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Instruments and Techniques

Production of Chronic Atrioventricular Block in Dogs Without Thoracotomy

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AUTHORS' SYNOPSIS. *Total heart block was produced in dogs without thoracotomy by means of a formaldehyde injection into the bundle of His. The method was successful in 22 out of 24 experiments. It is a useful model for haemodynamic studies in the intact animal.*

Experimental atrioventricular (AV) block in dogs is a versatile research model and numerous methods for its production have been devised. With only two exceptions (Williams and Lambert, 1964; Fisher, Lee, Christianson, and Kavaler, 1966) all these methods use thoracotomy, with or without atriotomy, as the operative approach. Thoracotomy, however, produces important cardiovascular changes, for left ventricular volume and cardiac output decline, and heart rate, pulmonary vascular resistance, and ventricular ejection fraction all rise upon opening the chest ((Rushmere, Finlayson, and Nash, 1954; Fermoso, Richardson, and Guyton, 1964; Coles, Buttigliero, and Gergely, 1965). All these facts make exact cardiological evaluation of acute experimental AV block difficult, since immediate and late effects of thoracotomy become superimposed on the primary change in cardiac dynamics.

These observations have prompted us to develop a new method of block production in dogs. This method does not require thoracotomy, produces only a small myocardial lesion, and results in a permanent AV block. In this paper, which represents a further extension of our first report about experimental AV block (Turina and Babotai, 1967), we describe percutaneous production of chronic AV block in dogs. Stability of the block is confirmed by long-term observations, and the histological changes in the acute and chronic phases of experimental heart block are reported.

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Methods

Twenty-two mongrel dogs, weighing between 17 and 33 kg were used. In 11 dogs, the block was produced in an acute experiment under non-sterile conditions. Thirteen dogs were operated upon under sterile conditions and allowed to recover; duration of the block and long-term histological changes were studied in these animals.

Anaesthesia was induced with sodium pentobarbital (Pentothal) 10–15 mg/kg. Each animal was placed on its left side with the neck slightly elevated, and the right external jugular vein was exposed through a small incision. A stainless-steel cannula, 35 cm long (Fig. 1) was introduced into the right atrium under fluoroscopic guidance, until its tip rested slightly superior to the septal tricuspid leaflet, anterior to the coronary sinus.

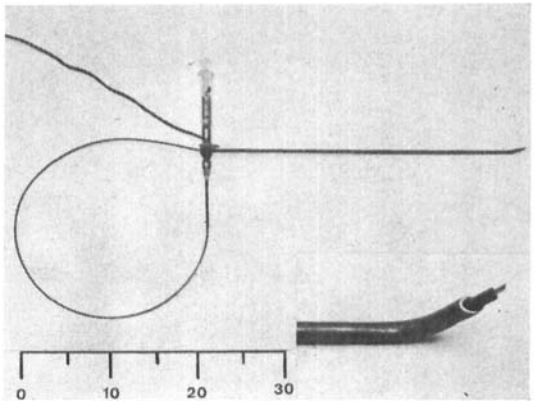

Fig. 1. Block cannula with the needle catheter inserted; formaldehyde syringe and ECG connection are attached to the cannula. Insert: cannula tip with the needle catheter protruding. Scale: metric.

