

The Wedensky Effect in the Human Heart*

AGUSTIN CASTELLANOS, JR., LOUIS LEMBERG, DOUGLAS JOHNSON,
AND BAROUH V. BERKOVITS

From the Department of Medicine, Section of Cardiology, University of Miami School of Medicine, and the Division of Electrophysiology, Jackson Memorial Hospital, Miami, Florida, U.S.A.

Artificial electrical stimulation has proved to be of great value in understanding electrophysiological events occurring in the human heart (Linenthal and Zoll, 1962; Gerbaux and Lenègre, 1964). Until the advent of the various types of pacemakers, progress in the clinical arrhythmias had been made either by interpolation from animal experiments or by careful analysis of certain tracings in which the various parameters could not be controlled at will (Katz and Pick, 1956). Several authors have shown the presence of a supernormal phase (Linenthal and Zoll, 1962; Walker, Elkins, and Wood, 1964) and of a vulnerable phase (Castellanos, Lemberg, and Gosselin, 1965a; Castellanos, *et al.*, 1965b) under controlled conditions in man. The significance of these findings relative to the genesis of naturally occurring arrhythmias was stressed in the corresponding articles. One mechanism that has been implicated in the origin of arrhythmias is the Wedensky effect. This was first described in neuromuscular studies by Wedensky as a prolonged lowered threshold of excitability induced by a strong stimulus (1886). Its occurrence in the human heart has not been adequately proved. The introduction of the Wedensky effect in clinical cardiology is credited to Scherf *et al.* (Scherf and Schott, 1953; Scherf, Blumenfeld, and Yildiz, 1962). They reported that under certain conditions one impulse could trigger a second impulse without invoking vulnerability or supernormality. These authors considered that such a phenomenon, and not a re-entry mechanism, could adequately explain the origin of extrasystoles occurring late in the cardiac cycle. Scherf and Schott (1953) believed that extrasystoles were due primarily to a disturbance of cardiac excitability, not of conductivity.

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In view of its potential clinical significance, we decided to determine, by means of intracardiac electrical stimulation, whether the Wedensky effect could occur in the human heart.

SUBJECTS AND METHODS

Seven patients with atherosclerotic heart disease and complete heart block with slow idioventricular rhythms were studied. Intermittent episodes of Adams-Stokes seizures and/or some degree of heart failure were present in all subjects. A specially constructed tetrapolar catheter electrode was used in 4 cases.* The length of this catheter was 125 cm. with four platinum electrodes, one at the distal portion. The distance between the second and third electrodes was 2.5 cm. and that between the third and fourth was 1 cm. All electrodes were completely insulated from each other. The terminals of the distal set were connected to a commercial pacemaker.† The terminals of the proximal set were connected to a second artificial pacemaker.† The stimuli provided by this second instrument were synchronized to the R wave produced by the driving pacemaker and delivered after every third or fourth driving beat. Special precautions were taken so as to ensure that all electrical instruments connected to the patient were at the same ground potential in respect to the power line (Starmer, Whalen, and McIntosh, 1964). In 3 patients a single unit for paired and coupled electrical stimulation was used.† This instrument was isolated from the ground by means of a magnetically shielded isolation transformer. The stimulators (of the type used clinically) delivered underdamped, 2.5 msec. pulses, with voltages ranging between 0 and 25 for interval use.

The catheter tip was passed into the right pulmonary artery so that the stimulating electrodes were located within the right ventricular cavity. The threshold stimulus or energy required to produce a ventricular response when falling outside the refractory period of the

*U.S. Catheter and Instrument Corporation, White Plains, New York.

† American Optical Company, Chelsea, Massachusetts.

