Role of ventricular premature beats in initiation and termination of atrial arrhythmias

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Clinical observations in 5 patients are presented of 42 episodes of atrial arrhythmias after ventricular premature beats which had occurred 0.04-0.10 sec. after the onset of the P wave. In experiments in dogs, catheter electrodes were introduced into the right atrium and right ventricle through the jugular vein under chloralose (0.10 g./kg.) anaesthesia, and 5,000 pacemaker impulses were analysed. With impulses exceeding three times the diastolic impulse threshold, no arrhythmias were observed either in the case of atrial or ventricular stimulation - apart from the pacemaker pararrhythmia. During acetylcholine infusion (0.8-1.0 mg./min.), atrial stimulation elicited atrial arrhythmias in 32.6 per cent of the cases where the impulses occurred in the period of atrial vulnerability. In cases of ventricular stimulation the pacemaker-induced ventricular premature beats occurring 0.04-0.11 sec. after the onset of the P wave were followed by atrial arrhythmias in 16.9 per cent of cases. It is suggested that ventricular premature beats occurring in the area of the P wave, which are vulnerable for the atrium, should be termed the 'R on P phenomenon'. In 7 instances in 2 patients it was noted that supraventricular arrhythmias stopped immediately after the premature ventricular beats.

There are two main ways of inducing ectopic tachycardias, atrial and ventricular flutter, or fibrillation by electrical impulse. The first involves stimulation of the myocardium with high frequency, the second, stimulation in the vulnerable period of the heart cycle (Ferris, King, and Spence, 1936; Wiggers and Wégria, 1940; Leeds, Mackay, and Mooslin, 1951; Burn, Vaughan Williams, and Walker, 1955; Lown *et al.*, 1963; Haft *et al.*, 1968; Yamada *et al.*, 1968).

Ventricular extrasystole or pacemaker beats in the territory of the T wave of the electrocardiogram are the clinical equivalent of the electrical stimulus applied during the vulnerable period. This phenomenon - 'R on T' (Smirk and Palmer, 1960) - is often followed by various ventricular arrhythmias (Schmidt, 1952; Lown, Kosowsky, and Klein, 1968; Watanabe and Dreifus, 1968; Büchner and Effert, 1968; Csapó, Békássy, and Lónyay, 1970). Several reports deal with the importance of atrial extrasystoles in the induction of

atrial arrhythmias as well (Killip and Gault, 1965; Hager and Schley, 1966; Reynolds *et al.*, 1967; Haft *et al.*, 1968; Büchner and Effert, 1968; Büchner, 1969). This problem and the stopping of supraventricular arrhythmias by premature beats have been analysed in detail in the case of WPW syndrome (Durrer *et al.*, 1967; Massumi, Kistin, and Tawakkol, 1967; Zeff and McGowan, 1969). In the following report we are presenting our observations on eliciting atrial arrhythmias by ventricular premature beats in clinical material and in animal experiments.

Subjects and methods

The clinical observations have been performed in our intensive care unit. Patients with arrhythmia and those after electrocardioversion have been continuously monitored on an electrocardiogram built into the central monitoring system of Hellige.

Mongrel dogs weighing 10-14 kg. were used in our animal experiments. A pacemaker electrode was introduced into the right atrium and hence into the right ventricle through the jugular vein

Received 8 June 1970.

Animal results In the course of our animal experiments in 10 dogs, a total of 5000 pacemaker impulses was analysed.

Fifteen hundred pacemaker impulses were recorded without acetylcholine pretreatment, consisting of 400 atrial and 1100 ventricular stimuli. Sixty-two per cent of the atrial stimulations affected the refractory period of the cycle, and 38 per cent elicited extrasystoles. Neither after the stimuli in the refractory period nor after pacemaker extrasystole were any arrhythmias observed.

Of the ventricular stimuli, 52 per cent affected the refractory period, while 48 per cent elicited ventricular premature beats. No arrhythmias have been elicited by the stimuli affecting the refractory period. In 0.8 per cent of the cases of pacemaker-induced extrasystole, repeated spontaneous premature beats were registered.

