The Nature of the RS-T Segment Displacement as Studied with Esophageal Leads

III. The Effects of Digitalis

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The electrocardiographic changes, with particular reference to the RS-T segment and T wave, in surface leads and in esophageal leads reflecting left ventricular cavity potentials, are studied in 7 persons with and without heart disease, before and after the administration of digitoxin. After the administration of digitoxin, the RS-T segment depression in precordial leads and in esophageal leads reflecting the potentials of the posterior surface of the left ventricle, are regularly associated with RS-T segment elevation in esophageal leads reflecting left ventricular cavity potentials. The possible roles played by myocardial involvement due to digitalis, modification of the monophasic curves, and the reduction of the human ventricular gradient are discussed.

Changes in electrocardiograms of animals and humans induced by digitalis were reported upon shortly after introduction of the string galvanometer, but it was not until the publications of Cohn and coworkers that the significance of the T wave alterations due to digitalis was emphasized. Subsequently, other investigators published their observations of the changes in the T wave and RS-T segment in the three standard leads in both normal and diseased hearts, using varying doses and different preparations of digitalis. A regular sequence of changes in the T wave and RS-T segment induced by digitalis was described by McMillan and Bellet in 1932. These changes consisted essentially of progressive lowering of the height of the T wave with subsequent depression of the RS-T segment, and finally diphasic or inverted T waves. These authors also observed that smaller doses of digitalis were required to produce T-wave and RS-T segment changes in the electrocardiograms of older persons, especially with diseased hearts, than in young persons. The electrocardiographic changes in the precordial leads due to digitalis have been described in several reports.

The significance and nature of the T wave and RS-T segment alterations due to digitalis have been the subject of much controversy. The demonstration of myocardial damage in animals following the administration of very large doses of digitalis has served to support the school of investigators ascribing the changes in the T wave and RS-T segment to myocardial involvement, with possible resultant delay in conduction. Other authors ascribe the RS-T segment and T wave changes to modification in the form of the monophasic curves or to a reduction of the human ventricular gradient towards a more normal level.

Though the changes in the T wave and RS-T segment due to digitalis have been adequately described for surface leads, only a few observations have appeared as to the nature of the electrocardiographic changes occurring within the ventricular cavities. Because of the anatomic relationship and proximity of the esophagus to the left atrium and ventricle, esophageal electrocardiography affords a readily available method for the study of potentials of the human left ventricular cavity and posterior left ventricular surface. In previous studies it has been demonstrated that esophageal electrocardiography affords a readily available method for the study of potentials of the human left ventricular cavity and posterior left ventricular surface. In previous studies it has been demonstrated that esophageal electrocardiography affords a readily available method for the study of potentials of the human left ventricular cavity and posterior left ventricular surface. 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Fig. 1A. J. B. 54 year old man with hypertensive heart disease. Records were taken prior to digitoxin administration. (All records were taken at 1 mv. = 10 mm. sensitivity.) All electrocardiograms were recorded simultaneously.

Fig. 1B. Records were taken after the administration of 3.2 mg. of digitoxin. Note RS-T segment depression in Leads I, II, V_L, V_F, and V_1 through V_6. RS-T segment is slightly elevated in V_R. Note striking T-wave alteration as compared with control record 1A.
Fig. 2A. Esophageal electrocardiograms recorded prior to the administration of digitoxin to patient J.B. E₂ is recorded at lower esophageal level. E₆ and E₁₀ are recorded at left atrial level and reflect left ventricular cavity potentials. Note presence of intrinsic atrial deflection. E₁₄ is recorded at supracardiac level.

Fig. 2B. Esophageal electrocardiograms recorded subsequent to digitoxin administration. RS-T segment is depressed in E₁ and E₂ and markedly elevated in E₆ and E₁₀. Note changes in T-wave contour.

Esophageal electrocardiograms recorded at certain atrial levels reflect RS-T segment changes occurring within the left ventricular cavity. This level is characterized by the recording of a ventricular QS or Qr pattern accompanied by an intrinsic atrial deflection. Similar ventricular patterns have been obtained with catheters placed inside the human and animal left ven-
tricular cavity. In the present study, the simultaneous recording of esophageal leads with standard and unipolar extremity and precordial leads was employed to investigate the nature of RS-T segment and T wave changes due to digitalis.

METHODS

The method of recording multiple esophageal electrocardiograms has been described in more detail elsewhere. In brief, it consists of the introduction of an esophageal electrode containing 15 fine wires, each separately connected to external metal bands 1.75 cm. apart. An electrocardiogram was recorded at each of these fifteen levels before and after the administration of digitoxin, Lead E2 reflecting left posterior ventricular surface and Ec reflecting the supraventricular level. Three esophageal electrocardiograms were recorded simultaneously, the selected esophageal electrocardiogram being recorded with any desired combination of precordial or other esophageal leads. The three standard leads, VR, VL, VF, and six unipolar precordial leads were recorded before and after the administration of digitoxin.