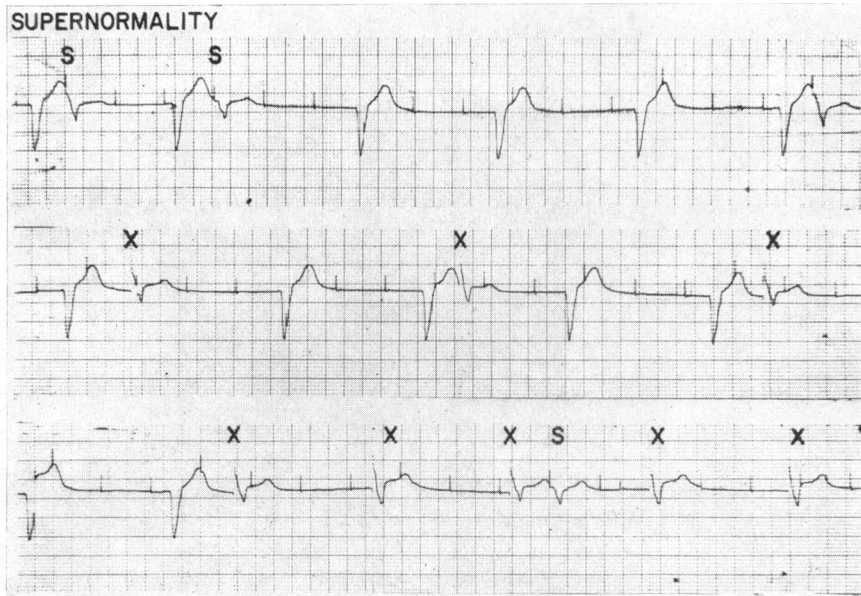


FIG. 1.—Supernormal phase of excitability exposed by intracardiac stimulation in a patient with apparent complete heart block. The top strip, obtained during idioventricular beating, shows ventricular responses following only those stimulus artefacts occurring during the final portion of the T wave or slightly after. Stimuli of high intensity (X) were applied in the middle strip. No after-effects were noted. The lower strip shows how subthreshold responses become suprathreshold during the supernormal phase (terminal portions of the T wave) of the “strong” stimuli. This is not a true Wedensky effect.

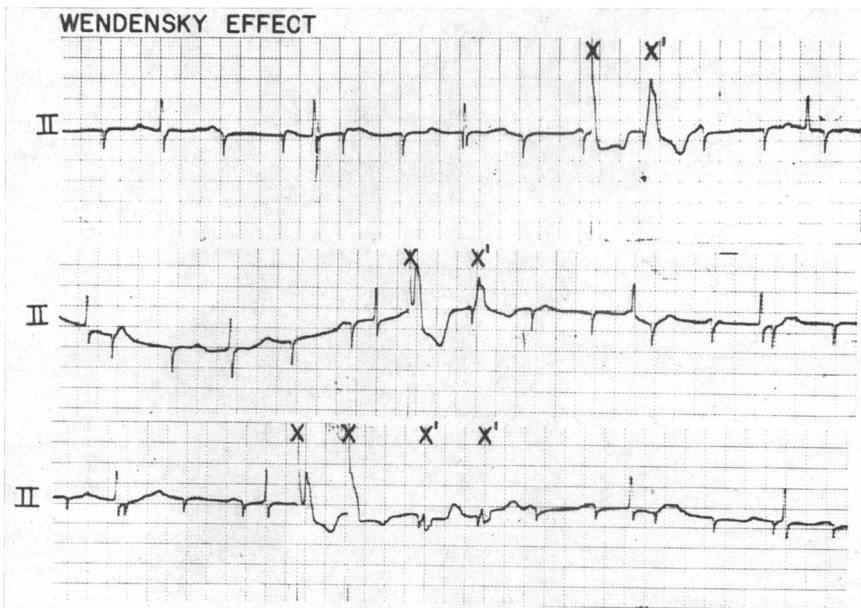


FIG. 2.—Wedensky effect in the human heart. The upward deflections are the spontaneous QRS complexes, presumably of A-V nodal origin. The downward-directed spikes are the subthreshold stimulus artefacts from the artificial pacemaker. Note that stimuli that are seven times above threshold (marked with an X) and that do not occur in the vulnerable phase of natural beats, are able to evoke responses (X') from previously subthreshold stimuli. These responses occur well after the end of the T wave of the strong shock, hence ruling out vulnerability and supernormality as the underlying mechanisms.

spontaneous beat was determined. The intensity of the driving pacemaker was adjusted at will. The distance between the driving and testing stimuli was progressively shortened by adjusting the delay time, so as to map out ventricular excitability. The supernormal phase was studied by scanning the cycle, with the intensity of the test pacemaker being slightly below threshold.

