Re-entrant Ventricular Arrhythmias in the Late Myocardial Infarction Period

3. Manifest and Concealed Extrasystolic Grouping

NABIL EL-SHERIF, M.D., RALPH LAZZARA, M.D., RONALD R. HOPE, M.D., AND BENJAMIN J. SCHERLAG, PH.D.

SUMMARY Re-entrant beats with regular extrasystolic grouping were seen in 44% of dogs 3–7 days following ligation of the anterior descending coronary artery. Utilizing direct recordings of the re-entrant pathway (RP) from the epicardial surface of the infarction zone, we found extrasystolic grouping to be based on characteristic tachycardia-dependent conduction disorders in a potentially RP. Trigeminy and quadrigeminy were related, respectively, to a 3:2 and 4:3 Wenckebach-like conduction cycle in a RP. However, quadrigeminy could also be due to an underlying bigeminal rhythm with concealment of alternate re-entrant beats, i.e., concealed bigeminy. A bigeminal rhythm was the result of a 2:1 conduction pattern in a re-entrant pathway with a sufficient degree of conduction delay during the conducted beat of the 2:1 cycle to result in re-entry. A trigeminal or quadrigeminal rhythm could change to a bigeminal rhythm on critical shortening of the cardiac cycle. Fixed and variable coupling were related, respectively, to stable and changing conduction pattern in a re-entrant pathway. On the other hand, extrasystolic grouping could be concealed due to either block in the re-entrant pathway or entrainment in a small area of the closely bordering normal zone.

THE TERM EXTRASYSTOLIC GROUPING as utilized in this study refers to extrasystoles that occur in repetitive patterns during a basic cardiac rhythm, e.g., the sinus rhythm. In this case, one (or more) extrasystoles may follow every sinus beat (bigeminy), every other sinus beat (trigeminy), every third sinus beat (quadrigeminy), etc. A majority of these extrasystoles show relatively fixed coupling. However, variable coupling, as well as other characteristic variations in coupling, e.g., gradual lengthening of coupling of successive beats may also be seen.

The mechanism of extrasystolic grouping is probably the one aspect of disorders of the cardiac rhythm that captured the interest of a majority of clinical electrocardiographers and experimental electrophysiologists alike. Three possible mechanisms have been proposed in the literature to explain extrasystolic grouping:4–6 1) a parasystolic mechanism; 2) extrasystolic focal activity by which a center is triggered by the preceding impulse to fire one or more extra beats; 3) a re-entrant mechanism. Over the years, the attempts to solve the controversy over the mechanism of extrasystoles centered essentially around two means: 1) commonly, deductive analysis of clinical records and, 2) less commonly, experimental designs in which extrasystoles were created by various artificial means.

Of the three postulated mechanisms for extrasystolic grouping, the parasystolic mechanism was disputed as a plausible explanation of a majority of clinical extrasystoles despite earlier claims to the contrary. Since in both remaining mechanisms of triggered focal activity and re-entry, the extrasystole depends basically on a preceding cardiac impulse, both mechanisms may assume similar characteristics in clinical records. Even, in certain experimental designs, the differentiation between the two mechanisms may be extremely difficult probably because of limitations of the recording techniques.

Recently, we have shown that dogs studied 3–7 days following a major transmural myocardial infarction, represent a remarkably stable model for re-entrant ventricular arrhythmias and one in which systematic electrophysiologic and pharmacologic studies could be conducted. In these dogs re-entry was demonstrated through direct recording of the electrical activity of the re-entrant pathway(s). Continuous electrical activity originating from the infarction zone was shown regularly and predictably to bridge the diastolic interval between the re-entrant beat and the preceding impulse, as well as between consecutive re-entrant beats. In previous reports, we analyzed the conduction characteristics in the infarction zone as well as examined in detail the electrophysiologic mechanisms for initiation and termination of re-entrant ventricular arrhythmias. In these experiments, periods of extrasystolic grouping were frequently demonstrated. The ability to record directly the electrical activity of the re-entrant pathway offered a unique opportunity for a close scrutiny of the mechanism of re-entrant beats with extrasystolic grouping.

Material and Methods

The results included in this study were obtained from 50 adult mongrel dogs that were studied 3–7 days following ligation of the left anterior descending artery just distal to the anterior septal branch. All dogs showed evidence of a transmural infarction that involved the subepicardial layer of muscle. In these dogs recordings were obtained from the epicardial surface of the infarction zone (IZ) and adjacent normal zone (NZ) utilizing a specially designed composite electrode as well as multiple close bipolar electrodes. Details of the surgical procedure and the recording techniques are described elsewhere. In addition to the electrograms, two standard electrocardiographic (ECG) leads were recorded, specifically leads II and aVR. All records were obtained on a multichannel oscilloscopic photographic recorder (E for M, DR-8) at paper speeds of 25–200 mm/sec. Electrocardiograms were recorded with the preamplifier set for frequen-
cies of 0.1–200 cycles/sec and bipolar electrograms were recorded with filter frequencies of either 40–200 cycles/sec or 12–200 cycles/sec. Measurements were accurate within ±3 msec at a paper speed of 200 mm/sec.

