nic) and of antipyrine was compared following the intravenous administration of the 2 substances to 12 normal humans. The antipyrine space averaged 1.8 liters higher than the NAAP space (Table III).

Use of NAAP for the measurement of body water in the dog. NAAP disappears from the dog at a rate of about 20% per hour. Only about 60% of the NAAP administered to a dog can be accounted for in the urine; the remainder is metabolized. Only the extrapolation procedure, therefore, can be applied to the dog. A dose of about 50 mg per kg will result in plasma levels which can be measured accurately.

Summary. The use of N-acetyl 4-aminoantipyrine (NAAP) in the measurement of body water has been explored. The substance is uniformly distributed in the various tissues in close proportion to the water content, its metabolism is negligible and it is excreted slowly. The volumes of distribution of antipyrine and NAAP were compared in normal human subjects and the values found to agree well. NAAP has certain advantages over antipyrine: it is negligibly bound to plasma proteins; the value for body water may be calculated from a single plasma sample and a urine sample; its colorimetric estimation obviates the need for an ultraviolet spectrophotometer.

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Characteristic Pressure Pulses Recorded with an Esophageal Balloon in Experimental Mitral Insufficiency in Dogs.* (18929)

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This is a study of the pulsation attributable to cardiac activity which can be recorded in the esophagus at the level of the left atrium. It was undertaken to investigate the potentialities of the technic with regard to the diagnosis and possible quantitation of mitral insufficiency. The work of earlier investigators(1-3) along these same lines had not succeeded in conclusively establishing the origin and form of the various pulse waves observed in the esophagus nor was their relationship to events occurring within the left atrium ever clearly demonstrated. Even the work of Taquini(4) and of Puddu and Sibilia(5) was not completely convincing, though it tended to show that a characteristic pattern could be observed in mitral insufficiency in humans. The curves which they obtained, however, showed comparatively minor alterations from those found in normal individuals. Moreover, the patterns did not resemble either the left atrial pressure or volume curves obtained experimentally by Wiggers in dogs with acute mitral insufficiency(6).

All earlier recording had been done with air filled latex balloons attached to elastic rubber tubing. The pressure sensitive element was a rubber diaphragm. Such elastic, air filled systems allow for substantial volume displacement, and therefore record volume changes but do not accurately portray pressure variation. To render the apparatus more sensitive to pressure change the volume displacement permitted in the system was reduced by employing (1) a water filled balloon and completely water filled system; (2) polythene tubing; (3) a relatively rigid pressure

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sensitive element, *i.e.* Sanborne electromanometer.

It was also observed that as the balloon was distended with successive volumes of fluid, a point was reached beyond which equal increments of volume resulted in decreasing increments of pressure within the system. Therefore, when recordings of the pulse pressure within the esophagus were made, the balloon was distended to that degree at which least increases of volume resulted in greatest increases of pressure. At first latex condoms were used. Later it was found that heavier rubber such as that in rubber gloves gave a more desirable pressure volume relationship.

This is certainly in no sense a rigid, isometric system since both the balloon and the esophagus itself are distensible. However, it is more so than the previously used elastic, air systems and the tracings obtained are surprisingly similar to pressure tracings obtained simultaneously within the left atrium.

Method. The esophageal tube consisted of a length of polythene tubing whose inner diameter was 3.5 mm. One end was sealed and 2 openings into the lumen were cut in the sides of the tube about 3 cm from the sealed end. The rubber balloon was secured to the tube so as to cover both openings. A 3-way stopcock, attached to the open end of the tube, served to connect it with a saline filled syringe and the lead tubing leading to the pressure transducer. All pressures were recorded with Sanborne electromanometers and a 4-channel Sanborne direct writing electrocardiograph. Paper speed was 50 cm per sec. so that each small vertical division represented 0.02 sec.

Pens were aligned so as to write synchronously. Since both the esophageal and atrial pressures were transmitted approximately equal distances through fluid filled rigid tubing, it was felt that no differences in timing existed.

Adult dogs were anesthetized with nembutal. Endotracheal and esophageal tubes were inserted The esophageal balloon was distended with saline as previously described. This resulted in a static pressure within the system of between 9 and 17 mm of Hg. Tracings were then taken at various levels within the esophagus. Intermittent positive pressure respiration was begun, the chest was opened and the balloon was fixed at the level of the left atrium. A left, superior pulmonary vein was ligated distally and a No. 8F cardiac catheter inserted through it into the left atrium. Simultaneous atrial and esophageal pressure curves and lead II of the electrocardiogram were then recorded. Mitral insufficiency was then produced through an incision in the atrial appendage. At the conclusion, the dogs were sacrificed and the hearts examined to verify the degree and location of the lesions.

