curves, and intracavitary potentials. Some adults and most children have veins too small to allow passage of the usual double lumen catheter electrode.

During the procedure of introducing the catheter, electrocardiographic tracings from the tip of the catheter are valuable in determining the exact anatomical location of the tip. We have found that changes in the contour of the P and QRS complexes may be a more reliable index of the location of the tip of the catheter than either the fluoroscope or the pressure curve, especially in the region of the lower right atrium near the tricuspid valve, or in the coronary sinus.

Summary. A new technic is described to obtain intracavitary cardiac potentials through the single lumen saline filled cardiac catheter without use of the usual copper wire electrode. If the exploring terminal of an electrocardiograph is connected to the open arm end of a column of blood or saline in a catheter which has been introduced into the cavity of the heart, and if the indifferent electrode is connected to a central terminal, the completed curve will represent chiefly the fluctuations of intra-cardiac potential at the tip of the catheter.

Prior to submitting this article for publication we were unaware of the report of Kisch *et al.*, *J. Mt. Sinai Hosp.*, 1948, **15**, 257, who described a similar technic although he advocates the introduction of a thin wire into the catheter to avoid a.c. interference.

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17079. Reflex Modulation of Heart Rate on Closure and Opening of an A-V Fistula.*†

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Branham[1] described the well known slowing of the heart rate which ensues upon temporary obliteration of an A-V fistula by digital compression. The reverse phenomenon, *viz.*, increase in heart rate, also takes place when the pressure is released. That the vagus nerves are the efferent pathway of the reflex arc responsible for this reaction has been demonstrated by Weber,[2] Lewis and Drury,[3,4] and Holman,[5] by use of atropinization techniques. While it is logical to infer that the sinus and aortic nerves constitute the afferent arcs from the arterial side, the possibility that afferents from the venous side may also be concerned has not been excluded. Since closure of an A-V fistula causes a fall, and opening a rise of central venous pressure,[6] such changes in pressure could evoke reflex alterations in heart rate if the Bainbridge reflex is operative. The question as to which afferent pathways are dominantly and subdominantly concerned was therefore resubmitted to experimental study.

Method. Dogs varying in weight from 10 to 12 kilos were anesthetized with chloralose because this anesthetic increases the sensitivity of the cardio-inhibitory mechanism, whereby the vagal tone is well maintained. An

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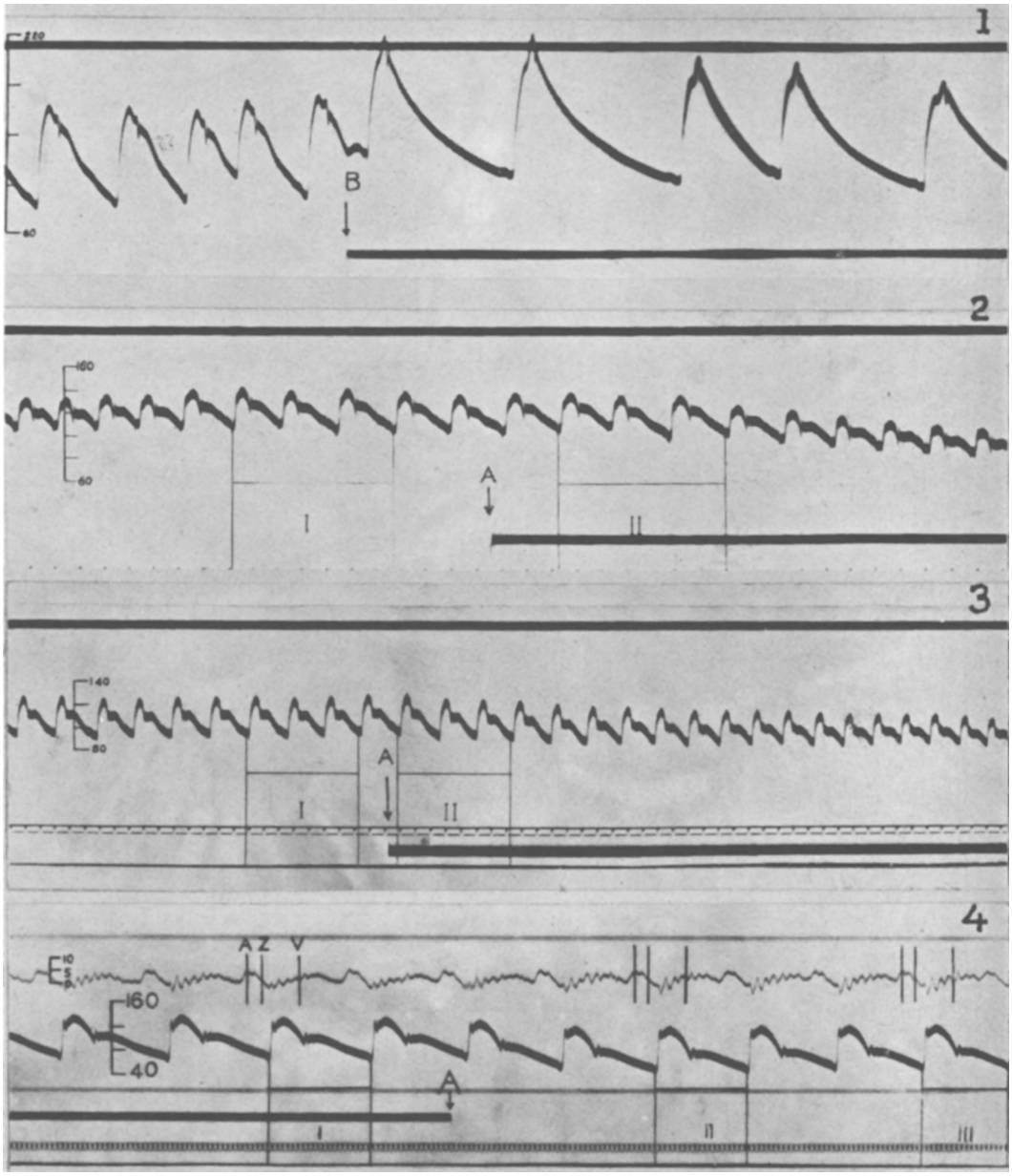