Recordings were obtained during spontaneous sinus rhythm, vagal-induced cardiac slowing, and atrial, His bundle or ventricular pacing, as well as premature stimulation. Details of the pacing procedures and procedures to slow the heart rate are described elsewhere. The onset and termination of ventricular arrhythmias were monitored in the ECG leads as well as the corresponding changes in the NZ and NZ electrograms. In this study periods of extrasystolic grouping as defined in the introduction were closely analyzed.

**Results**

Out of 50 experiments that showed re-entrant ventricular arrhythmias, 22 experiments showed periods of re-entrant beats with extrasystolic grouping. In 14 experiments, a critical fast heart rate (atrial pacing at 170–225 beats/min) was necessary for the occurrence of extrasystolic grouping. In the remaining eight experiments, extrasystolic grouping was seen during spontaneous sinus rhythm and/or relatively slow heart rates (80–170 beats/min). In both groups of experiments, however, the extrasystolic grouping was always related to characteristic patterns of tachycardia-dependent conduction disorder in a potentially re-entrant pathway (RP) in the infarction zone (IZ).

**Extrasystolic Grouping at Relatively Fast Heart Rates**

Figure 1 was taken from an experiment that showed no re-entrant ventricular beats during spontaneous sinus rhythm. Ventricular re-entry could be produced either following a premature beat with a critical range of coupling intervals or during a critical range of rapid heart rates induced by atrial pacing. Tracings from top to bottom represent standard leads II and aVR, an electrode catheter recording of the His bundle electrogram (Hbeg) and composite electrode recordings from the infarction zone (IZeg) and adjacent normal zone (NZeg). Panel A illustrates two sinus beats at a cycle length of 420 msec followed by an atrial premature impulse (PI) with a coupling interval of 270 msec that resulted in a re-entrant ventricular beat. During sinus rhythm the NZeg was a relatively sharp multiphasic deflection with a duration approximately equal to the QRS duration in surface leads. On the other hand, the IZeg consisted of a multiphasic deflection lasting longer than the QRS in surface leads. Thus, the second part of the IZeg, which was represented by a distinct relatively sharp deflection (marked by an arrow), was inscribed in the early part of diastole during the ST-T segment. As was explained elsewhere, in all experiments it was observed that the first part of the composite IZeg (the first 20–30 msec) remained essentially unchanged at all cardiac cycles provided that there was no change in the QRS configuration in surface leads. This part represented activation of relatively normal myocardium. The later part of the IZeg showed characteristic changes on shortening of the cardiac cycle length. This part reflected delayed activation in the IZ and is referred to in this study as the IZ potential. Exact repetition of the same configuration of the IZ potential in consecutive sinus beats (marked by arrows in panel A) was taken to represent a 1:1 conduction pattern in the IZ.

During the atrial premature beat, the IZ potential was replaced by a continuous series of low amplitude asynchronous spikes ending with a relatively sharp deflection (marked by an arrow) bridging the entire diastolic interval between the atrial premature beat and the re-entrant ventricular beat. The continuous asynchronous spikes recorded by the IZeg reflected the electrical activity of the entire re-entrant pathway in the IZ. This electrical activity was not recorded in the NZeg obtained from the closely adjacent NZ. The late sharp spike that was recorded immediately preceding the inscription of the ventricular deflection of the re-entrant beat in both the surface ECG and NZeg probably reflected the electrical activity of the terminal part of the re-entrant pathway. This deflection can serve as a marker of conduction in the re-entrant pathway.

Figure 1, panels B and C, was recorded during atrial pac-
ing at a cycle length of 300–310 msec. This cardiac cycle length was associated with characteristic changes in the IZ potential and the occurrence of re-entrant beats with extrasystolic grouping (trigeminal and quadrigeminal rhythms in panels B and C respectively). Analysis of the IZeg shows that the trigeminal rhythm in panel B was related to a 3:2 Wenckebach-like conduction pattern of the IZ potential. The opening beat of the Wenckebach cycle was associated with a more synchronized sharp IZ potential. During the second beat of a 3:2 Wenckebach-like cycle, the IZ potential was replaced by a continuous series of asynchronous spikes ending with a relatively sharp spike immediately preceding the re-entrant beat which replaced the third beat of the Wenckebach cycle. The ventricular deflection of the re-entrant beat in the IZeg was approximately equal to the QRS duration in surface leads and was not followed by an IZ potential. The sinus beat that immediately followed the re-entrant beat showed once more a relatively synchronized IZ potential and represented the opening beat of the next 3:2 Wenckebach-like cycle. Regular repetition of these cycles caused a trigeminal rhythm with an almost constant coupling interval of 260–265 msec. On the other hand, panel C shows that the quadrigeminal rhythm was related to a 4:3 Wenckebach-like cycle of the IZ potential. In this case, in contrast to the trigeminal rhythm in panel B, the second beat of the cycle showed a limited degree of fractionation and delay of the IZ potential that extended for only the first half of the diastolic interval. During the third beat of the cycle the IZ potential showed further delay in diastole that ended in a re-entrant beat which replaced the fourth beat of a 4:3 Wenckebach-like cycle.