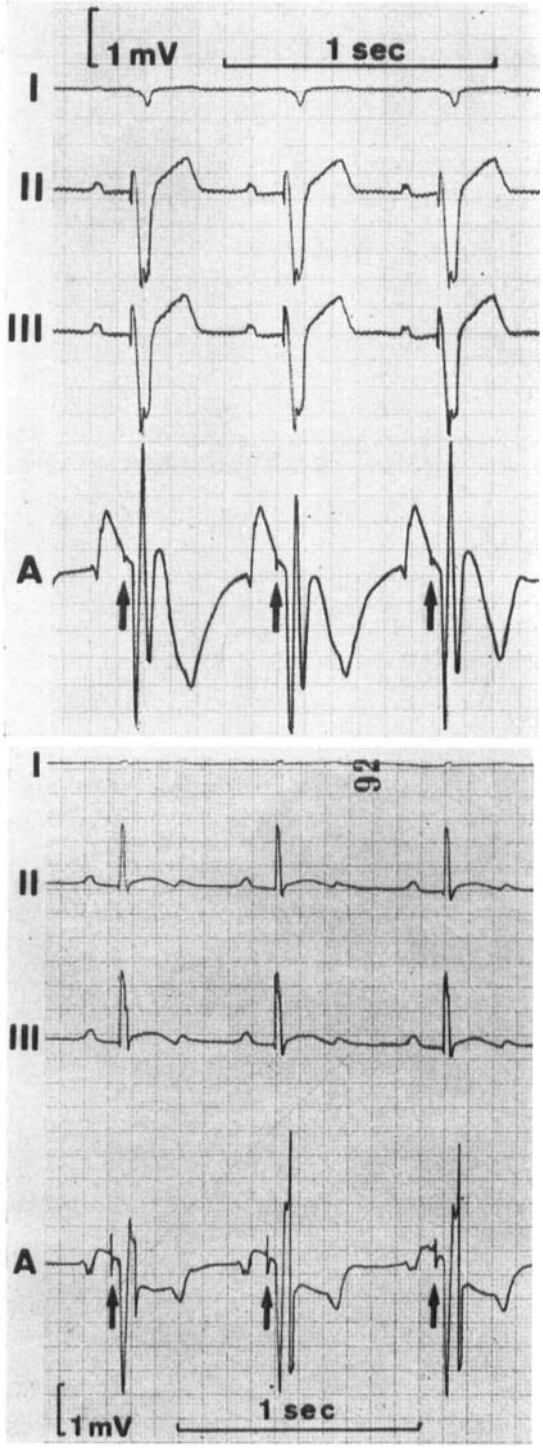

Fig. 2. Bundle potentials, as recorded with the cannula. Arrows denote the depolarization of the bundle of His. I, II, III = extremity leads; A = atriogram.

Electric insulation of the cannula was achieved by covering it with a non-conductive paint. Only the tip of the cannula was left bare of insulation, acting as an exploring electrode to record potentials from the nodal region. The cannula was connected to the precordial lead of a standard ECG recorder (Mingograf 81 by Elema Schönander); the extremity leads were recorded simultaneously and displayed on the oscilloscope screen and on a paper strip, together with intra-atrial electrocardiogram (atriogram). A No. 7 catheter with a needle mounted on its tip (see insert, Fig. 1) was filled with 40% formaldehyde solution and threaded through the cannula until the nedle reached the end of the cannula. Under fluoroscopic guidance and continuous registration of atriograms, characteristic potentials from the bundle of His were looked for with small movements of the cannula tip. According to Pruitt and Essex (1960) and to Hoffman, Moore, Stuckey, and Cranefield (1963) these potentials consist of a fast, predominantly negative deflection of the QRS complex (Fig. 2). Upon locating the bundle, the needle-tipped catheter was advanced through the cannula until the needle became firmly embedded in the myocardium. Under continuous ECG registration 0·2–0·3 ml. formaldehyde was injected into the myocardium at this site. Within a few seconds, sometimes after a burst of ventricular or supraventricular extrasystoles, a total AV block appeared (Fig. 3).

In acute experiments, animals were kept under observation for 6–12 hr after a stable AV block had been produced; after this time they were killed. The follow-up period in long-term experiments ranged between eight and 64 days. Recordings were made in awake animals every two weeks after the block production. Extremity and precordial leads were analysed for heart rate, conduction disturbances, and for origin of the ventricular impulse. A QRS complex wider than 0·08 sec was usually associated with a heart rate of less than 50/min; in precordial leads the ventricular activation time was delayed and bundle branch block pattern was recorded over one of the ventricles. This was considered as conclusive of infra-bifurcational rhythm. On the other hand, a normal QRS complex, heart rate of more than 50/min, and a normal ventricular activation time were diagnosed as supra-bifurcational rhythm (Wyss, Holzmann and Schaub 1961).

Results

Our overall results of block production are summarized in Table 1. There was one failure out of 11 acute experiments and one failure out of 13 long-term experiments. In both of these animals no identification of the bundle was possible. One animal was lost 10 min after the block had been produced: intra-atrial manipulation of the cannula gave rise to a ventricular tachycardia, which progressed to fibrillation within a few seconds. In about half of all the experiments only one formaldehyde injection was needed to procure the block. In the other half a second injection was

