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Cardiac Tamponade: Fluid and Pressure Effects on Electrocardiographic Changes.* (30852)

JIMMIE C. TONEY† AND SAMUEL N. KOLMEN
Department of Physiology, University of Texas Medical Branch, Galveston

The production of cardiac tamponade by the introduction of gas or liquid into the pericardial space results in both hemodynamic(1, 2,3) and electrocardiographic changes(4,5,6, 7). The electrocardiographic changes are of interest since they are used empirically as criteria for the diagnosis of cardiac tamponade or pericarditis. Among the changes involved are decreased QRS voltage(6,7), elevated RS-T segment and inverted T wave(5, 6). The decreased QRS voltage currently is attributed to decreased conduction through the pericardial space(6,7); whereas, the other electrocardiographic changes are thought to result from mechanical injury of the sub-epicardial muscle layers(8).

This study was undertaken to evaluate these explanations of the empirical observations. Studies performed included the effect of a) increased fluid volume in the pericardial sac, b) altered volume conduction, c) positional changes of the heart, and d) diminution of right atrial inflow on electrocardiographic recordings and on arterial and venous pressures.

Methods. Mongrel dogs, used without regard to age, sex, or weight, were anesthetized with sodium pentobarbital (30 mg/kg body weight) by intravenous injection. A tracheostomy and thoracotomy were performed. After the midsternal thoracotomy was begun the dogs were ventilated by a Harvard 607 positive pressure respirator using ambient air. Standard limb leads were recorded in all procedures by the use of needle electrodes.

Central venous pressure was recorded with a polyethylene catheter (Clay-Adams PE 240) inserted through the right external jugular vein. The open end of the catheter was positioned in the superior vena cava approximately 3 cm cephalad to the right atrium. Arterial pressure was recorded from the arch of the aorta by a catheter inserted through the left femoral artery. Intrapericardial pressure was measured by a cannula sewn through the pericardial sac (Fig. 1). All pressures were transmitted through P23AC Statham strain gauges to a Grass model 5 polygraph as were the electrocardiographic findings. The recordings were obtained at a paper speed of 25 mm/sec. The data were analyzed by the "t" test for paired samples (9). A "P" at the 0.05 level was considered to be significant.

Procedures. In all instances a control record of at least 15-minute duration was obtained prior to any of the following procedures. Data were collected for at least 2 minutes after initiation of the experimental procedure. Each animal served as its own control.

Series A. An increase in pericardial pressure was imposed on 4 dogs using nitrogen gas under a maintained pressure head of 55 mm of Hg.

Series B. An increase in pericardial pressure was imposed on 7 dogs using a high-conductance liquid (Ringer's solution or serum) under a maintained pressure head of 55 mm of Hg. Conductance of these liquids was between 1.16×10^{-2} and 1.25×10^{-2} mhos,

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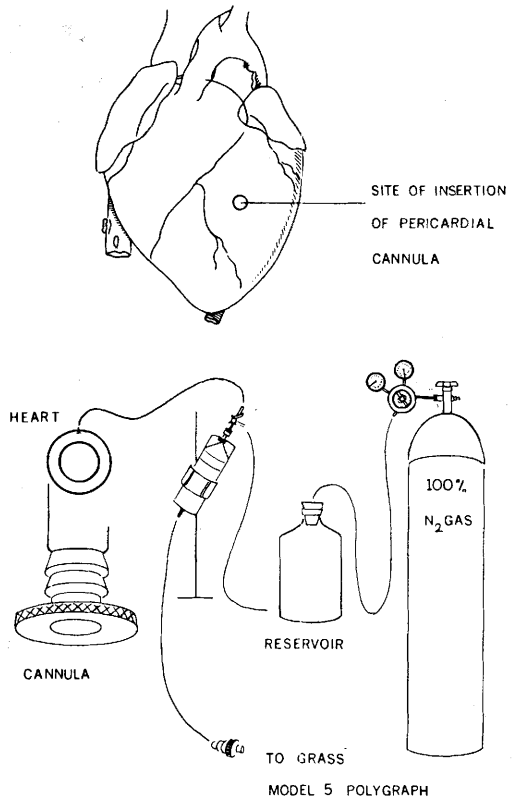

FIG. 1. Schematic diagram of tamponade preparation.

Series C. An increase in pericardial pressure was imposed on 8 dogs using a low-conductance liquid (mineral oil or 10% sucrose) under a maintained pressure head of 55 mm of Hg. Conductance of these liquids was less than 4×10^{-6} mhos.

Series D. An infusion of a liquid into the pericardial space without a measurable decrease in arterial pressure was performed on 5 dogs. The infusate used was 10% sucrose or mineral oil.