Figure 2 was obtained from the same experiment shown in figure 1. Figure 2, panel A, was recorded during a regular trigeminal rhythm as shown in figure 1, panel B. The first part of the record shows a 3:2 Wenckebach-like cycle of the IZ potential that ended in a re-entrant ventricular beat. This was followed by five sinus beats before the next re-entrant beat near the end of the record. Analysis of the IZeg shows that two successive 3:2 Wenckebach-like cycles of the IZ potential occurred between the two consecutive manifest re-entrant beats. During the second beat of the first 3:2 Wenckebach-like cycle the IZ potential showed lesser degree of conduction delay compared to the same beat during manifest trigeminal rhythm (both the first and last 3:2 Wenckebach-like cycles in the record). This relatively limited degree of delay of the IZ potential probably did not provide sufficient time for recovery of the terminal part of the re-entrant pathway for manifest re-entry to take place. Figure 2, panel A, thus illustrates an example of concealed trigeminy. On the other hand, the standard ECG leads in figure 2, panel B, also illustrate the presence of five sinus beats between two consecutive manifest re-entrant beats, the same as in panel A. Analysis of the IZeg, however, shows that this was not an example of concealed trigeminy as shown in panel A but was rather due to a longer 6:5 Wenckebach-like cycle of the IZ potential.

Figure 3 was obtained from the same experiment shown in figures 1 and 2. The first part of panel A was obtained from a record showing a quadrigeminal rhythm during regular atrial pacing at a cycle length of 300 msec. The quadrigeminal rhythm in this record differed from the one shown in figure 1, panel C, in having two consecutive re-entrant beats instead of one at the end of the 4:3 Wenckebach-like cycle of the IZ potential. Atrial pacing was abruptly terminated in the last part of the record during the second beat of a potential 4:3 Wenckebach-like cycle. With resumption of the relatively slower sinus rhythm there was immediate improvement of conduction in the IZ as revealed in the IZeg by the inscription of a more synchronized sharp IZ potential close to the major ventricular deflection (marked by arrows). The re-entrant ventricular arrhythmia was terminated at the same time that IZ potential improved.

Figure 3, panel B, shows that the re-entrant ventricular arrhythmia also disappeared at a faster pacing rate. The first
part of the record illustrates atrial pacing at a cycle length of 235 msec. The surface ECG leads showed no evidence of ventricular re-entry. The IZeg, however, showed a 2:1 block of the IZ potential. During the conducted beat of a 2:1 cycle there was marked delay of the IZ potential with the terminal sharp spike of the fractionated IZ potential (marked by an arrow) superimposed on the initial ventricular deflection of the next beat. Analysis of the NZeg reveals evidence that the delayed electrical activity in the re-entrant pathway did in fact re-excite the immediately adjacent NZ as revealed by the change in configuration of the NZeg (marked X). This represents an example of concealed bigeminy. The difference between the concealed bigeminy in figure 3, panel B, and the concealed trigeminy in figure 2, panel A, is in the level at which concealment took place. In figure 2, panel A, concealment probably occurred within the re-entrant pathway in the IZ. Re-entry was confined, in figure 3 panel B, to the NZ immediately adjacent to the IZ. The fact that there was no detectable change in the QRS configuration in figure 3, panel B, suggests that the area of the NZ re-excited by the delayed electrical activity in the IZ was relatively small and did not influence the basic activation pattern of the whole ventricle.

The later part of figure 3, panel B, illustrates the marked effect slight changes in the cardiac cycle length had on conduction in the IZ. Slight lengthening of the cardiac cycle from 235 to 255 msec in the middle of the record was immediately followed by a lesser degree of conduction delay of the IZ potential compared to that during the 2:1 conduction sequence. The next cardiac cycle of 295 msec was followed by marked conduction delay of the IZ potential which resulted in a ventricular fusion beat with a coupling interval of 300 msec. Thus slowing of the atrial pacing rate changed the 2:1 conduction pattern of the IZ potential to a 3:2 Wenckebach-like cycle. At the end of panel B, constant atrial pacing at a cycle length of 310 msec resulted in a 4:3 Wenckebach-like cycle that ended in a re-entrant beat with a coupling interval of 255 msec, similar to that during regular quadrigeminy in figure 1, panel C. Thus, while relatively constant cardiac cycles may be associated with re-entrant beats with almost fixed coupling intervals (fig. 1), alterations in the cardiac cycle can result in significant variation of the coupling interval of re-entrant beats.

Figure 4 was taken from the same experiment shown in figures 1–3. The figure shows an interesting pattern of conduction in the re-entrant pathway and helps to illustrate the effect of the re-entrant beat on conduction in the IZ of the following sinus impulse. Panels A and B represent a continuous tracing and illustrate a regular trigeminal rhythm (beats 1 to 7) with gradual increment of the coupling interval of the re-entrant beats. This resulted in a successively greater degree of ventricular fusion with more activation of the ventricles by the supraventricular impulse. The barely perceptible changes in the QRS configuration of beat 7 compared to a sinus beat hardly betray the occurrence of partial re-entry. However, the NZeg of this beat clearly shows that the NZ closely adjacent to the IZ was re-excited by the delayed electrical activity in the IZ was relatively small and did not influence the basic activation pattern of the whole ventricle.