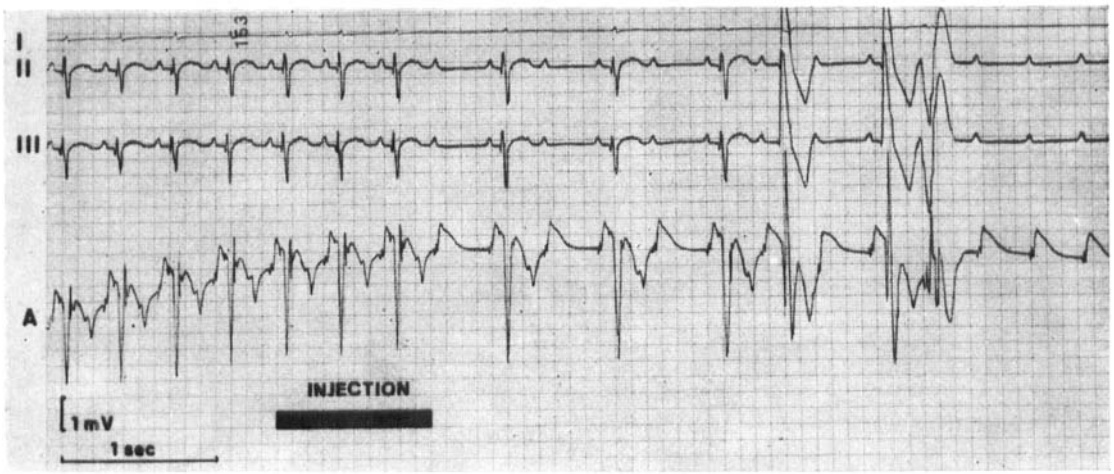

Fig. 3. Percutaneous block production in continuous ECG recording. In first seven P waves atriograms show bundle spikes; after formaldehyde injection a 2:1 block appears, which after three ventricular extrasystoles progresses to total AV block. Symbols as in Fig. 2.

needed; this happened if the needle was only loosely embedded and the first injection was not properly deposited into the myocardium.

Table 1. *Results of AV Block Production*

	Acute experiments (no. of animals)	Chronic experiments (no. of animals)
Successful	10	12
Unsuccessful	1	1

In chronic AV block the heart rate varied between 37 and 53/min; nine animals showed an infra-bifurcational and three a supra-bifurcational rhythm pattern. Six dogs were observed for one to two weeks and another six between 50 and 64 days. The total heart block was permanent; none of the animals reverted to sinus rhythm during the observed period.

In acute AV block subendocardial bleeding at the injection site was invariably observed. Micro-

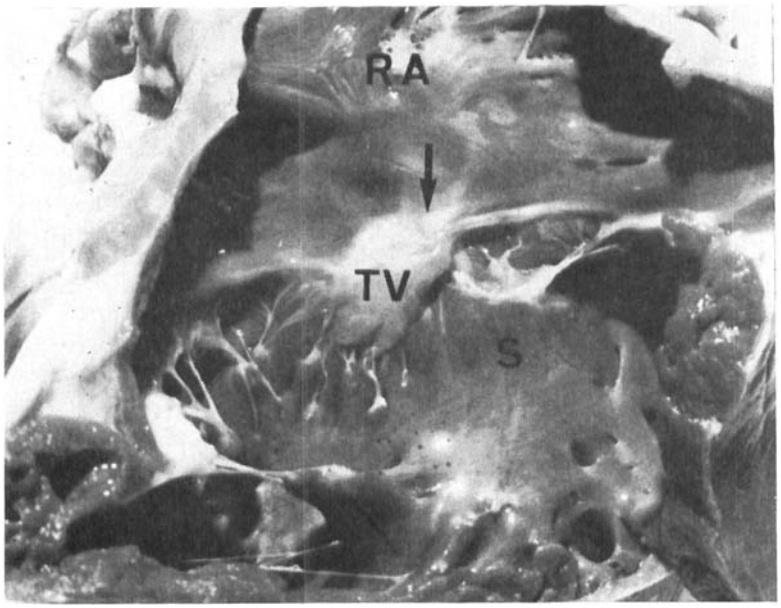

Fig. 4. Gross appearance of the heart with an AV block of two months' duration. RA = right atrium; TV = septal tricuspid leaflet, S = septal portion of the right ventricle. Arrow denotes the site of injection.

scopically an "*in-vivo* formaldehyde fixation" could be noted, consisting of interstitial bleeding and oedema, cellular shrinking, and thrombosis of blood vessels. Within a few days parietal thrombosis of the atrial wall over the injection site developed, and histiocyte-rich granulation tissue appeared on the edges of formaldehyde-impregnated area. Eight to nine weeks after the block production a fibrotic scarring in the region of the bundle was noted (Fig. 4); this reaction sometimes proceeded to the production of cartilage. The bundle of His showed different degrees of fibrosis in all animals. Extension of formaldehyde impregnation varied widely: in eight dogs, only a pea-sized area was affected; the bundle of His was destroyed, but the AV node and both bundle branches were intact (Fig. 5). In five animals a more widespread necrosis and fibrosis was found, due to diffusion of formaldehyde into the surrounding structures. In these dogs fibrotic changes were noted in right atrial wall, AV node, the whole of the bundle of His and proximal parts of both bundle branches, aortic ring, septal tricuspid leaflet, and the uppermost portion of the ventricular septum.

