Extensive Intraventricular Conduction Defect

EXPERIMENTAL PRODUCTION WITH DESTRUCTION OF TOTAL PURKINJENET SYSTEM OF THE CANINE RIGHT VENTRICLE

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The bundle-branch and Purkinje-net system of the canine heart can be visualized by the application of iodine solution to the endocardial surface. The Purkinje-net fibers are distributed throughout most of the subendocardial surface of the right ventricular wall. The conduction tissue is selectively stained light brown or dark blue, depending upon the iodine content of the solution. The bundle branch and Purkinje net form a continuous system of fibers that stain in an identical fashion. Iodine solutions have been found to cause immediate and permanent right bundle-branch block when applied to the endocardium overlying the bundle-branch tissue.

The present experiment was undertaken with the assumption that conduction would be similarly blocked in the Purkinje tissue by the iodine staining reaction. The conduction defect produced by this procedure is described and compared to that of right bundle-branch block. Destruction of the Purkinje-net system was demonstrated by histological examination.

Methods

Experiments were performed on 14 medium-sized mongrel dogs under intravenous pentobarbital anesthesia (25 mg./Kg.). A complete experiment was performed as follows: A control 12-lead electrocardiogram was obtained. The heart was exposed through a fourth right intercostal thoracotomy. The azygos vein was ligated. The pericardium was opened and marsupialized. All areas of the right ventricular surface could be made accessible by slight retraction of the pericardium. A needle electrode, inserted into the left ventricular cavity through its free wall, served as a unipolar time-reference lead. Potentials from this electrode were recorded simultaneously with all direct ventricular surface recordings. Contiguous bipolar and unipolar recordings were obtained with an exploring electrode from 18 to 34 points distributed over the right ventricular surface and from two points over the left ventricular surface. Careful note was made of the anatomical position of each recording point.

The septal area of the right ventricular cavity was exposed by retraction of the tricuspid valve, through a right atriotomy, in the normothermic animal with temporary cardiac inflow and outflow occlusion. The right bundle branch was stained for optimum definition by applying a small cotton sponge, dampened with Lugol's solution, to the endocardium overlying the bundle branch. It was then severed with a capsulotomy knife. The atrial incision was closed with a Satinsky clamp and the circulation restored. The direct ventricular surface (bipolar and unipolar) recordings and the limb leads were repeated after resumption of a sinus rhythm.

The right ventricular cavity was again exposed, evacuated of blood, and filled with Lugol's solution, diluted 1:10 or 1:20 with saline. Irrigation with this solution was continued for about 15 seconds. The cavity was flushed with saline and circulation again restored. The electrocardiographic studies were repeated after resumption of a sinus rhythm. The chest was closed, following which a 12-lead electrocardiogram and a tetrahedral vectorcardiogram were obtained. The animal was allowed to recover. A 12-lead electrocardiogram was obtained one or two weeks following surgery. The electrocardiogram, vectorcardiogram, and direct ventricular surface recordings were again repeated four to six weeks after the surgical procedure. The animal was then sacrificed. The heart was examined for gross pathological changes.

Eight hearts were fixed in 4 per cent buffered
FIGURE 1

Contrast between the normal canine endocardial and subendocardial myocardium (left) and that in experimental Purkinje-net block (right). Weigert-van Gieson's stain. X 100.

Normal: Note the thin endocardium and subendocardium with Purkinje-net block. Experimental (five weeks following the endocardial application of 1:10 Lugol's solution): Note the marked fibroelastic hypertrophy of the endocardium and subendocardium with disappearance of the Purkinje nets.

formaldehyde. Blocks were then taken for histological examination from the following areas: right anterior wall adjacent to the anterior septal surface, right anterior wall over the parietal band, inferior wall in the center region between the apex and base, and from the mid-septal region at the junction of the sinus and conus. Single sections were cut from the first three blocks, and serial sections were cut from the septal block. Every tenth section was retained. Alternate sections were stained with hematoxylin and eosin and Weigert-van Gieson's stain.

Five animals died or were sacrificed after the initial complete electrocardiographic studies. The ventricular surface recordings following acute Purkinje block were omitted in four of the early experiments.