Panel A shows that the IZ potential of the sinus beat that immediately followed a re-entrant beat (i.e., the opening beat of the following 3:2 Wenckebach-like cycle) was closely coupled to the major ventricular deflection. The first sinus beat in panel B which followed the fifth re-entrant beat showed a slightly more separation of the IZ potential from the major ventricular deflection denoting more conduction delay in the IZ. This became more noticeable in the sinus beat that followed the sixth re-entrant beat. Finally, the sinus beat that followed the seventh re-entrant beat revealed
significant conduction delay of the IZ potential, however, not sufficient to re-excite the NZ. This was followed by block of the IZ potential of the next sinus beat with subsequent resumption of a 3:2 Wenckebach-like conduction cycle ending with the re-entrant beat #8. This beat was again followed by a concealed 2:1 conduction pattern in the IZ.

Thus a regular trigeminal rhythm due to successive 3:2 Wenckebach-like cycles showing a cycle-to-cycle increment of conduction delay in the re-entrant pathway was finally interrupted by alternating 2:1, 3:2, 2:1 cycles respectively. Refractoriness of the terminal part of the re-entrant pathway in the wake of the markedly delayed conduction of the seventh and eighth re-entrant beats probably explains why the immediately following sinus beats showed significant conduction delay in the same pathway, thus setting the stage for the following 2:1 cycle.

**Extrasystolic Grouping during Spontaneous Sinus Rhythm and/or Relatively Slow Heart Rates**

Figure 5 was obtained from an experiment that showed re-entrant ventricular beats with extrasystolic grouping during spontaneous sinus rhythm (usually a heart rate of 120–170 beats/min in the anesthetized dog). Both sinus slowing and sinus tachycardia resulted in the disappearance of the arrhythmia. Figure 5, panel A, was recorded during vagal-induced sinus slowing. The IZ potential (marked by an arrow) was regularly inscribed following every sinus beat in a 1:1 conduction pattern. Figure 5, panel B, shows that release of vagal stimulation with gradual acceleration of the heart rate was associated with a beat-to-beat increased fractionation and delay of the IZ potential (marked by arrows). The last sinus beat was followed by a markedly delayed IZ potential that resulted in a re-entrant ventricular rhythm. The fractionated IZ potential bridged the entire diastolic interval between the sinus and re-entrant beats. Figure 5, panel C, shows that when the basic heart rate was kept constant at 133–136 beats/min (cycle length of 445–450 sec) a regular quadrigeminal rhythm developed. The latter was related to the regular succession of a 4:3 Wenckebach-like conduction pattern of the IZ potential.

Figures 6 and 7 were obtained from the same experiment shown in figure 5 and represent recordings during spontaneous sinus tachycardia. Panels A and B in figure 6 and
Figure 6. Panels A and B were obtained from the same experiment shown in figure 5 during spontaneous sinus tachycardia. Both panels show essentially a bigeminal rhythm due to a 2:1 conduction pattern of the IZ potential resulting in marked fractionation and delay of the potential following every sinus beat. The three successive sinus beats in panel A which may have been interpreted as concealed bigeminy from the surface ECG were in fact due to a 4:3 Wenckebach-like conduction cycle of the IZ potential. On the other hand, the five successive sinus beats in panel B were indeed a manifestation of concealed bigeminy.

Figure 7. Recordings obtained from the same experiment shown in figure 5 and 6 during a slightly faster sinus rate (a cycle length of 375 msec). The record illustrates a bigeminal rhythm at the beginning and the end of the record with a period of five consecutive sinus beats in between. In contrast to panel A, the IZeg reveals that this arrangement was indeed an example of concealed bigeminy. The IZeg shows that every sinus beat was regularly followed by a fractionated and delayed IZ potential in a regular 2:1 conduction sequence. However, only following the first, seventh, and ninth cardiac (sinus) beats was the fractionated IZ potential markedly delayed resulting in a ventricular re-entrant beat. By contrast, there was relatively less degree of delay of the IZ potential that followed the third and fifth cardiac (sinus) beats which failed to result in re-entry. This would suggest failure of conduction in the terminal part of the re-entrant pathway.

Figure 6, panel B, was recorded during a slightly faster sinus rate (a cycle length of 385 msec). The record illustrates a bigeminal rhythm with every sinus beat being regularly followed by a very late coupled ventricular beat resulting in varying degrees of ventricular fusion except in the middle of the record where three sinus beats occurred in a row. The latter arrangement may superficially suggest an example of concealed bigeminy. The IZeg shows that the bigeminal rhythm was related to a 2:1 conduction pattern of the IZ potential whereby each sinus beat was followed by a fractionated and delayed IZ potential that extended up to the ventricular beat that showed very late but fixed coupling. However, what simulated a concealed bigeminy in the middle of the record was in fact due to a period of 4:3 Wenckebach-like conduction pattern of the IZ potential.