Series E. A decrease in venous return to the right atrium by simultaneous and complete ligation of the vena cava and azygos vein was imposed on 8 dogs.

Series F and G. An alteration in the position of the heart within the thorax was accomplished by the use of a lifting ligature secured in the pericardial sac in 4 dogs. The lifting ligature was sewn into the pericardial sac at the same site used in the tamponade procedures to secure the catheter into the pericardial sac (Fig. 1). Two procedures were performed on each animal. These were: (Series F) a pull of the ligature administered perpendicular to the surface of the heart and (Series G) a pull administered parallel to the surface of the heart. The perpendicular pull was one sufficient to move the apex of the heart 1-2 cm anteriorly, and the parallel pull was with an equivalent force.

Series H. In this series of 4 dogs the electrodes were placed in closer proximity to the heart in order to compare the potential differences of these electrodes with the potential differences of standard limb lead II. In 2 of the dogs the potential difference between an electrode catheter in the right atrium and an electrode catheter in the left ventricle was compared with lead II of the same dog. In the remaining 2 dogs, the potential difference between the electrodes inserted in the left and right ventricular wall was compared with lead II of the same dog. The tamponade procedure described in Series B was then performed on these animals.

Results. Fig. 2-9 illustrate typical recordings of lead II obtained with each procedure. Table I incorporates the mean per cent change and standard deviation for measurements in each series. The measured variables include mean arterial pressure, central venous pressure, heart rate, P-wave amplitude, R-wave amplitude, S-T segment deviation, and T-wave amplitude.

In Table I (Series A, B, C and H) it will be noted that successful induction of tamponade resulted in an increase in central venous pressure, a decrease in mean arterial pressure, and a slight decrease in heart rate. Similar changes were also observed with respect to Series E and F. The amplitude of the P-wave increased and the R-wave decreased in each series in which hemodynamic changes occurred and were unchanged when no hemodynamic alterations were observable (Table I, Series D and G).

The changes with respect to the S-T segment were not as uniform as those presented above (Table I). The S-T segment shifted above the base line when hemodynamic changes occurred and when additional fluid

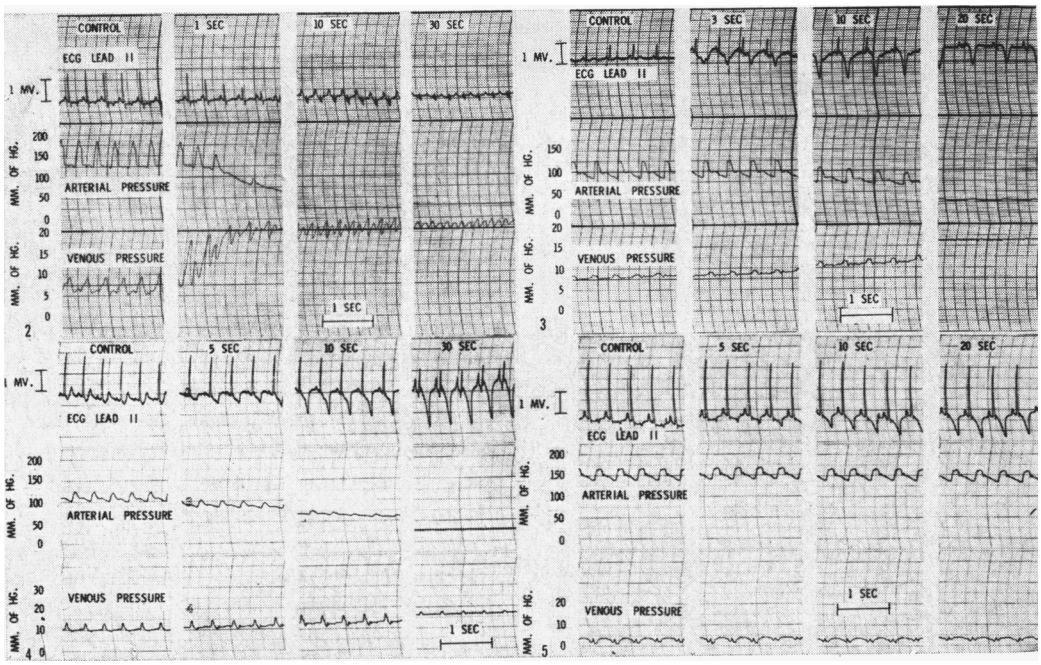

FIG. 2. Nitrogen gas tamponade.
FIG. 3. High conductance liquid tamponade.
FIG. 4. Low conductance liquid tamponade.
FIG. 5. Liquid into pericardial space without arterial pressure decrease.