FIG. 1. Aortic pressure pulses showing the effect of closing (B) an A-V shunt on aortic pressure and heart rate. Time, 0.2 sec.

FIG. 2 and 3. Effect of closing an A-V shunt (A) during stabilization of arterial pressure by simultaneous withdrawal of blood. Time, 0.2 sec.

FIG. 4. Effect of opening an A-V shunt (A) on right atrial pressure (upper) and aortic pressure (lower). Time, 0.02 sec.

initial dose of 75 mg per kilo was followed by 15 mg per kilo every hour. Bilateral anastomoses were made between the femoral artery and femoral vein of each side. These vessels were first cannulated and then joined by rubber tubing. A hemostat was used to open and close the circuit thus produced. Optical manometers of adequate sensitivity

and calibrated against a mercury manometer under static conditions were used to register aortic pressure pulses. Mean blood pressure was determined by planimetry of 3 successive heart cycles.

Experiments. Control reactions were first recorded by simply opening and the closing arterio-venous shunts. It was observed that there was always an increase in heart rate with fall of arterial pressure on opening the shunts, and a lowering of the heart rate with rise of arterial pressure on closing the shunts. Fig. I illustrates an experiment in which closing of the shunts at B caused diastolic pressure to rise immediately and the heart rate to slow to a pronounced degree.

In all of these control experiments it was found that the change in heart rate on opening of the shunts took place within 1 to 5 beats (average 1.4 seconds), and maximum slowing developed within 3 beats after closure of the shunts. The fact that this slowing of the heart rate is always preceded by a rise of pressure on closing the shunts naturally suggests that the carotid sinus and aortic nerves constitute the afferent pathways.

To test this hypothesis an effort was made to maintain arterial pressure constant after closure of the shunts. By repeated trials it was found that this could be accomplished in a reasonably satisfactory number of experiments by inserting a Y-tube into one of the A-V anastomoses, through which blood could be withdrawn from the animal at the moment that the venous limb of the Y was closed. By this expedient the animal could be bled from the femoral artery at a rate adjusted to counteract the normal rise in arterial pressure. While it was difficult to maintain an absolutely constant level of mean arterial pressure before and after closure of the shunts in all cases, a sufficient number of records were realized in which no changes or only insignificant alterations in arterial pressure took place. A plot of all experiments in which arterial pressure rose, essentially remained unchanged, or fell, indicated that slowing of the heart rate always accompanied a definite rise in arterial pressure. The change in heart rate on fall of arterial pressure was not so uniform. When this was less than 5 mm Hg acceleration was not a constant feature. In 4 cases moderate acceleration was observed, and in 6 a definite slowing. Two records free from sinus arrhythmia are reproduced in Fig. 2 and 3. In both of these the change in heart rate is strikingly small as compared to that shown in Fig. 1. Calculation showed that in the curve of Fig. 2 a slight slowing of the heart rate takes place without any rise in arterial pressure. Actual measurement revealed a reduction during period II which would be equivalent to 5 beats per minute as compared to period I, in spite of a fall in mean pressure of 3 mm Hg. In Fig. 3 the slowing is even less, being equivalent to two beats per minute with a fall of mean arterial pressure of only 1 mm Hg.