Panels A to C in figure 7 were arranged to show the effect of spontaneous acceleration of the sinus rate. Figure 6, panel A, was recorded during a sinus cycle length of 385 msec. The standard ECG leads show essentially a bigeminal rhythm with every sinus beat being regularly followed by a very late coupled ventricular beat resulting in varying degrees of ventricular fusion except in the middle of the record where three sinus beats occurred in a row. The latter arrangement may superficially suggest an example of concealed bigeminy. The IZeg shows that the bigeminal rhythm was related to a 2:1 conduction pattern of the IZ potential whereby each sinus beat was followed by a fractionated and delayed IZ potential that extended up to the ventricular beat that showed very late but fixed coupling. However, what simulated a concealed bigeminy in the middle of the record was in fact due to a period of 4:3 Wenckebach-like conduction pattern of the IZ potential.

Figure 6, panel B, was recorded during a slightly faster sinus rate (a cycle length of 375 msec). The record illustrates a bigeminal rhythm at the beginning and the end of the record with a period of five consecutive sinus beats in between. In contrast to panel A, the IZeg reveals that this arrangement was indeed an example of concealed bigeminy. The IZeg shows that every sinus beat was regularly followed by a fractionated and delayed IZ potential in a regular 2:1 conduction sequence. However, only following the first, seventh, and ninth cardiac (sinus) beats was the fractionated IZ potential markedly delayed resulting in a ventricular re-entrant beat. By contrast, there was relatively less degree of delay of the IZ potential that followed the third and fifth cardiac (sinus) beats which failed to result in re-entry. This would suggest failure of conduction in the terminal part of the re-entrant pathway.

Figure 7, panel A, was recorded during a sinus cycle length of 365 msec and shows a regular bigeminal rhythm related to a 2:1 conduction pattern of the IZ potential. The
IZeg reveals that the configuration of the terminal part of the fractionated IZ potential was approximately the same in all beats. On the other hand, the configuration of the first half of the fractionated IZ potential (marked by an arrow) appears to differ from beat-to-beat sometimes in an alternating fashion. Because the composite electrode averaged the recordings of multiple close bipolar sites, this observation may suggest that part of the recorded fractionated IZ potential may represent electrical activity in area(s) in the IZ that may not participate in the re-entrant pathway. This functional dissociation of conduction in the IZ will be further emphasized in a later figure.

Figure 7, panel B, shows that further acceleration of the sinus rate resulted in a bigeminal rhythm with a greater degree of ventricular fusion. This is explained by the fact that the re-entrant pathway conduction time closely approached the cardiac cycle length which resulted in more activation of the ventricles by the conducted supraventricular impulse. This explanation is further confirmed in figure 7, panel C, which shows that on slight further abbreviation of the sinus cycle length manifest ventricular bigeminy disappeared. Analysis of IZeg showed that there was still a 2:1 conduction pattern of the fractionated IZ potential, the latter extended up to the ventricular deflection of the following sinus beat. However, the very terminal part of the IZ potential that was consistently inscribed before each manifest re-entrant beat had disappeared. This would strongly suggest that the very terminal part of the re-entrant pathway was regularly pre-excited by the conducted supraventricular impulse approaching from the NZ.

It is important to stress the difference in the mechanism of concealed bigeminy shown in figure 6, panel B, and figure 7, panel C. Thus, in the former situation, the re-entrant impulse probably failed to conduct in the terminal part of a potentially re-entrant pathway. By contrast, in figure 7, panel C, there was probably no failure of propagation of the re-entrant impulse but rather a pre-activation of the terminal part of the re-entrant pathway by the following sinus beat when the basic sinus cycle length was shorter than the re-entrant pathway conduction time.

**Functional Dissociation of Conduction in the Ischemic Zone during Extrasystolic Grouping**

Analysis of the composite electrode recording from the IZ during the bigeminal rhythm in figure 7, panel A, provided suggestive evidence of functional dissociation of conduction in the IZ. In over 50% of the experiments, however, clear evidence of dissociated conduction in the IZ was revealed by analysis of simultaneous recording of the composite and one or more of the close bipolar electrodes.

This is illustrated in figure 8. Panel A shows simultaneous recordings from the IZ by a composite electrode (IZeg-Comp) and a close bipolar electrode (IZeg-Bip) obtained during spontaneous sinus rhythm at a cycle length of 490 msec. Both the IZeg (Comp) and the IZeg (Bip) revealed a 1:1 conduction pattern of a slightly delayed but relatively sharp IZ potential (marked by arrows). Panel B shows that atrial pacing (PI) at a cycle length of 420 msec resulted in a regular trigeminal rhythm with two successive re-entrant beats following every second sinus beat. The first re-entrant beat was clearly premature and had a fixed coupling interval of 320 msec (100 msec shorter than the basic cardiac cycle length of 420 msec). On the other hand the second re-entrant beat followed the first one after a cycle length of 440 msec, slightly longer than the basic sinus cycle length. The IZeg (Comp) reveals that the trigeminal rhythm was related to a 3:2 Wenckebach-like conduction pattern of the IZ potential with the first re-entrant beat replacing the blocked beat of the 3:2 cycle. A continuous series of low amplitude multiple asynchronous spikes bridged the entire diastolic interval between the sinus and first re-entrant beats as well as between the two successive re-entrant beats with a large amplitude relatively sharp component of the IZ potential inscribed in the later part of the diastolic interval (marked by straight arrows). Analysis of the IZeg (Bip) revealed that its IZ potential (marked by curved arrows) maintained a 1:1 conduction pattern during the 3:2 Wenckebach-like cycle depicted by the IZeg (Comp) while the IZ potential failed to be inscribed during both re-entrant beats. This strongly suggests that the close bipolar electrode was reflecting the electrical activity of a localized functionally dissociated area of the IZ that clearly did not participate in the 3:2 Wenckebach-like cycle in the re-entrant pathway depicted by the IZeg (Comp). The latter electrogram, in contrast to the close bipolar recording, averaged the recordings from multiple close bipolar sites.