A careful search for the Wedensky effect was made in all cases. During idioventricular beating the intensity of one pacemaker was kept slightly below threshold. Once this procedure had been accomplished, a "strong" synchronized or unsynchronized stimulus from the second artificial pacemaker, with an intensity of about 15 to 20 times threshold, was administered intermittently. Its effects on subsequent, previously subthreshold, impulses were noted. In one patient, once supernormality was detected, a synchronized stimulus was placed late in the R-R cycle, and then the intensity of the driving impulse suddenly increased.

RESULTS

The duration of the refractory periods and of the vulnerable phase will be reported elsewhere (Castellanos *et al.*, 1965b). A supernormal phase ranging from 160 to 195 msec. was observed in 4

patients during artificial pacing, but in only 3 of these during idioventricular beating. In 2 patients subthreshold responses could attain threshold values only when they fell in the supernormal phase of the contraction elicited by the "strong" shock (80 to 140 msec. after the peak of the T wave) (Fig. 1). The latter were delivered after the end of the vulnerable phase of natural beats. A true Wedensky effect was found twice: in one, the previously subthreshold impulses produced a response 160 to 260 msec. after the end of the T wave of the strong shock (Fig. 2); in another patient it was noted that subthreshold impulses, which occurred well after the end of supernormality (260 msec. after the end of the T wave), could elicit a response when the intensity of the driving stimulus was increased from 2 times above threshold to 15 times above threshold (Fig. 3). Such an increase of the intensity of driving pulses determined that all stimuli of similar subthreshold intensity (which previously did not provoke a response) were now able to do so, at any position of the cycle after the end of the refractory period.

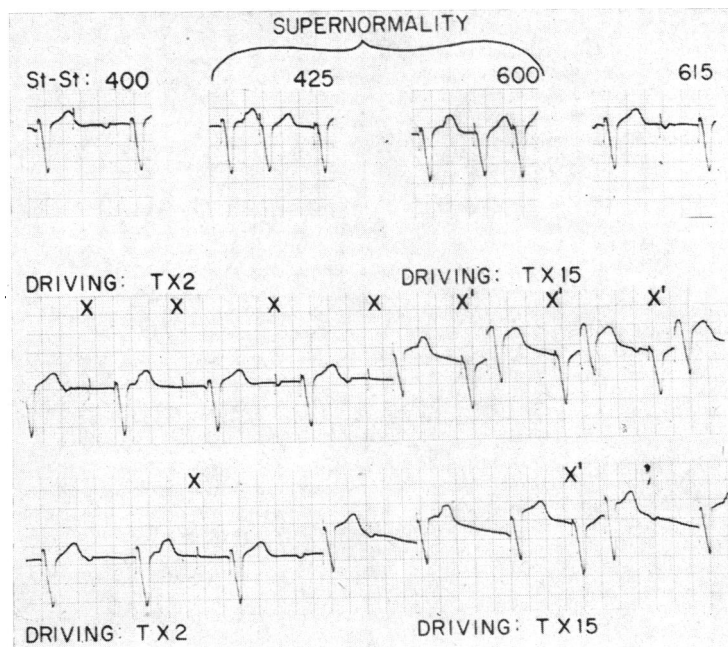


FIG. 3.—The supernormal phase of excitability is shown in the top strip. Note that impulses falling in the refractory period, as well as those occurring 615 msec. after the driving stimulus, do not produce a response. The responses occur only during the supernormal phase, that is, from 425 to 600 msec. after the driving stimulus. Hence, the duration of this phase of excitability is 175 msec. The lower two strips show the Wedensky effect in the human heart. Subthreshold impulses occurring well after the end of supernormality (740 msec. from the driving stimulus) do not produce a response at X, when the intensity of the driving impulses is only twice threshold. However, they are able to become suprathreshold toward the right of the strips when the intensity of the driving impulse is increased to 15 times above threshold.