Each patient was given 1.2 mg. of digitoxin as an initial oral dose, followed by the administration of 0.2 three times a day or 0.1 mg. four times a day until toxic symptoms or electrocardiographic changes appeared. In no case was the above dosage maintained for longer than seven days.

The group of patients studied consisted of 3 young persons with no evidence of heart disease, and 4 patients with various degrees of cardiac enlargement. The latter group included 1 patient with rheumatic aortic stenosis and 3 patients with essential hypertension. None of these patients had taken any digitalis preparation previously, nor were there any symptoms of angina pectoris or cardiac decompensation.

RESULTS

In 3 of the patients with cardiac disease the electrocardiograms before the administration of digitoxin were essentially normal. The RS-T segments recorded in precordial leads and in the esophageal leads at the posterior left ventricular surface and at atrial level were isoelectric. In these 3 patients the following electrocardiographic changes occurred after the administration of 3.0 to 3.2 mg. of digitoxin:

1. RS-T Segment.

Depression of the segments occurred in Leads I and II, precordial leads V1 through V6 (figs. 1A and 1B), and in lower esophageal leads (E3 to E4) reflecting posterior left ventricular surface potentials (figs. 2A and 2B; only E4 and E5 shown). The depression was most marked in Leads V4 through V6 and in the lower esophageal leads. Elevation of the RS-T segment occurred in esophageal leads E1 through E10 at atrial level (only Ec and E10 shown in figs. 2A and 2B), in supraventricular leads E12 through E15 (only Ec shown in figs. 2A and 2B) and in Lead VR. The elevation was most marked in esophageal leads at atrial levels reflecting left ventricular cavity potentials.

2. T Waves.

The T waves in the standard, precordial and lower esophageal leads became markedly diminished in amplitude, or diphasic (minus-plus) in contour. In esophageal leads reflecting left ventricular cavity potentials the T waves, which had been inverted prior to the administration of digitoxin, became diphasic (plus-minus) in configuration.

3. The Q-T Intervals.

Subsequent to digitoxin administration there was definite shortening of the Q-T interval after correction for changes in heart rate.

In the one patient with aortic stenosis an electrocardiographic pattern of left ventricular hypertrophy was present in the control record, consisting of high voltage of the QRS complex, deeply inverted T waves and RS-T segment depression in Leads I, II, V3 through V6, and in the lower esophageal leads. In esophageal leads at atrial level, reflecting left ventricular cavity potentials, the RS-T segment was elevated and the T wave upright. Following the administration of digitoxin, there was no essential change in the T wave. However, the RS-T segment became more depressed in Leads I, II, V3 through V6 and lower esophageal leads, and more elevated in esophageal leads at atrial level. The Q-T interval became shortened.

In 3 patients without any evidence of heart disease, only minimal lowering of the T waves occurred in the surface leads following digitoxin administration. No significant RS-T segment alterations were noted.

In no instance was the RS-T segment depressed in esophageal leads at atrial level re-
fleeting left ventricular cavity potentials either before or after digitoxin administration, nor were there any changes noted in the configuration or duration of the QRS complex.

**Discussion**

From the data which have been presented it is apparent that following the administration of digitoxin the RS-T segment depressions in standard, precordial and lower esophageal leads—the latter reflecting posterior left ventricular surface potentials—were regularly associated with RS-T segment elevation in esophageal leads reflecting left ventricular cavity potentials. The proximity of the esophageal leads at atrial level to left ventricular cavity potentials, and at lower esophageal levels to the posterior surface of the left ventricle, probably accounts for the more marked RS-T changes seen in these leads. The T wave changes in esophageal leads reflecting left ventricular cavity potentials were the opposite of those seen in precordial and lower esophageal leads.

Digitalis in the doses administered had no effect on the configuration or duration of the QRS complex. The persistence after digitalis administration of the ventricular QS or Qr pattern at left atrial levels, representing left ventricular cavity potentials, would indicate that conduction in the left bundle branches remained normal, since delay in conduction in the left bundle branch would be accompanied by initial positivity in the left ventricular cavity. Hence, digitalis did not affect the process of depolarization or conduction in the bundle branches in the present study.

Various investigators have demonstrated that injury to the endocardial aspect of the heart produces depression of the RS-T segment in epicardial leads and elevation of the RS-T segment in intracavity leads. It has also been shown that spontaneous or induced coronary insufficiency affects preponderantly the subendocardial myocardium with resultant RS-T segment depression in left precordial leads. It has also been shown by us that in induced coronary insufficiency, the RS-T segment elevation in esophageal leads reflecting left ventricular cavity potentials probably indicates predominant involvement of the subendocardium.