Recordings were made with an oscilloscopic photographic recorder (Electronics for Medicine, White Plains, New York) at paper speeds of 75 mm./sec. for the standard electrocardiograms and 150 mm./sec. for the ventricular surface recordings.

The bipolar recordings were obtained with an exploring electrode consisting of two silver wires separated by a distance of less than 1 mm. and embedded in an epoxy resin probe with a smooth recording surface. The unipolar direct recordings were obtained from one of the poles of this bipolar electrode.

The sequence of right ventricular surface activation was determined by measuring the interval from the onset of the Q wave in the reference lead to the onset of the intrinsic phenomenon recorded from the exploring electrode. This usually corresponded to the peak of a bipolar monophasic complex. Measurements were made with a 60 X optical magnifier.

The conduction defect produced by the application of iodine to the endocardium was compared to that following cutting of the right bundle branch in the same open-chest animal. The standard 12-lead electrocardiograms of the closed-chest animals with chronic Purkinje-net block were compared to electrocardiograms from 20 animals with chronic right bundle-branch block produced under direct vision in a previous experiment.

Results

The endocardium of the right ventricle was found to be sclerotic on gross pathological examination. Histological examination revealed that a process of fibroelastic proliferation had occurred in both layers of the endocardium. This was associated with a disappearance of the Purkinje nets (fig. 1). The terminal penetrating Purkinje and transitional cells were still in evidence but diminished in number. The subendocardial myocardium showed minimal to moderate focal fibrosis. Further changes in the myocardium, which are considered to be secondary to the endocardial changes, consisted of focal necrosis with hem-
Right ventricular surface activation with acute right bundle-branch block (left) and acute Purkinje-net block (right). This animal demonstrates extreme lateral spread of surface depolarization following the production of Purkinje-net block. Time is in msec.

orrhage and dilatation of thin-walled vascular channels. These changes were of 24 to 48 hours' duration and are not considered to be directly pertinent to the electrocardiographic findings in the acute phase of the experiment.

The control electrocardiographic studies were normal in all animals. The QRS intervals were of 38 to 55 msec duration, with no evidence of pre-existing block.

Right ventricular surface activation was delayed following interruption of the right bundle branch. Earliest surface activation occurred in the septal areas. The right ventricular wall was depolarized in a generally cephalad (apex to conus) direction. The last area to be activated was the conus and, occasionally, the superior lateral area of the right ventricular wall (fig. 2, left). No change in the time of activation was recorded from the left ventricular surface.

The application of Lugol's solution to the endocardium produced no significant further delay in activation of the septal margins of the right ventricular wall. However, there was a further delay in activation of the remaining free wall of the right ventricle. Depolarization occurred generally in a more lateral (septal to right atrial) direction. The last areas to be activated were the mid and superior lateral regions near the atrioventricular (AV) groove (fig. 2, right). The greatest delay, as compared to right bundle-branch block, occurred in the mid and inferior lateral regions of the right ventricular wall. No change in the time of activation was recorded from the left ventricular surface.

Right bundle-branch block produced typical electrocardiographic changes in the open-chest limb leads and resulted in a QRS interval of 70 to 85 msec. duration. Purkinje-net block produced a further increase of the QRS interval to 95 to 110 msec. duration in the open-chest limb leads.

Purkinje-net block produced a characteristic electrocardiographic pattern. Delayed right ventricular activation produced a wide, rather low voltage, terminal deflection which was easily differentiated from that of right bundle-branch block. This change was evident in all leads but was best demonstrated in lead V1'. Figure 3 compares the electrocardiographic patterns of Purkinje-net block with that of typical canine chronic right bundle-branch block. Particularly characteristic are the changes in leads V1'' and V1. There is an increase in the QRS interval. The terminal deflection has rather low voltage, increased duration, and tends to be flat at its apex, in contrast to the tall, peaked, terminal deflection of right bundle-branch block.

Currents of injury were not evident, and except for a change in the QRS interval, there was no change in the basic wave form of the QRS complex between the electrocardiograms taken immediately after surgery and those taken four to six weeks following surgery.