COMMENTS

Arrhythmias induced iatrogenically by means of electronic instruments have provided pertinent evidence relative to the mechanism of naturally-occurring disorders of rhythm (Linenthal and Zoll, 1962; Gerbaux and Lenègre, 1964; Castellanos *et al.*, 1965a, b). For instance, pacemaker-induced repetitive firing can be compared with a similar phenomenon occurring when a spontaneous premature ventricular contraction falls before completion of the T wave (R on T phenomenon) (Smirk and Palmer, 1960; Tavel and Fisch, 1964.)

The existence of a supernormal phase of excitability in the human heart can adequately account for some of the ectopic ventricular contractions encountered clinically (Linenthal and Zoll, 1962). In these instances it is believed that a cell or group of cells under the influence of injury, ischæmia, or drugs can develop subthreshold activity that can only manifest itself during the periods of lowered threshold following a previous contraction (Scherf and Schott, 1953). This mechanism could explain extrasystoles with a short coupling. On the other hand, parasystoles would occur if the local responses were able to attain suprathreshold intensity by themselves, without requiring a lowering of threshold induced by a previous beat. Hence, parasystole appears in any moment of the heart cycle outside the refractory period. It is obvious, however, that supernormality cannot be invoked in the genesis of coupled extrasystoles occurring late in the cycle. The prolonged lowering of threshold (exceeding the supernormal phase) induced by a strong stimulus (Wedensky effect) could well explain the mechanism of those extrasystoles without implying the existence of a re-entry phenomenon.

Working with a nerve-muscle preparation, Wedensky (1886) found that when the nerve was stimulated by subthreshold stimuli, the muscle failed to respond. Yet, when one strong induction shock was applied to the nerve so that a muscular contraction occurred, the previously subthreshold responses were then able to elicit responses. Mogendowitsch (1930) was able to precipitate the Wedensky effect when crystals of sodium chloride, instead of faradic stimulation, were applied to the nerve. This author believed that subthreshold impulses, formed in the area of application of the crystals, became suprathreshold after application of the shock.

Samojloff (1930) considered that the activating effect of the induction shock could last as long as 0.5 sec., hence ruling out supernormality as the underlying mechanism. Goldenberg and Rothberger (1933) were the first to apply Wedensky's explanation to the origin of cardiac arrhythmias.

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Working with excised Purkinje fibres of the dog, they found that iatrogenically-induced subthreshold responses were able to become suprathreshold after a strong induction shock. The first half of Fig. 5 of Goldenberg and Rothberger is very similar to Fig. 2 of this communication. This is to be expected since our technique is very similar to theirs.

The phenomenon under consideration was found in 2 of the 7 patients with advanced A-V block in whom the study was performed under controlled conditions. It should be emphasized that the results of studying ventricular excitability by means of transvenous electrical stimulation should be interpreted with caution when working with sub (near) threshold stimuli. Because the electrode is not attached to the ventricular muscle it moves freely in the ventricular cavity. Therefore the possibility must be considered that conversion of subthreshold to suprathreshold stimuli could be due to a closer contact of the catheter with the endocardial surface induced by the stronger shock. However, animal experiments performed by Goldenberg and Rothberger (1933) who used a similar technique to the one presented in this communication but with the recording electrodes in contact with the Purkinje fibres under study, and the fact that certain phases of excitability, such as the supernormal period, can be detected with exteriorized intramyocardial electrodes (Linenthal and Zoll, 1962), seem to indicate that the Wedensky effect is a true property of the heart (appearing in certain conditions) and does not represent a technical artefact (Scherf and Schott, 1953).

CLINICAL IMPLICATIONS

The possibility that this phenomenon could explain clinically-occurring arrhythmias has been further studied in our department by analysing the duration of the asystole interval, or the recovery of idioventricular automaticity, after a period of rapid electrical stimulation in patients with complete A-V block. Under normal conditions, the depression of impulse formation produced by the artificial stimulation provokes a transient ventricular asystole after cessation of stimulation (Fig. 4, top strip). This pause, which is dependent on the rate of the idioventricular rhythm, is always longer than the basic R-R distance (De Saint Pierre *et al.*, 1963). The asystole interval was seen to be shortened after digitalization in 1 of 3 patients thus studied (Fig. 4, bottom strip). This means that active impulse formation, not seen during idioventricular beating, could very likely have been induced by the artificial current.