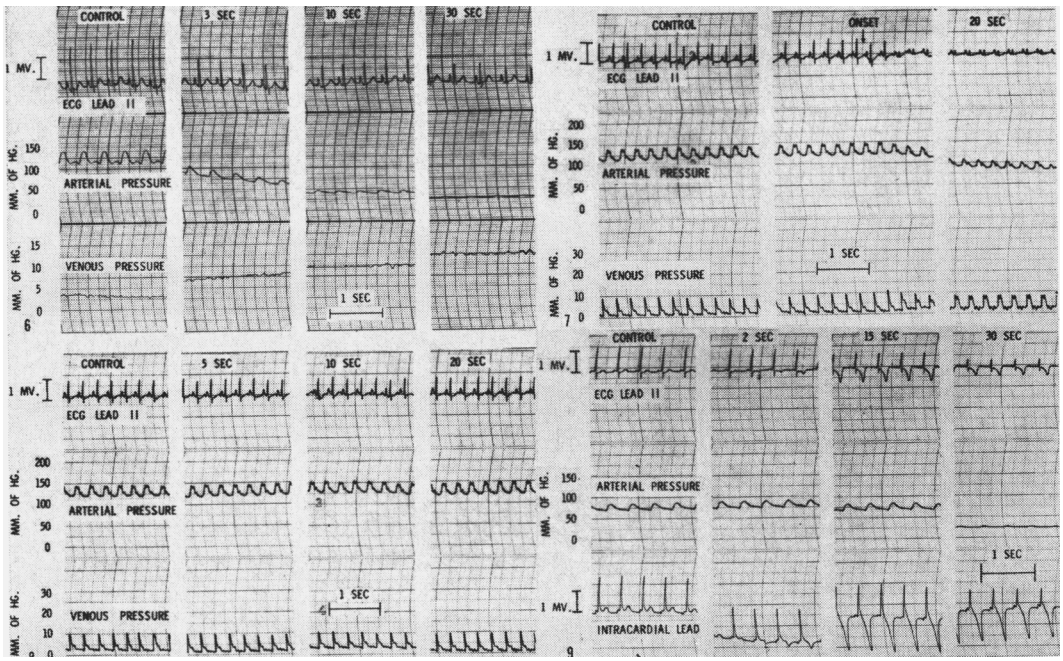

FIG. 6. Venous ligation.
FIG. 7. Lifting ligature in the pericardial sac, perpendicular pull.
FIG. 8. Lifting ligature in the pericardial sac, parallel pull.
FIG. 9. High-conductance liquid tamponade, ECG electrodes in right atrium and left ventricle.

TABLE I. Compilation of Hemodynamic and Electrocardiographic Changes.*

Series	P-wave amplitude	R-wave amplitude	S-T segment	T-wave	Heart rate	Arterial pressure	Venous pressure
A: Tamponade with nitrogen gas	+44% ± 20 P = .05	−80% ± 8 P = .001	0	0	−11% ± 2 P = .01	−80% ± 4 P = .001	+128% ± 63 P = .01
B: Tamponade with high-conductance liquid	+38% ± 32 P = .05	−80% ± 19 P = .001	Elevated	−540% ± 31 P = .001	−22% ± 14 P = .01	−74% ± 13 P = .001	+131% ± 64 P = .01
C: Tamponade with low conductance liquid	+66% ± 28 P = .001	−57% ± 26 P = .001	"	−488% ± 23 P = .001	−17% ± 17 P = .001	−78% ± 3 P = .001	+148% ± 57 P = .001
D: Liquid in pericardial sac, no decrease in arterial pressure	0	0	Variable	−423% ± 18 P = .001	0	0	0
E: Venous ligation	+36% ± 25 P = .01	−65% ± 16 P = .001	Depressed or 0	+ 62% ± 52 P = .05	−23% ± 19 P = .05	−61% ± 16 P = .001	+488% ± 259 P = .01
F: Ligature in sac, perpendicular pull	+32% ± 2 P = .001	−67% ± 3 P = .001	0	− 46% ± 5 P = .001	0	−56% ± 5 P = .001	+ 50% ± 4 P = .001
G: Ligature in sac, parallel pull	0	0	0	0	0	0	0
H: Tamponade with high conductance liquid, electrodes on or in heart	+33% ± 3 P = .001	−68% ± 3 P = .001	Elevated	−523% ± 36 P = .001	−27% ± 6 P = .01	−69% ± 3 P = .001	Not measured

* Mean percent change ± standard deviation. P value <0.05 considered significant. 0 = No change.

was present in the pericardial sac (Table I, B, C, H). If only one of the foregoing conditions was present, the S-T segmental changes were variable or absent (Table I, A, D, E, F). The application of positive pressure to the pericardial space in itself was not adequate to cause an S-T segment change (Table I, A).