The effects of pacemaker impulses during acetylcholine infusion were twofold:

(a) Of a total of 1000 atrial stimuli, 446 induced atrial extrasystoles. From the 554 impulses affecting the refractory period, 98 coincided with the descending limb of the R wave and with the S wave or with the start of the ST segment (period of atrial vulnerability); 32 of these (32.6%) elicited atrial fibrillation (Fig. 6), the atrial fibrillation ceasing on discontinuing acetylcholine infusion.

(b) Of 2500 ventricular stimuli, 950 affected the refractory period and elicited neither premature beats nor other arrhythmias; 1550 pacemaker impulses induced premature ventricular beats, and 172 stimuli applied 0.4–0.11 sec. after the onset of the P wave induced ventricular premature beats; in 29 cases (16.9%) this was followed by atrial fibrillation (Fig. 7), disappearing spontaneously in 1 case, while in the others it disappeared on discontinuing acetylcholine infusion. Apart from these occasions, pacemaker-induced premature beats were never followed by atrial arrhythmias.

Discussion

As early as 1936 Ferris *et al.* had already focused attention on the arrhythmia-producing effect of electrical stimuli applied in the repolarization period of the cardiac cycle. Later, the vulnerable periods of the cardiac cycle were precisely defined, first in animal experiments, and later in patients with pacemakers and after cardioversion (Wiggers, 1940; Wiggers and Wégria, 1940; Lown *et al.*, 1963; Haft *et al.*, 1968); in the atria this includes the descending limbs of the R and S waves, and in the ventricles the ascending

FIG. 3 Atrial extrasystole (AEs) after 'R on P' ventricular extrasystole (VEs) and parasystole (VPs).

limb of the T wave. Electrical impulses applied in the vulnerable periods often induce various types of arrhythmias (Wiggers and Wégria, 1940; Lown *et al.*, 1963; Lown, Kleiger, and Wolff, 1964; Büchner, 1969).

In the course of our own observations, patients with a tendency to such atrial arrhythmias have been found after ventricular extrasystoles and parasystoles occurring on the descending limb of the P wave or immediately thereafter. This type of ventricular premature beat may be analysed electrophysiologically as follows (Fig. 8): as is well

FIG. 4 Serial atrial premature beats (salve) following 'R on P' ventricular premature beat (VEs). Sr., sinus rhythm; A.Ar., atrial arrhythmia. (Reproduced by kind permission of the Editor of Orvosi Hetilap.)

known, the impulse is conducted not only in the atrioventricular direction but in the reverse direction as well, and the orthograde and retrograde conduction times are equal, i.e. $PQ = QP$ (Bussan, Torin, and Scherf, 1955; Linenthal *et al.*, 1962; Siddons and Sowton, 1967). In Fig. 8 the schematically represented ventricular premature beat appears 0.05 sec. after the onset of the P wave. Considering the high speed of ventricular conduction, the time required to cover the distance between the origin of the impulse and AV node is negligible. By measuring the $QP (=PQ)$ distance from the onset of the premature beat (the starting point of its R wave), we can define approximately the point when the impulse reached the atria. In Fig. 8, the PQ interval was 0.16 sec.; thus the impulse of ventricular excitation reached the atria approximately 0.21 sec. after the P wave, during the S wave of the electrocardiogram; in other words in the vulnerable period of the atria. The ventricular premature beat was followed by atrial arrhythmia (Fig. 4). In the course of 38 observed episodes, the premature ventricular beats preceding the atrial arrhythmias occurred after the P wave (P-Es distance) by 0.04 to 0.10 sec. The PQ interval varied between 0.16 and 0.18 sec. in our cases. Thus the impulse of the ventricular premature beats reached the atria approximately 0.20 to 0.28 sec. after the onset of the P wave, which corresponds to the period of atrial vulnerability. For the identification of this type of ventricular premature beat the name 'R on P phenomenon' is suggested – on the analogue of 'R on T phenomenon', as introduced by Smirk and Palmer (1960). The vulnerability of these premature ventricular beats may be expressed by the following formula:

$$\frac{PQ + PE_s}{PS} = Q$$

where PQ is the length of atrioventricular conduction, PE_s denotes the distance between onset of the P wave and that of the premature beat, and PS is the distance between the onset of the P wave and the endpoint of the S wave. The ventricular premature beat is vulnerable in respect of the atrium if the value of the quotient (Q) is between 0.7 and 1.2.

