refractory period, as measured, later remained constant over a period of many weeks.

References

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