It is tempting to accept the corollary that the small changes in heart rate which still persist when arterial pressure remains stabilized is occasioned by the Bainbridge reflex. Before this assumption may be accepted, however, it is important to establish that venous pressure is in fact reduced by closure of a shunt. For this reason, several experiments were carried out in "open chest" animals in which right atrial pressure was recorded by an optical manometer. No convincing evidence of a significant change of right atrial pressure was obtained. Fig. 4 shows one of the curves obtained on opening the A-V shunt. It is obvious that right atrial pressure is not significantly affected. Careful measurements of the original curves revealed a rise of pressure equal to 6 mm H_2O at A, of 8 mm H_2O at Z, and no alteration at V.

Discussion. In a sense it was disappointing to find that the A-V shunts employed in these experiments were apparently not large enough to cause a sufficient change of right atrial pressure to test the operation of the Bainbridge reflex. They do not therefore exclude the possibility that such reflexes may operate when larger shunts exist which apparently do cause an elevation of right atrial pressure.[7] This occurrence was fortunate in another way; it pointed out the difficulty of estab-

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lishing the existence of such a reflex in a crucial way. Had a material fall of right atrial pressure taken place in these experiments while arterial pressure was kept from rising, no one would have contested the conclusion that the Bainbridge reflex is responsible for the degree of slowing shown in Fig. 2 and 3. Having unwittingly devised an experiment in which neither right atrial nor arterial pressure altered significantly, it becomes apparent that these changes in heart rate must be attributed to still a different factor.

The possibility has been suggested[8,9] that differences in pulse pressure, aside from alterations in mean arterial pressure, may operate to cause reflex alteration in heart rate. However, this factor is also excluded in the curves of Fig. 2 and 3, in which the pulse pressure likewise remains unaltered before the heart rate slows. In short, the slight subsidiary changes in heart rate which are still found upon compression of an A-V fistula remain undetermined.

Summary. An attempt was made to determine whether reflexes other than those from arterial pressor receptors are concerned in modulation of the heart rate when an A-V fistula is closed or opened. In dogs under chloralose anesthesia, bilateral A-V shunts were established between femoral arteries and veins, one of which being so arranged that blood could be drained from the animal from the arterial side during closure of the shunt in an amount sufficient to stabilize arterial pressure at a fairly constant level.

In such experiments it was found that slight slowing of the heart rate still occurs on closing a shunt even when arterial pressure falls a little and the pulse pressure is unaffected. Since supplementary experiments of a similar type failed to reveal significant changes in right atrial pressure, changes in central venous pressure were also excluded. These experiments call attention to the difficulty of establishing the operation of the Bainbridge reflex in a crucial manner.

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17080. A Newcastle Disease Virus (NDV) Hemolysin.

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The first observations of a virus hemolysin were those by Morgan, Enders, and Wagley[1] in regard to mumps virus. An hemolysin associated with Newcastle Disease Virus (NDV) has not hitherto been described, although its presence has been observed.[2] The methods employed in the present investigation were modifications of those described by Morgan *et al.*[1]

Dr. Erwin Jungherr kindly supplied the California strain of NDV (no. 11,914) used in all experiments. Infected allantoic and amniotic (AA) fluids were harvested together 36 hours after intra-allantoic inoculation of 10-day-old embryonated eggs with NDV. A single pool of fluids, stored in CO_2 ice, was used throughout. In hemagglutination (HA) tests, 0.5 cc of 0.25% hen erythrocytes was added to an equal amount of each virus dilution. Readings were taken after 1¼ hours at room temperature. Two per cent cells were used in hemolysis (HL) tests which were incubated for 2 hours at 37°C. Except for 1 test run at pH 6 (Table I), all dilutions were made in isotonic phosphate buffer pH 7.2.

Some properties of the NDV hemolysin are illustrated in Table I. Hemagglutination and hemolysis tests run on the original AA fluids served as controls. These were of especial

1 Morgan, H. R., Enders, J. F., and Wagley, P. F., *J. Exp. Med.*, 1948, **88**, 503.

2 Florman, A. L., personal communication.