The functional dissociation of conduction in the IZ is further emphasized in figure 9, panel A, obtained from the same experiment shown in figure 8 during atrial pacing at a slightly faster rate. The standard ECG lead illustrates two re-entrant beats at the beginning and end of the record with four successive sinus beats in between, an arrangement that does not conform with either concealed bigeminy or concealed trigeminy. Analysis of the IZeg (Comp), however, readily provides the electrophysiologic mechanism by showing the succession of a 2:1 block and a 3:2 Wenckebach-like

**Figure 8.** Recordings obtained from a different experiment showing functional dissociation of conduction in the infarction zone (IZ) during regular extrasystolic grouping as revealed by analysis of simultaneous recordings from the IZ by a composite electrode (IZeg-Comp) and a close bipolar electrode (IZeg-Bip).
cycle. On the other hand, IZeg (Bip) revealed a regular 1:1 conduction pattern of its IZ potential (marked by curved arrows), in a clear illustration of the functional dissociation of conduction in the IZ. Alternation of a 2:1 block and 3:2 Wenckebach-like cycles was not an uncommon finding in this study and could result in a host of arrangements of manifest re-entrant beats.

Figure 9, panel A, illustrates that the two re-entrant beats had variable coupling intervals with the second late-coupled beat showing some degree of ventricular fusion. This contrasted with the fixed coupling during the trigeminal rhythm shown in figure 8. The variable coupling in figure 9, panel A, can probably be explained on the basis of the relatively complex conduction sequence that separated the two re-entrant beats. On the other hand, the fixed coupling in figure 8 was due to the presence of a relatively stable simple succession of 3:2 Wenckebach-like cycles. This clearly illustrates that in the same experiment re-entrant beats with both fixed and variable coupling could be seen related, respectively, to a relatively stable pattern or variable conduction patterns in the re-entrant pathway. A similar observation was shown in figure 3, panel B.

Effect of Preceding Cycle Length on Refractoriness in Ischemic Myocardium

Conduction in the IZ was consistently tachycardia dependent. There was, however, evidence that refractoriness in ischemic myocardium varied according to the length of the preceding cardiac cycle, with an increase of refractoriness following a long preceding cycle. This is illustrated in figure 9, panel B, which was obtained from the same experiment shown in figure 8 and figure 9, panel A. The record shows atrial pacing at a basic cycle length of 375–380 msec. The IZeg (Comp) reveals that the two successive re-entrant beats in the middle of the record were related to a long Wenckebach-like conduction cycle in the re-entrant pathway with a beat-to-beat increment of the fractionation and delay of the IZ potential (marked by straight arrows).

Analysis of the IZ potential in the IZeg (Bip), (marked by curved arrows) revealed a 1:1 conduction pattern during the initial long Wenckebach cycle. The IZ potential was blocked following the two re-entrant beats. A compensatory pause of 540 msec followed the second re-entrant beat and the IZ potential was again inscribed close to the major ventricular deflection of the sinus beat after the pause. However, in the next sinus beat (marked X), the IZ potential failed to be inscribed. This sinus beat had a cycle length of 380 msec, 5 msec longer than consecutive sinus cycles at the beginning of the record during which the IZ potential was showing a 1:1 conduction pattern. The sinus beat was, however, preceded by the long compensatory cycle of 540 msec that followed the second re-entrant beat. This would suggest that the long preceding cycle was followed by an increase of the refractory period of that area of the IZ represented by the IZ potential in the IZeg (Bip) resulting in block of conduction of the cardiac impulse at a cycle length that was previously associated with a 1:1 conduction pattern. On the other hand, the long compensatory pause did not result in block in the re-entrant pathway depicted by the IZeg (Comp). The latter, instead, showed conduction delay and manifest re-entry in a 3:2 Wenckebach-like conduction pattern similar to that shown in panel A. This suggests that the degree of lengthening of refractoriness following a long preceding cycle may not be regularly distributed in different areas of the IZ.

In the above experiment, similar changes in refractoriness and conduction of the IZ potential in the IZeg (Bip) could be also demonstrated during regular atrial pacing at cycle lengths between 330–380 msec when a single long pause of 500–540 msec was introduced by interruption of one pacing cycle. Also in this experiment, as in several other experiments in which both composite and close bipolar recordings were analyzed, the effect of a long preceding cycle length on refractoriness and conduction in the IZ could be better demonstrated by changes in the IZ potential in the close bipolar rather than the composite electrode recording. This could be probably explained by the fact that the close bipolar recording reflected the electrical activity of a rather
localized area of the IZ while the composite electrode averaged the recordings of multiple close bipolar sites. With the frequent demonstration of functional dissociation of conduction in the IZ with different areas of the IZ possibly responding differently to changes in refractoriness and conduction in relation to the preceding cycle length, an averaged recording of these areas, understandably, may not yield consistent results.