The administration of very large doses of digitalis preparations to animals has produced myocardial damage, which was reported by Bückner and by Dearing, Barnes and Essex as being chiefly localized to the subendocardium. Some investigators have attributed the electrocardiographic changes produced by digitalis to myocardial involvement, mainly univentricular in localization, as a possible result of reduced coronary blood flow. From the observation of McMillan and Bellet and from the data of the present investigation it is apparent that electrocardiographic alterations due to digitalis are much more readily produced in older persons with diseased hearts than in normal young persons. Whether digitalis further aggravates an already damaged myocardium in patients with or without coronary artery disease is difficult to evaluate. It is interesting to note that "coronary" contour of the T wave may be produced by digitalis in diseased hearts. Also, of some importance may be the fact that RS-T segment changes, similar to those seen in coronary insufficiency, have been observed in normal persons following exercise subsequent to the administration of digitalis, although absent prior to digitalis.

Whether all these changes are due to the direct action of digitalis on the myocardium or result from a reduction of coronary blood flow because of vagal effects is not definitely known. Anatomic lesions following therapeutic doses of digitalis have not been observed in the human or animal heart. It is conceivable that digitalis produces a gradient of myocardial involvement with therapeutic doses causing a biochemical or electrolytic disturbance rather than histologic alteration of the subendocardium. In the present study the RS-T segment became depressed in the precordial leads and in the lower esophageal leads reflecting the posterior surface of the left ventricle and became elevated in esophageal leads reflecting left ventricular cavity potentials following digitalis administration. The RS-T segments had been isoelectric prior to the digitalis. The RS-T segment in Lead V4 became elevated subsequent to digitalis administration. Similar
elevations in Lead VR have been noted in coronary insufficiency\textsuperscript{26, 47} and may be seen in published records following digitalis therapy.\textsuperscript{48} Since Lead VR usually represents predominantly ventricular cavity potentials the RS-T segment deviations are probably similar to those occurring within the ventricular cavities. The above findings, in accord with those of others, indicate that digitalis may produce myocardial involvement affecting predominantly the subendocardial aspect of the heart.

Some authors have attributed the RS-T segment and T wave changes following digitalis administration to modification of the monophasic action potential curves.\textsuperscript{22, 33, 49} These authors believe that the electrocardiogram is a resultant of two monophasic curves, which because of digitalis effects lost their plateau component, with the curves becoming shorter in duration. This would indicate that the repolarization process occurs much more rapidly. Some investigators state that this is especially evident in the endocardial component of the monophasic curves.\textsuperscript{49} These concepts may help to explain the shortening of the Q-T interval and the peculiar configuration of the RS-T segment and T wave in the majority of the patients receiving digitalis (figs. 1 and 2). Although there is some experimental evidence to support the view that digitalis modifies the monophasic curves, some investigators have criticized this explanation, believing that the electrocardiographic changes due to digitalis are a result of myocardial damage.\textsuperscript{19, 20}

Employing the concept of ventricular gradient as advanced by Wilson, Macleod, Barker and Johnston\textsuperscript{46} it has been proposed by Ashman\textsuperscript{21} that the RS-T segment and T wave changes due to digitalis are normal physiologic phenomena dependent upon the relative magnitude of the manifest mean area of the QRS complex (A\textsubscript{QRS}) and of the ventricular gradient (G). In the human heart the presence of a ventricular gradient, which accounts for the upright T wave, is due to the lack of uniformity of the effective duration of the excited state between endocardium and epicardium, especially concerning the repolarization phase.\textsuperscript{41}

In all probability the repolarization process is normally slower in the endocardial than the epicardial aspect of the heart. Local variations in the uniformity of the effective duration of the excited state may lead to RS-T segment and T wave changes.\textsuperscript{50, 51}

According to Ashman, digitalis tends to abolish the human ventricular gradient, so that the time-course of depolarization and repolarization of the cardiac regions is almost equalized. Following the administration of digitalis, the process of repolarization may be shortened most in regions in which it lasted longest,\textsuperscript{22} with repolarization of the subendocardial aspect commencing before depolarization of the epicardial surface has been completed.\textsuperscript{24}

**SUMMARY**

1. Digitalis was administered to 7 patients with and without heart disease.
2. The electrocardiographic changes following digitalis consisted of depression of the RS-T segment in precordial and lower esophageal leads, the latter reflecting the posterior left ventricular surface.
3. The RS-T segment became elevated in esophageal leads, reflecting left ventricular cavity potentials, following digitalis administration.
4. The nature of these changes is discussed.

**ACKNOWLEDGMENT**

We wish to express our appreciation to Dr. Arthur M. Master for his cooperation in making this study possible.

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Circulation. 1950;2:921-928
doi: 10.1161/01.CIR.2.6.921
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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:
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