Results. The curves obtained in 18 normal animals and in 8 following the production of mitral insufficiency are sufficiently similar so that a detailed description of representative samples will illustrate the main features of the entire group.

In Fig. 1 are shown: (A) esophageal pulsation in the normal animal with closed chest, (B) same animal after the pericardium has been opened, (C) same animal following the production of mitral insufficiency. The first pulse wave tracing (A) is typical of that observed in the intact animal. It is characterized by a positive presystolic wave which follows the onset of the P wave of the electrocardiogram by 0.04 to 0.06 sec. It is similar in contour and timing with the wave of atrial systole observed in the atrium itself. This is followed by a series of rapid oscillations, which occur during the first heart sound and probably represents its low frequency components. The exact onset of ventricular systole is difficult to judge exactly. During the period of ventricular systole, the pressure either falls somewhat as in this illustration or remains at the level reached at the end of atrial systole. The curve then rises in a gentle slope and a second set of rapid oscillations is superimposed upon its summit. These are found to occur during the second heart sound and to just precede the fall in pressure which marks the reopening of the mitral valve.

The tracings seen in Fig. 1B show that the opening of the pericardium has not modified the pulse contour appreciably and the same

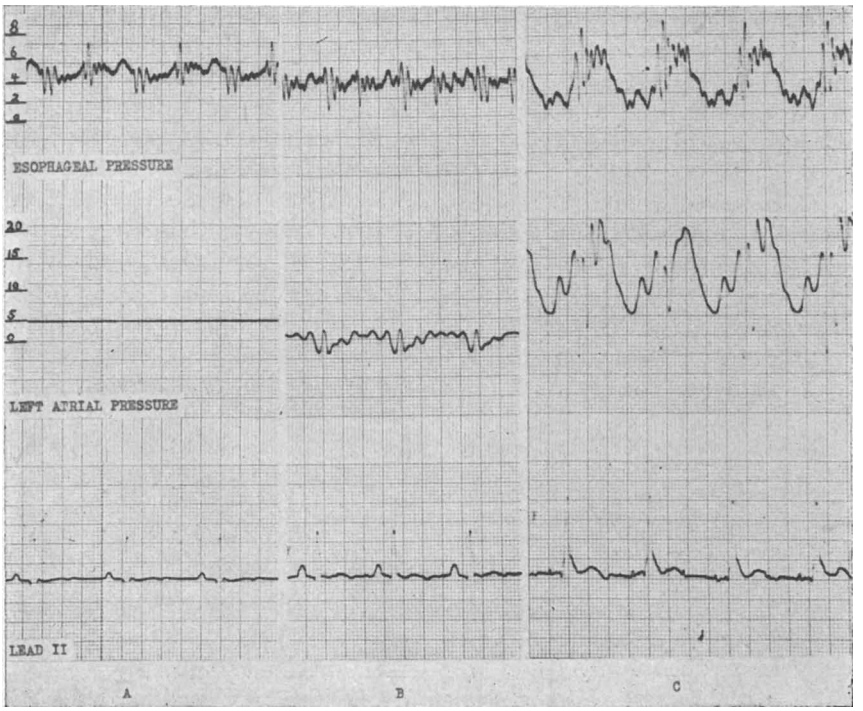

FIG. 1. A. Esophageal pressure tracing and Lead II of electrocardiogram in a dog with a closed chest. B. Esophageal (above) and left atrial (middle) pressure tracings in the same dog after pericardium had been opened. C. Pressure tracings following production of mitral insufficiency, showing characteristic early pressure elevation and sustained systolic plateau.

general features are noticed as in Fig. 1A. The pressure curve obtained directly from the atrium (middle trace) needs no comment. The only noticeable feature is the pronounced wave of mitral closure. This has been observed similarly by Wiggers in dogs(6).