Discussion
Pathophysiology of Re-entry with Manifest and Concealed Extrasystolic Grouping
This study has shown that extrasystolic grouping of re-entrant beats is based on characteristic tachycardia-dependent conduction disorders in a potentially re-entrant pathway in the IZ. At a critical narrow range of cardiac cycle lengths, a potentially re-entrant pathway can conduct in a Wenckebach-like pattern characterized by a beat-to-beat increment in conduction delay. If the cardiac impulse is sufficiently delayed, the bordering NZ will recover excitability and may become re-excited by the delayed electrical activity. The shortest Wenckebach-like sequence is a 3:2 conduction pattern. This is the basic mechanism for trigeminal rhythms (fig. 1B). In no single experiment was trigeminy related to a 3:1 conduction pattern in a re-entrant pathway. Quadrigeminy is due to a 4:3 Wenckebach-like conduction pattern (fig. 1C). However, a quadrigeminal rhythm in the surface ECG may be the result of a regular 2:1 conduction cycle in a re-entrant pathway with manifest re-entry only in alternate cycles, i.e., a form of concealed bigeminy. Although longer Wenckebach-like cycles could occasionally be seen (fig. 2B), it is rare for a regular penta- or hexageminy to be due to successive 5:4 or 6:5 conduction ratios respectively. Regular hexageminy, however, can be a manifestation of concealed trigeminy (fig. 2A). On the other hand, the not uncommon regular alternation of 3:2 and 2:1 conduction cycles can give rise to a host of patterns that may or may not simulate concealed bigeminy or trigeminy (fig. 9A).

A bigeminal rhythm is due to a characteristic 2:1 conduction pattern in a potentially re-entrant pathway. From an electrophysiologic point of view, a 2:1 cycle represents a greater degree of conduction disorder compared to a Wenckebach-like conduction pattern. Thus, a Wenckebach-like pattern in a re-entrant pathway will consistently change into a 2:1 conduction at relatively shorter cardiac cycle lengths. Certain pathways will exhibit a significant degree of conduction delay during the conducted beat of a 2:1 cycle (figs. 3B, 6, and 7). The conduction delay may be sufficient to re-excite the bordering NZ, giving rise to a re-entrant beat following every conducted sinus beat in a bigeminal arrangement (figs. 6 and 7). In these experiments, a trigeminal or quadrigeminal rhythm due to a 3:2 or 4:3 Wenckebach-like conduction patterns, respectively, may change to a bigeminal rhythm on shortening of the cardiac cycle length (compare fig. 5C with figs. 6 and 7). In other experiments, however, the change from a Wenckebach-like conduction pattern in a potentially re-entrant pathway to a 2:1 ratio will be associated with less conduction delay during the conducted beat of the 2:1 cycle thus negating the chance for re-entry. These experiments may show trigeminy or quadrigeminy at a certain cardiac cycle length but will not exhibit a bigeminal rhythm.

Re-entrant beats with extrasystolic grouping can disappear at both relatively slow and fast heart rates. At a slower heart rate a potentially re-entrant pathway will allow conduction of the cardiac impulse in a 1:1 pattern with significantly less conduction delay than is necessary for re-entry to occur (figs. 3A and 5A). On the other hand, re-entry may disappear on increasing the heart rate due to one of two basic mechanisms: 1) A faster rate may result in a 2:1 or higher degree of conduction block in a potentially re-entrant pathway with the conducted beat showing less conduction delay, thus negating the chance for re-entry. Also a faster rate may result in complete (paroxysmal) block in the re-entrant pathway. 2) At a faster rate the re-entrant pathway conduction time may approach, equal, or exceed the basic cardiac cycle length. In this case, re-entry may be concealed due to entrainment in a small part of the closely bordering NZ by the activation wavefront of the next supraventricular impulse advancing from the NZ (fig. 3B). At still shorter cycles, re-entry may be actually confined to the re-entrant pathway whose terminal part may be pre-excited by the advancing wavefront from the NZ (fig. 7C). This type of rate-related concealed re-entry can be suspected from the surface ECG. Usually the re-entrant beats will show very late coupling resulting in various degrees of ventricular fusion complexes. Slight acceleration of the heart rate will result in fusion beats with less and less aberrant QRS configuration until finally only supraventricular QRS complexes are recorded (see fig. 7). The reverse order will be seen on gradual slowing of the heart rate.

The term concealed re-entry was first coined by Mack and Langendorf and Langendorf et al. Utilizing deductive analysis of clinical records, these authors suggested that the cardiac impulse can be blocked within the re-entrant pathway. Cranefield et al. later demonstrated concealed re-entry in in vitro models and suggested that the re-entrant impulse can block either in the re-entrant pathway or the closely bordering normal zone. The present study has documented the presence of both types of concealed re-entry.