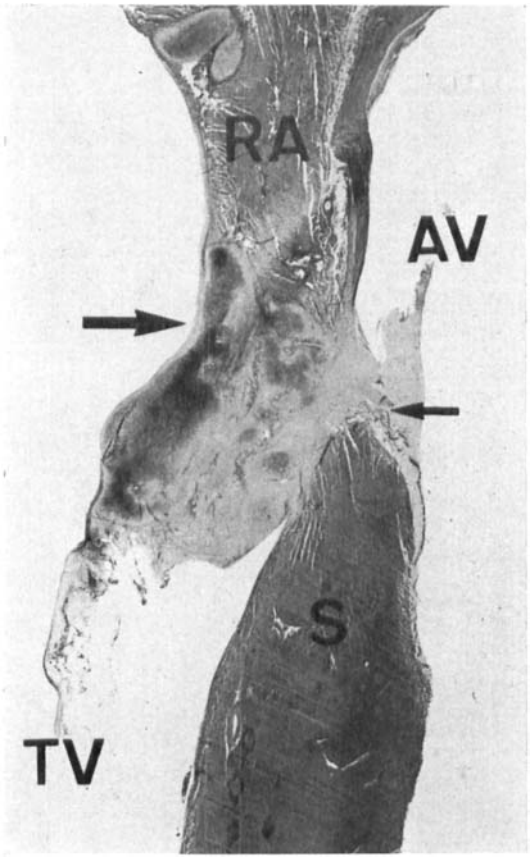

Fig. 5. Cut through the AV border of a dog heart with total AV block, two months after the block production. A pea-sized granuloma with cartilaginous transformation is found on the injection site. The base of the septal tricuspid leaflet (TV) is thickened. Bundle of His lies in the granuloma, the left bundle branch (small arrow) can be recognized on the left side of the ventricular septum (S). Bigger arrow: injection site; RA = right atrium, AV = aortic valve.

Discussion

Williams and Lambert (1964) were the first to develop a method for AV block production without thoracotomy. They identified AV nodal deflection by means of intracardiac potentials; injection of formaldehyde or procaine was used to block impulse conduction. No details of the procedure or the percentage of successful block productions were given. Fisher *et al.* (1966) produced the block by means of formaldehyde injection in the region where the bundle of His was presumed to be. These authors used only fluoroscopic guidance for their orientation and their success rate was about 50%. Brutsaert (1966) tried electrocoagulation of the bundle of His via a catheter-tip electrode, but he was also hampered by the lack of identification of the bundle of His. Cruze and Schiebler (1963) devised a two-stage procedure, which eliminated the acute, but not chronic changes due to thoracotomy; their method is, however, too complicated for routine laboratory work.

With our method, block production was accomplished in a very short time and animals recovered rapidly. Widespread fibrotic changes found in five dogs indicate, nevertheless, that the utmost care must be exercised in injecting only the smallest amount of formaldehyde needed; this will limit the necrosis to the bundle of His only. Three possible complications can arise from an excessive formaldehyde injection, namely tricuspid and aortic regurgitation, due to fibrosis, and pulmonary embolism from the atrial wall thrombosis. This last complication was never encountered; in our present haemodynamic studies we could not detect any aortic incompetence either.

Deliberate production of an AV block in humans, followed by a pacemaker implantation, has been reported several times in the last few years (Chardack, 1964; Gianelli, Ayres, Gomprecht, Conklin, and Kennedy, 1967; Slama, Blondeau, Aigueperse, Cachera, Degorges, and Abbou, 1967). It was used as a last, admittedly heroic, measure to control an otherwise refractory supraventricular tachycardia. In all these operations open-heart surgery had to be done, and percutaneous block production could have achieved the same effect in a much simpler way. If a local anaesthetic agent

like procaine be used, only a temporary AV block results (Williams and Lambert, 1964), and a short-term control in selected cases of supraventricular tachycardia can thus be envisioned.

Summary

Production of an atrioventricular block in dogs without thoracotomy is based on electrocardiographic identification of the bundle of His and its destruction with a small amount of formaldehyde. A long steel cannula, serving as exploring electrode, is used for identification; it is introduced into the right atrium via the right external jugular vein. When the cannula tip records characteristic bundle potentials, a needle-tipped catheter is pushed through the cannula and advanced into the myocardium. Through this catheter 0·2–0·3 ml. 40% formaldehyde is injected, whereupon total heart block appears. The method was successful in 22 out of 24 experiments. This block is permanent; none of the surviving animals reverted to sinus rhythm even after two months of observation. In chronic experiments, endocardial thickening and fibrosis appear in the bundle region; extension of fibrosis varies widely, according to the amount of formaldehyde injected. In eight dogs only a pea-sized granuloma was found in the place where injection had been made; the other five animals showed localized necrosis and a certain degree of fibrosis in the surrounding structures. The utmost care has to be exercised in injecting only the smallest amount of formaldehyde needed; this limits destruction to the bundle of His only.

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