The tracings seen in Fig. 1C, following the cutting of the valve, give unmistakable evidence of mitral insufficiency both in the esophageal (top) and the atrial (middle) pressure tracings. In both, a positive wave of atrial systole is easily identified. The beginning of ventricular contraction is signalled by a sharp rise of pressure beginning 0.04 sec. after the Q wave of the electrocardiogram. The atrial pressure curve displays several marked pressure oscillations during the early phase of ventricular ejection, then a sustained late systolic plateau is seen wherein the atrial pressure maximum is reached. Finally, a rapid fall in pressure marks the opening of the mitral valve. The approximate mean atrial pressure has risen from 0 mm of Hg to about 12 mm of Hg. The pulse tracings obtained synchronously in the esophagus display, with minor differences, the same features as the atrial curve itself. Evidence of the regurgitation jet early in the course of ventricular ejection is shown by the early, sharp elevation of the curve. The late systolic plateau followed by the precipitous descent of the curve also parallel the atrial pressure curve very closely.

There was no attempt made to maintain a constant basal pressure line or zero line in esophageal tracings, and these tracings were arbitrarily centered. The chief interest lay in the determination of the form of the pulse wave and in the calculation of the pulse pressure. This proved to be 13 mm Hg in the atrium and 5.5 mm Hg in the esophagus.

Fig. 2 shows a series of tracings, obtained successively as this animal was bled to death. It is seen that both the mean atrial pressure and the pulse pressure resulting from the regurgitation jet, decline in the successive trac-

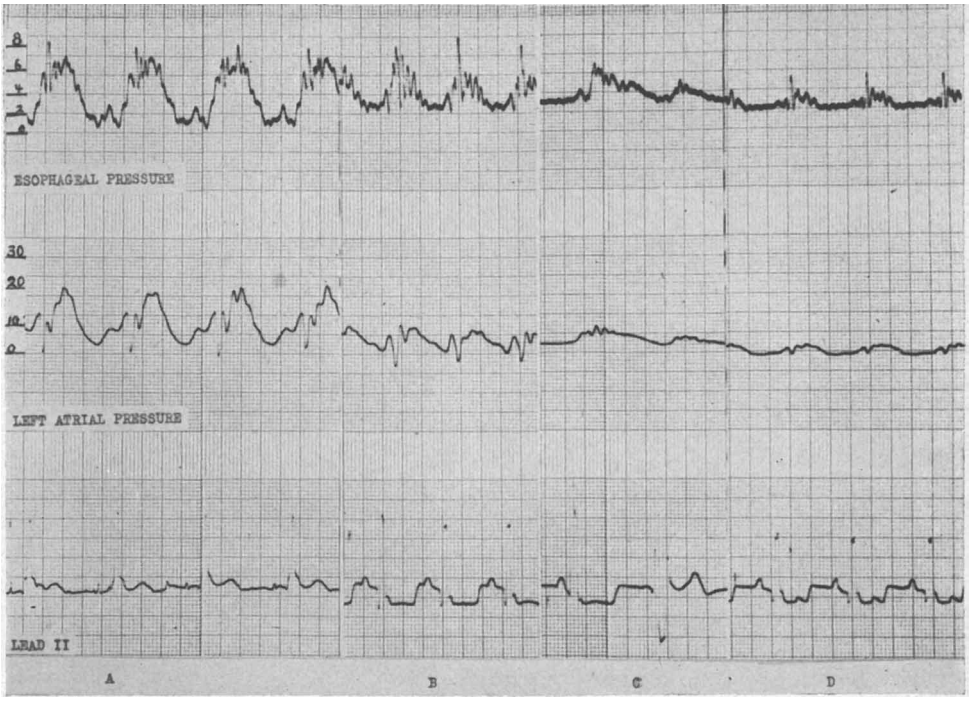

FIG. 2. Tracings A, B, C, and D show successive decline of pulse pressure as the animal was bled to death.

ings. This decline in pulse pressure is almost linearly reflected in the esophageal pulse curve.

In order to demonstrate that the elevated pressure seen during ventricular systole in the esophageal tracings was not somehow due to an arterial impact, the aorta was compressed at its roots. Fig. 3 shows the tracings obtained in another dog in whom mitral insufficiency had been produced, just prior to compression of the aorta (A), during compression (B), and as the aorta was released (C). The compression of the aorta resulted in an increase in the maximum atrial pressure from 16.6 mm of Hg to 110 mm Hg. This is an increase of more than 600%. The pressure in the atrium just prior to ventricular systole increased from —3 mm of Hg to 40 mm Hg. The pulse pressure in the atrium during ventricular systole, therefore, increased from 19.6 mm of Hg to 60.0 mm of Hg. This phenomenon of an increased regurgitation pressure following increase of peripheral resistance was originally shown by Wiggers(6).