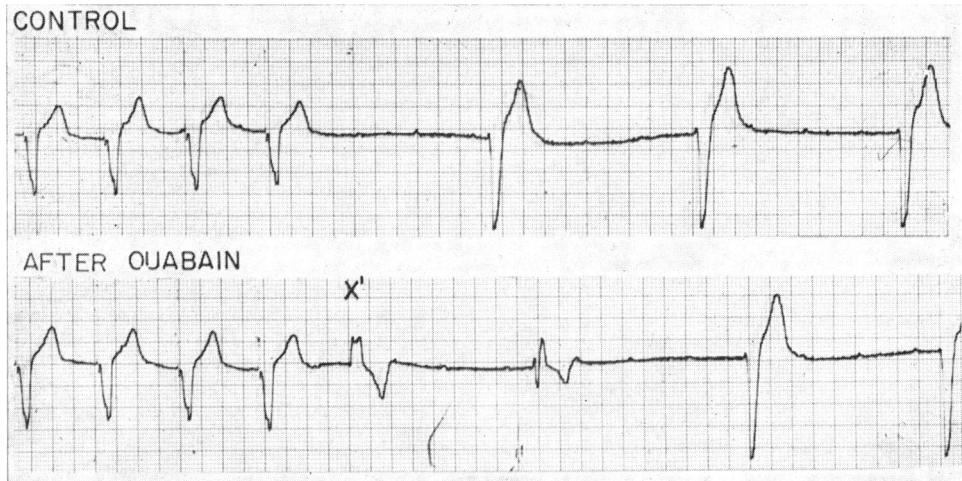


FIG. 4.—Recovery of idioventricular automaticity after artificial electrical stimulation in a patient with complete A-V block. The upper strip shows the expected asystole after cessation of stimulation. The lower strip, obtained after digitalization, shows the shortening of the asystole interval by the appearance of a “premature” ventricular contraction (X').

Animal experiments performed by Scherf (1926, 1930) and Scherf *et al.* (1954) seem to favour this hypothesis. Ventricular ectopic beats were induced by a single electrical or mechanical impulse in dogs that were given large amounts of quinidine, especially when the animals were also treated with minimal doses of barium or aconitine. The abnormal beats were believed to arise in the stimulated area. Rubio and Rosenblueth (1955) produced a slow A-V nodal rhythm by ligating the sinus node of several dogs. Thereafter they observed that some impulses arising in the ventricles and travelling in a V-A direction were able to produce active A-V nodal responses. In their studies on the production of ventricular fibrillation by direct currents, Wégria and Wiggers (1940) stressed that shocks of short duration produced responses that could not be differentiated from those of induction shocks or condenser discharges. Currents of longer duration could, however, stimulate at both the opening and the closing. Additional secondary responses, considered to be after-effects of either opening or closing, were occasionally seen in some of their illustrations. Wégria and Wiggers (1940) believed that spontaneous premature beats, which tended to augment with increasing current duration, were due to after-effects of direct currents. In fact, they emphasized that there were two types of electrically-induced ventricular fibrillation. In the systolic type either the opening or closing fell during the vulnerable phase of the normal beats. On the other hand, diastolic fibrillation occurred after the end-systole of the normal beats. One of the mechanisms by

which this type of fibrillation could occur was seen whenever closure fell in the absolute refractory period (producing no response), and opening early in diastole yielding the expected QRS complex. Fibrillation would ensue if a second, *spontaneous* response (an after-effect of opening) fell in the vulnerable period of the former.