In our experiments in dogs we intended to reproduce our human observations. In healthy untreated animals, pacemaker impulses exceeding by three times the diastolic impulse threshold failed to produce arrhythmias with atrial and ventricular stimulation. Acetylcholine increases the susceptibility to atrial arrhythmias, and it has been noted by a number of authors that, under the effect of

FIG. 5 Atrial fibrillation after ventricular ('R on P') extrasystole and restoration of sinus rhythm after ventricular extrasystole. Sr., sinus rhythm; AF, atrial fibrillation; VEs, ventricular extrasystole; AE_s, atrial extrasystole.

FIG. 6 Atrial pacemaker stimulation during acetylcholine infusion in animal experiment. The second stimulus which is affecting the descending limb of the R wave induces atrial fibrillation. Pm, pacemaker stimulus; AF, atrial fibrillation.

FIG. 7 Ventricular pacemaker stimulation during acetylcholine infusion. Pacemaker premature beats occurring 0.04 to 0.11 sec. after the onset of the P wave elicit atrial fibrillation. Abbreviations as in Fig. 5 and 6.

acetylcholine, pacemaker stimulation of the atrial musculature causes atrial fibrillation (Burn, 1957; Holland, Burn, and Schümann, 1957; Rand and Walker, 1958; West and Cox, 1960; Yamada *et al.*, 1968). This persists until the effect of acetylcholine stops.

By applying atrial pacemaker stimulation during acetylcholine infusion we have determined the period of atrial vulnerability, and this had been found to agree with the data already published: beats affecting the descending limb of the R wave and the S wave caused atrial fibrillation in 32.6 per cent of our cases. In the course of pacemaker stimulation of the right ventricular musculature, it has been found that pacemaker premature beats following the P wave by 0.04 to 0.11 sec. are followed by atrial fibrillation in 16.9 per cent of the cases. The PQ interval of our animals varied between 0.14 and 0.17 sec.; the impulses of these ventricular premature beats reached the atria 0.18 to 0.28 sec. after the onset of the P wave; in other words in the period of atrial vulnerability. The values of the quotient $(PQ + PEs)/PS$ were in the case of premature beats between 0.7 and 1.2.

In the case of Durrer *et al.* (1967), supra-ventricular tachycardia associated with the WPW syndrome was terminated by right ventricular pacemaker extrasystole when the stimulation followed the onset of Q wave by 0.40–0.46 sec. Masumi *et al.* (1967) terminated supraventricular tachycardias developing during heart catheterization by extrasystoles similarly timed. Zeff and McGowan (1969) reported cases of supra-ventricular tachycardia successfully treated by prolonged pacing of the right ventricle. In our own cases we have seen 7 episodes in 2 patients where atrial arrhythmias were interrupted by a spontaneous ventricular premature beat and this was followed by restoration of sinus rhythm (Fig. 4 and 5). These ventricular premature beats occurred in each case 0.42 to 0.46 sec. after the Q wave. No similar phenomena have been encountered in our animal experiments.

Summarizing our clinical observations and our animal experiments, it can be concluded that in states susceptible to atrial arrhythmias these can be elicited either by atrial pacemaker stimulation in the period of atrial vulnerability or by spontaneous or pacemaker-induced ventricular premature beats occurring 0.04–0.11 sec. after the onset of P wave. These ventricular premature beats form a fusion PQRS complex with the preceding P wave very similar in its appearance to the WPW syndrome. It might therefore be

$$Q = \frac{PQ + PEs}{PS} = \frac{0.16 + 0.05}{0.23} = \frac{21}{23} = 0.91$$

FIG. 8 Schematic illustration of an 'R on P' premature beat (which is visible in Fig. 3 in the second line). ARP, absolute refractory period; RRP, relative refractory period. See text for discussion.

assumed that a similar mechanism could play a role in triggering supraventricular tachycardias associated with WPW syndrome. Our clinical observations support the possibility that where supraventricular paroxysmal rhythmic disturbances stop spontaneously, the spontaneously occurring ventricular premature beat might also play a role. We agree with Durrer *et al.* (1967) that the impulse of the premature ventricular beat, by reaching the atrioventricular node or the atria, disrupts the circus movement or else defibrillates the atria.

The author is grateful to Mrs. Mária Lozsádi for preparing the electrocardiograms in our intensive care unit.

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