The pulse tracings from the esophagus show an elevation of maximum pressure (6 to 15.5 mm of Hg), elevation of the end diastolic filling pressure (0.6 to 6 mm of Hg) and increased pulse pressure (5.4 to 9.5 mm of Hg). There is, unfortunately, no linearity between the atrial and esophageal pressure values at the two levels. The ratio between the atrial and esophageal pulse pressures, for example, is 3.6 to 1 at low pressures and 6.3 to 1 at the high levels. This decreasing responsiveness at high levels of pressure is to be expected, since the balloon becomes progressively more distensable as the pressure within the system rises. However, at low pressure levels there is a rough correlation between the magnitude of the pulse pressure recorded within the atrium and that in the esophagus during ventricular systole. The average pressure ratio observed in the eight animals with mitral insufficiency was 3.3 to 1 with a range of 2.3 to 4.0. The range of pulse pressure variation in the atria was from 7 to 20 mm of Hg and that in the esophagus was 2.5 to 7 mm of Hg.

Summary and conclusions. Pulsations in

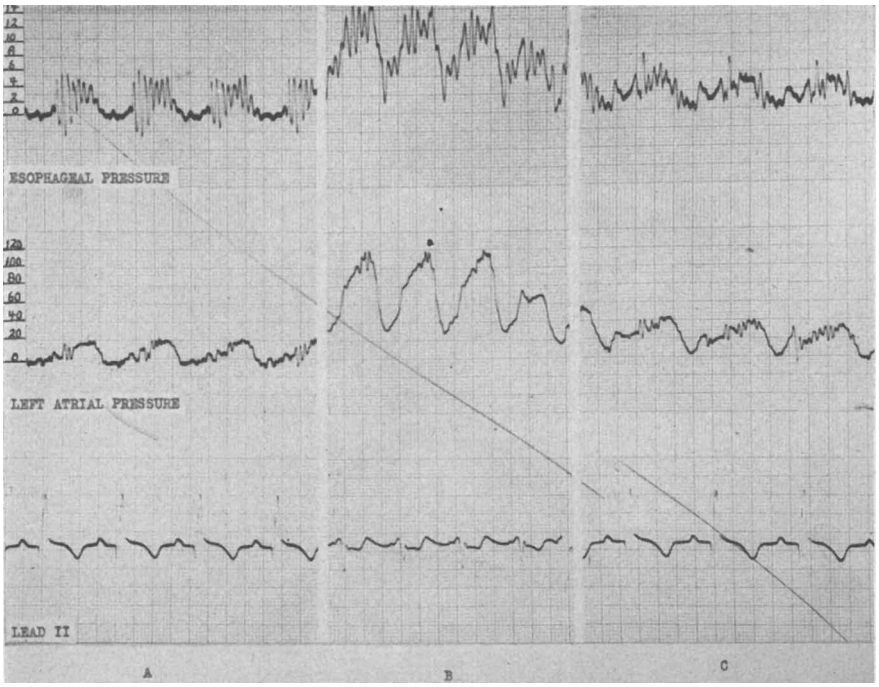

FIG. 3. A. Pressure tracings following production of mitral insufficiency. B. Pressure tracings in the same animal during compression of aorta at its root. C. Tracings after release of aortic compression.

the esophagus at the level of the left atrium and pressure pulses within the left atrium were simultaneously recorded in normal dogs and in the same animals following the production of mitral insufficiency.

An identifiable and consistent pattern in the esophageal tracings was observed in the normal animals. Following the production of mitral insufficiency, characteristic alterations of the esophageal pulse wave contour were observed. These very closely paralleled the pressure tracings obtained simultaneously within the left atrium itself.

It was also possible to detect a fall of the regurgitation pressure which resulted from hemorrhage or a rise which was produced by aortic compression. A ratio of approximately 3 to 1 was observed between simultaneously recorded atrial and esophageal pulse pressures in the dogs with mitral insufficiency.

It is suggested that the contour of the pulse waves of the esophagus at the level of the left atrium, recorded with this technic, closely reflects that of the pressure pulses of the left atrium and that, within limits, a pressure relationship of a quantitative nature exists.

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