In our own laboratory, experiments on dogs revealed that during the early stages of progressive intravenous digitalization, very strong shocks (20 times above threshold) were able to produce secondary responses occurring late in the cycle (Fig. 5). The latter depended on the coupling of the stimulus artefact to the preceding (spontaneous) R wave. The after-effects occurred when the stimulus artefact fell in the responsive part of systole and in early diastole (Fig. 6). Hence, vulnerability could be ruled out. Electrical stimulation was able to bring out the secondary responses at a time when they did not appear spontaneously (electrically exposed digitalis effects). With added progressive increments of ouabain, ventricular beats and ventricular tachycardia appeared spontaneously. We believe that “strong” shocks produce a prolonged lowering of the threshold well exceeding the supernormal phase. As increasing amounts of cardiac glycosides have a tendency to enhance automaticity by augmenting the slope of diastolic depolarization during phase 4 (Vassalle, Greenspan, and Hoffman, 1963), the sudden and marked, electrically induced, lowered threshold can account for the unexpected initiation of propagated responses at a time when automatic beats do not appear

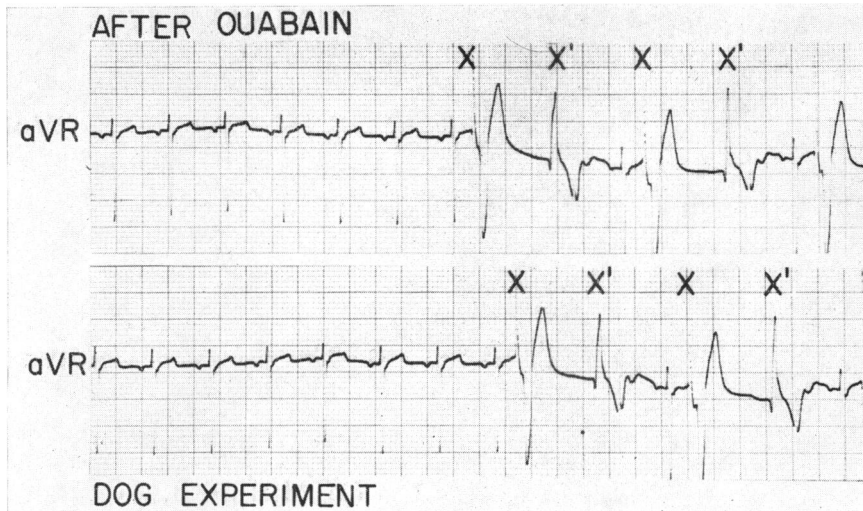


FIG. 5.—Ectopic beats appearing late in the cycle, induced by electrical stimulation, in a digitalized dog. Artificial stimuli occurring during the early part of the cycle are followed by the expected ventricular response as well as by a second response which occurs immediately before the P wave. Note that spontaneous extrasystoles were not seen in the absence of electrical stimulation (electrically exposed digitalis effects).

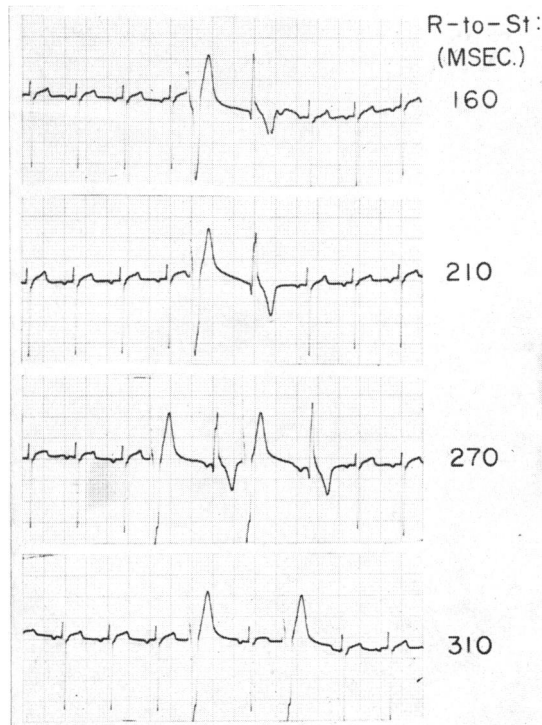


FIG. 6.—Isolated pacemaker stimuli produce a second spontaneous contraction late in the cycle. Note that the phenomenon occurs when the artificial stimulus is delivered outside the peak of the T wave, thus excluding vulnerability as the underlying mechanism.

spontaneously. Further administration of ouabain accentuates diastolic depolarization until spontaneous multifocal pacemaker activity is initiated.