The tetrahedral vectorcardiogram was characteristic. The terminal slow segment of block was oriented perpendicularly to the plane of the septum and right ventricular wall in a superior and slightly anterior direction, as in right bundle-branch block, and is best seen in the sagittal plane (fig. 4). Purkinje block produced increased slowing and lower voltage of this segment.

The chronic phase of Purkinje-net block showed the same general sequence of surface depolarization; however, there was a further delay of the right ventricular surface potentials. The QRS interval increased to 120
FIGURE 3
Electrocardiograms of canine chronic right bundle-branch block (upper, 1 to 3) and Purkinje-net block (lower, 4 to 6). The electrocardiograms of right bundle-branch block were obtained in a previous experiment. Time lines are 0.02 second.

FIGURE 4
Tetrahedral vectorcardiograms of acute right bundle-branch block (left) and acute Purkinje-net block (right). The tracings were obtained in an open-chest animal.
to 150 msec. This phenomenon has been observed with serial electrocardiograms in further experiments and is associated with the appearance of heart failure. This change usually is not seen before the third or fourth week. We believe, therefore, that the block is more reliably defined in the acute phase of the experiment.

**Discussion**

There is disagreement in the literature as to the functional importance of the Purkinje system in bundle-branch block. Rodrigues et al.\(^7\) believe that the delay in bundle-branch block occurs largely in the septum at the junction of right and left ventricular muscle and that the impulse enters the Purkinje system on the side of the block. Erickson et al.\(^8\) did not find this "synaptic" delay in the septum. Their investigations would indicate that the impulse enters the Purkinje system of the homolateral ventricle but with an abnormal pattern of Purkinje activation. Conrad and Cuddy\(^9\) found a prominent component of tangential spread in the right ventricular wall with little dependence on the Purkinje system in right bundle-branch block. Pruitt et al.\(^10\) in the isolated perfused dog heart, did not find any prolongation of the QRS complex greater than that of bundle-branch block after the instillation of various noxious agents into the left ventricular cavity and 5 per cent cocaine into the right and left ventricular cavities. They suggest that rapid subendocardial spread of the impulse may occur in the longitudinal axis of the muscle fibers in the presence of bundle-branch block. Recently, Venerose et al.\(^11\) have demonstrated Purkinje activation preceding muscle activation of the left ventricular septal surface in left bundle-branch block. This would indicate that the impulse does enter the homolateral Purkinje system and plays an important role in the depolarization process of the left ventricle in the presence of left bundle-branch block.

The results of the present experiment would give further support to the functional importance of the Purkinje system in right bundle-branch block. When the Purkinje-net system is blocked, there is a further increase in right ventricular activation time compared with that found in right bundle-branch block. An altered mode of mural depolarization occurs, suggesting an increased component of slower tangential spread of the impulse through the right ventricular wall.

The histological studies would indicate that the extensive iodine effect is well confined to the endocardium and Purkinje nets, with lesser involvement of the penetrating Purkinje and intermediate myocardial cells and only focal involvement of the subendocardial myocardium. However, the possibility that more extensive biochemical change has occurred in the subendocardial muscle, which would not be manifested in the histological studies, cannot be excluded. A factor of muscle-fiber block would then have to be considered.

It is probable that this block could be produced by a number of corrosive agents. The affinity of the conduction tissue for iodine makes this agent rather specific and allows it to be used in weak concentrations up to 1:40 of Lugol’s solution (5 per cent elemental I\(_2\) + 10 per cent KI). The block is inconsistent at 1:40 concentration because of further dilution by residual blood in the right ventricle. Solutions with NaI have been found to be as effective as Lugol’s solution.\(^5\)

The appearance of right ventricular failure was an unexpected finding and is under investigation at the present time.

**Summary**

Destruction of the entire canine right ventricular Purkinje-net system, by the introduction of dilute Lugol’s solution into the right ventricular cavity, results in an intraventricular conduction defect which is 20 to 30 msec. greater in duration than that of right bundle-branch block. The mode of right ventricular surface activation is altered. A characteristic electrocardiographic and vectorcardiographic pattern is produced. Histological studies confirmed the absence of Purkinje-net cells in animals with chronic block.
References


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