A 4- to 5-fold decrease in the amplitude of T-wave was observed in all animals receiving an additional volume of liquid in the pericardial space (Series B, C, D and H). Table I also illustrates the following: systemic pressures were altered in nitrogen gas tamponade (Series A) without any change in T-wave amplitude; systemic pressures were altered with a decrease in T-wave amplitude in all fluid tamponade series (Series B, C, D, F and H); systemic pressures were altered with an increase in the T-wave in the venous ligation series (Series E); and finally, there was a 4-fold decrease in the T-wave without an alteration of systemic pressures with sucrose or mineral oil injection (Series D). Although the above T-wave changes occurred within 2 minutes after initiation of the respective procedures, the onset of these changes occurred within 3-5 beats.

The changes in electrical potentials obtained from electrodes on or in the heart occurred simultaneously with those changes observed with standard limb lead II (Fig. 9). The changes associated with induction of tamponade in the Series H animals were similar to those observed in the Series B animals (Table I).

In Table I it will be observed that the pull perpendicular to the surface of the heart (Series F) resulted in electrocardiographic and hemodynamic changes described previously, whereas a pull parallel to the surface of the heart (Series G) failed to cause any changes.

Discussion. The results of this study are consonant with the widely known fact that in all procedures which produce a decrease in the venous return to the heart there is a decrease in arterial pressure and an increase in the central venous pressure. These hemodynamic changes can be attributed to an increase in the central resistance to venous return and the development of inflow stasis. This leads to a rise in central venous pressure, a decrease in cardiac output and a consequent fall in arterial blood pressure.

The electrocardiographic changes produced by procedures which decreased venous return are in agreement with those which have been reported to occur in pericarditis. These changes include a low voltage R-wave, an elevated S-T segment and a negative T-wave. The low voltage of the R-wave has been postulated(10) to be due to one or a combination of 3 circumstances: a change in the electrical properties of the tissues surrounding the heart, a change in the position of the heart, and an organic or functional "diffuse alteration" of the myocardium. The S-T segment and T-wave changes have been attributed to delayed repolarization at the epicardial surface(11) and to injury of the epicardial tissue(8).

In comparing tamponade with nitrogen gas (Table I, Series A) and tamponade with high or low conductance liquids (Series B, C, H), there are several obvious differences. The S-T segment showed no change with gas but was elevated with either liquid. The T-wave was unaltered with nitrogen gas but became inverted and increased in depth with the use of high- and low-conductance liquids. The introduction of liquid into the pericardial space without causing hemodynamic changes (Table I, Series D) also resulted in S-T segment and T-wave changes. Thus the S-T segment elevation and the T-wave inversion appear to be related to the presence of additional fluid in the pericardial space and independent of hemodynamic changes.

The changes in repolarization might be attributable to temperature differences arising from the introduction of gas or liquid. This possibility was negated in preliminary studies since introduction of liquids heated to 25°C and to 40°C failed to show significant differences in response.

On the other hand, amplitudes of the P and R waves were altered only in the experiments in which hemodynamic changes occurred. This was observed in the presence (B, C, H) or absence (A, E, F) of liquid; in the presence (A, B, C, H) or absence (E, F) of increased pericardial pressure.

Upon venous ligation, the S-T segment was depressed rather than elevated as in the liquid tamponade; the T-wave increased in amplitude rather than decreased as observed in the procedures involving liquid in the pericardial space. This reversal of direction during venous ligation appears to result from factors different than those involved in the fluid tamponade procedures. Changes in ion concentration extracellularly during the venous ligation procedures might account for the observed S-T segment and T-wave changes. Soloff *et al*(12) found that, with low (1-2 μg/kg) concentrations of potassium chloride injected into the left coronary artery, the T-wave would reverse direction; *e.g.*, an upright T-wave would become diphasic and finally negative, whereas at a higher concentration (6 μg/kg), the T-wave would increase in amplitude and there would be an elevation of the S-T segment. Thomas *et al* (13) reported that an elevation of the S-T segment often is associated with tall peaked T-waves and that tall T-waves are associated with hyperkalemia.