The striking resemblance between animal experiments and iatrogenic events occurring in man can be seen in Fig. 7. The electrocardiograms were obtained from a patient with atherosclerotic heart disease and second degree A-V block due to digitalis. Intracardiac pacing was considered because of intermittent complete A-V block and Adams-Stokes attacks. Initiation of pacing (Fig. 7) consistently provoked multifocal ventricular arrhythmias which were not seen in the control tracing. It is believed that digitalis effects were unmasked by artificial stimuli. The secondary responses to the first artificial stimuli could not be attributed to the presence of a vulnerable or supernormal phase.

The results of the present study reinforce Scherf and Schott's (1953) hypothesis that a disturbance of excitability, rather than a disturbance of conductivity (re-entry phenomenon), best explains the mechanism of ventricular extrasystoles occurring late in the cycle.

SUMMARY

Intracardiac electrical stimulation was used in 7 patients with apparent complete heart block, for the purpose of determining whether the Wedensky effect could occur in the human heart. A specially constructed quadripolar catheter connected to two separate pacemakers was employed four times. A

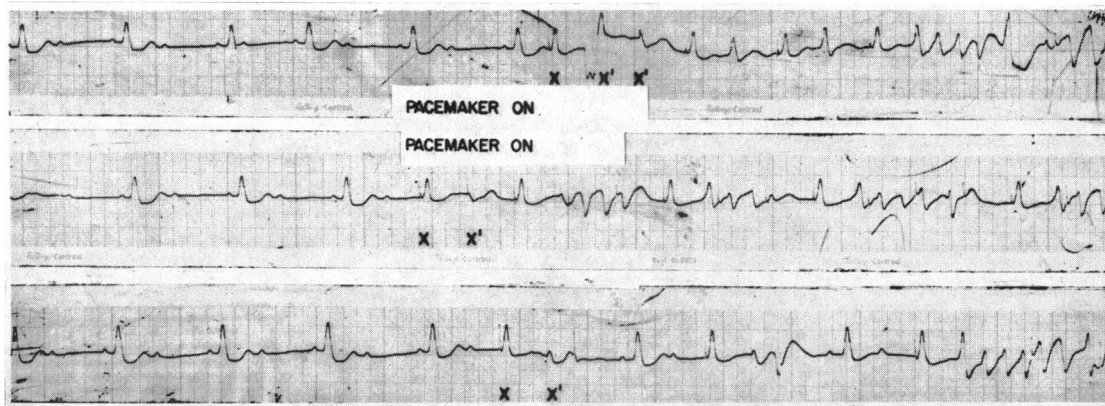


FIG. 7.—Appearance of multifocal ventricular beats after initiation of intracardiac pacing in a patient with arteriosclerotic heart disease and second-degree, as well as with intermittent complete, A-V block due to digitalis excess. The left portions of the three strips show predominant 2:1 A-V block. Extrasystoles are absent. Initiation of artificial pacemaking at X immediately induces the expected QRS complex. In addition, a second response, occurring at X' is followed by short runs of ventricular tachycardia. The events occurring here are very similar to those occurring in the experiments illustrated in Fig. 5.

synchronized unit for paired and coupled electrical stimulation was used in the rest of the cases.

Ventricular excitability was therefore studied in man under controlled conditions. A supernormal phase was detected four times. The Wedensky phenomenon, studied by a modification of Goldenberg and Rothberger's technique, was seen in two patients. The analysis of the pause that follows cessation of rapid electrical stimulation after digitalization, experiments performed in dogs, and occasional clinical cases with A-V block and varying degrees of digitalis effect, seem to corroborate the hypothesis of other investigators that electrical stimuli can produce, under certain conditions, secondary (late) responses in which the mechanism of vulnerability and supernormality cannot be invoked. Hence, a disturbance or excitability rather than an abnormality in conductivity (re-entry phenomenon) can best explain the origin of ventricular extrasystoles occurring late in the cycle.

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