This differentiation of the two levels of concealment may seem only a problem of semantics since in both situations the amount of excited tissue is so small that it is unlikely to alter the basic ventricular activation pattern and to be detected from surface recordings. However, the electrophysiologic mechanisms in both levels of concealment probably have different bases. It is reasonable to assume that conduction becomes incremental once the re-entrant impulse reaches and re-excites normal myocardium. Normal myocardium is known to recover excitability fairly synchronously and this incremental conduction is not at this stage likely to block because of differences in refractoriness. The only plausible mechanism for concealment in the closely bordering NZ is entrapment of the re-entrant impulse by the advancing activation wavefront of the next supraventricular impulse. This would require a re-entrant pathway conduction time that is only slightly shorter than the basic cardiac cycle length. In this case, re-entry occasionally became manifest it would take the form of a very late coupled or a fusion beat. In contrast, concealment due to block within the
re-entrant pathway does not require a delicate balance between the re-entrant pathway conduction time and the basic cardiac cycle length and manifest re-entrant beats do not have to be late coupled. Conduction in a re-entrant pathway is very slow and decremental in nature. Conduction can become even more decremental and block along the re-entrant pathway when a slight difference in refractoriness between the different components of the pathway occurs. This is more likely to happen at relatively short cardiac cycle lengths because of the tachycardia-dependent nature of conduction in the re-entrant pathway. However, it was clearly demonstrated in this study that during a remarkably constant basic cycle length, the re-entrant impulse may occasionally and unpredictably fail to complete conduction in the re-entrant pathway due to block along its way (figs. 2A and 6B). This underscores the tenuous nature of conduction among various components of the re-entrant pathway.

Attention was focused on the phenomenon of concealed extrasystoles when Schamroth and Marriott coined the term concealed bigeminy. These authors noted that in ECG records containing apparently haphazard distribution of extrasystoles, the interectopic intervals always consisted of an odd number of sinus beats thus suggesting that a bigeminal rhythm probably persisted in a concealed form. These authors later described records of concealed trigeminy and other recordings showing fluctuation between concealed bigeminy and trigeminy and attributed both manifest and concealed extrasystoles to a mechanism of triggered automaticity. More recent reports tried to explain the phenomenon on the basis of re-entry. However, some of the mechanisms suggested were speculative while the basic mechanism of Wenckebach-like conduction in a re-entrant pathway was not entertained.

Extrasytostol with Fixed and Variable Coupling

This study has shown that in the presence of a stable conduction pattern in a potentially re-entrant pathway, e.g., regular repetition of a 2:1 or 3:2 conduction sequences, the re-entrant impulse can retrace the same pathway in practically the same span of time and produce extrasytostoles with almost constant coupling. Considering the high degree of functional dissociation of conduction in the IZ and considering that the myocardium is a free syncytium with several potential alternative routes, the ability of the re-entrant impulse to precisely retrace the same complex pathway is truly a remarkable electrophysiologic phenomenon. A likely explanation is that under a stable condition the re-entrant pathway is probably shaped by a delicate difference of refractoriness and conduction characteristics of its various components, with the re-entrant impulse tending to pursue the line of least resistance. Once a re-entrant route is engraved, the passage of the re-entrant wavefront tends to perpetuate the same delicate balance of electrophysiologic properties that established it in the first place. On the other hand, different re-entrant pathway conduction times, and hence variable coupling intervals of extrasytostoles were frequently seen when there was a change in the conduction pattern in the pathway, e.g., a change from a 2:1 to a 3:2 conduction sequence. A change of conduction patterns can be easily induced by a minor or major alteration of the cardiac cycle length (fig. 3B). However, this change can also occur at remarkably constant cycle lengths (fig. 9A). In this case, the surface ECG will show sudden "unpredictable" variations in the coupling intervals. Extrasytostoles with variable coupling can still have the same QRS configuration if there is little or no change in the site of early breakthrough of the re-entrant impulse into the closely bordering NZ. The variation in coupling will be accounted for by changes along the re-entrant route but with a constant terminal pathway. Significant changes in the terminal pathway, as well, can conceivably explain both variations in coupling and QRS configuration of re-entrant extrasytostoles.

In summary, the present study provides a direct detailed analysis of the mechanism of re-entrant extrasytostic grouping in the in vivo heart. The study has documented the phenomenon of concealed extrasytostoles; however, it has also unequivocally established that the surface ECG is an inadequate means of analyzing the exact nature of the underlying concealed re-entry.

Acknowledgment

The authors would like to acknowledge the technical assistance of Mr. George Rodriguez and secretarial work of Miss Zoraya Ives.

References

7. Mack I, Langendorf R: Factors influencing the time of appearance of premature systoles (including a demonstration of cases with ventricular premature systoles due to reentry but exhibiting variable coupling). Circulation 1: 910, 1950
Re-entrant ventricular arrhythmias in the late myocardial infarction period. 3. Manifest and concealed extrasystolic grouping.
N El-Sherif, R Lazzara, R R Hope and B J Scherlag

Circulation. 1977;56:225-234
doi: 10.1161/01.CIR.56.2.225

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/56/2/225

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/