The series in which a pull was administered to the pericardial sac was taken to confirm or rule out the effects of changes in cardiac position on the EKG. A pull perpendicular to the anterior surface of the pericardial sac (Table I, Series F) resulted in an increase in amplitude of the P-wave (+32%), a decrease in amplitude of the R-wave (—67%), and a decrease in amplitude of the T-wave (—46%). The major effect seen here was an alteration of the position of the heart, causing the apex to lie more anteriorly than normal. In addition, there was some restriction of atrial filling due to pressure from the pericardial sac on the lateral aspects of the atria and due to crimping of the vena cavae. A pull on the sac parallel to the surface (Table I, Series G) resulted in none of the above changes; therefore, an increase in lateral pressure on the atria probably is not involved.

The P-wave increased in amplitude in all of the procedures that produced a decrease in arterial pressure. Lepeschkin(8) attributed an elevation of the P-wave to an increase of the muscle membrane potentials. He observed that an increase in amplitude of the P-wave may be caused by tachycardia, and that it could be recorded even after the heart rate returned to a normal rate. It is proposed that the increased amplitude of the P-wave might also be explained by an alteration of the anatomical axis of the heart, since a pull on the pericardial sac perpendicular to the surface of the heart at the point of attachment of a lifting ligature also increased the P-wave amplitude (Fig. 7). Perhaps this can be attributed to an increased amount of tissue in the plane of the recording electrodes.

To evaluate the role of volume conduction in lowering the amplitude of the R-wave, 4 animals were used in 2 additional tamponade procedures with electrodes on or in the heart in addition to the standard limb leads (Table I, Series H). In all 4 animals the electrocardiogram from the specially placed electrodes paralleled the pattern observed in the standard lead II (Fig. 9). The decrease in R-wave, elevation of the S-T segment, and inversion of the T-wave occurred simultaneously and to the same degree in both tracings. These results suggest that volume conduction is not contributory to the lowering of the amplitude of the R-wave.

Coronary flow was not a likely initiating factor in the P- and R-wave changes. In the procedures involving a decrease in arterial pressure there was a decrease in amplitude of the R-wave which occurred 4-6 heart beats prior to the decrease in arterial pressure (Fig. 2, 3, 4, 6, 7 and 9). Coronary flow most likely was reduced shortly thereafter and may have augmented the electrocardiographic changes observed.

The majority of the procedures involving an infusion of a liquid into the pericardial space showed an elevation of the S-T segment (Fig. 3, 4 and 9). This finding is consistent with those noted during pericarditis, and is suggestive of coronary insufficiency, particularly since the S-T segment elevation occurs late in the procedure and only after arterial pressure decreased to below 40 mm of Hg. Inadequate blood flow through the coronary arteries may have resulted from reduction in lumen diameter due to an in-

creased pressure on the epicardial surface and due to a decrease in pressure.

Summary. Dogs were subjected to various procedures in an attempt to clarify several existing theories about the electrocardiographic findings in pericarditis or cardiac tamponade. In this study changes in P- and R-wave amplitude are related to decreased arterial pressure and increased central venous pressure. Problems related to volume conduction are not involved in the decreased R-wave amplitude. The presence of additional fluid in the pericardial space results in S-T segment shift and T-wave inversion. Changes in the S-T segment require the additional factor of a systemic pressure change whereas the latter is independent of pressure changes. The shift in anatomical axis of the heart in a direction which impinges on the venous return to the right atrium will cause P- and R-wave changes and may be an important factor in the etiology of the electrocardiographic changes. Coronary insufficiency, on the basis of these studies, is not thought to be contributory to early electrocardiographic changes but may be of significance in later stages of pericarditis.

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Effect of Thymectomy in Newborn Rats Infected with Moloney Virus.* (30853)

NATALIE E. CREMER, DEE O. N. TAYLOR AND MARGARET MACGILLIVRAY†
(Introduced by Edwin H. Lennette)
Viral and Rickettsial Disease Laboratory, California Cancer Field Research Program, State Department of Public Health, Berkeley, Calif., and Children's Service, Massachusetts General Hospital, Boston

Thymectomy in mice as late as 31-71 days of age reduces the incidence of spontaneous leukemia in a high-leukemia stock of mice (1). Similarly, thymectomy reduces the incidence of induced leukemia in mice injected with a leukemogenic virus(2,3). Only a small percentage of mice thymectomized at 3-4 weeks of age and inoculated with a leukemogenic virus either as newborns or after thymectomy develop leukemia, and then only after a long latent period(4-6). Gross(7) reported that rats injected as newborns with Gross virus, passage A, and thymectomized at 10 days of age, are somewhat resistant to induction of leukemia but to a much lesser extent than are thymectomized mice. The present study was initiated to determine if thymectomy of rats at 24 hours of age, and prior to virus inoculation, would increase

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† Present address: Division of Human Genetics, Dept. of Pediatrics, Children's Hospital, Buffalo, N. Y.