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Received May 6, 1963. P.S.E.B.M., 1963, v113.

Chronic Catheterization of the Coronary Sinus. (28517)

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The effects on the coronary circulation of naturally occurring and pathological stresses can now be quantitated by means of an electromagnetic flowmeter chronically implanted on the left coronary artery of the unanesthetized resting or active dog(1). It seemed desirable, therefore, to attempt chronic catheterization of the coronary sinus to provide an accessible pathway for sampling coronary sinus blood in combination with the left coronary flow so as to permit simultaneous studies of left ventricular metabolism(2).

Methods and materials. Catheters were prepared from a 30 cm segment of polyvinyl tubing (I.D. .042 in., O.D. .074 in.) and a 9 mm segment of surflene tubing† (I.D. .042 in., O.D. .062 in.). One end of the surflene tubing was flanged to a dimeter of 3 mm by gentle heating. The polyvinyl segment at one end was enlarged by stretching it over the tip of a sharp-pointed hemostat, and sleeved over the non-flanged end of the surflene tubing, a distance of approximately 5 mm, thus forming a 1 mm groove between the end of the polyvinyl tubing and the surflene flange.

Previously trained mongrel dogs weighing 16-18 kg were anesthetized with intravenous pentobarbital (30 mg/kg). Respiration was maintained through an endotracheal tube connected to a positive pressure respirator supplied with room air. Although catheterization of the coronary sinus could be performed with greater facility through the right chest, a left thoracotomy was generally used.

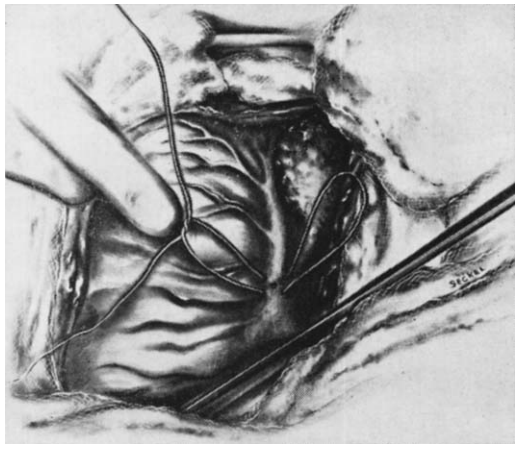

FIG. 1. Placement of horizontal mattress suture perpendicular to longitudinal axis of the coronary sinus.

This permitted simultaneous implantation of an aortic catheter for arterial pressure measurement, and of flow transducers on a coronary artery and the ascending aorta. The left chest was opened in the 4th intercostal space and the heart was suspended in a pericardial cradle. For clear visualization of the coronary sinus, the left ventricle was gently elevated and rotated anteriorly toward the right. A horizontal mattress suture (4-0) was placed superficially in the wall of the coronary sinus approximately 2.0 cm central to the coronary ostium (Fig. 1). An assistant made a preliminary hitch and held the free ends of the suture under slight tension while the operator held the opposing loop. This maneuver controlled and elevated the wall of the sinus, and thereby facilitated opening and cannulating the coronary sinus. A sharp-pointed 15-gauge needle was used to

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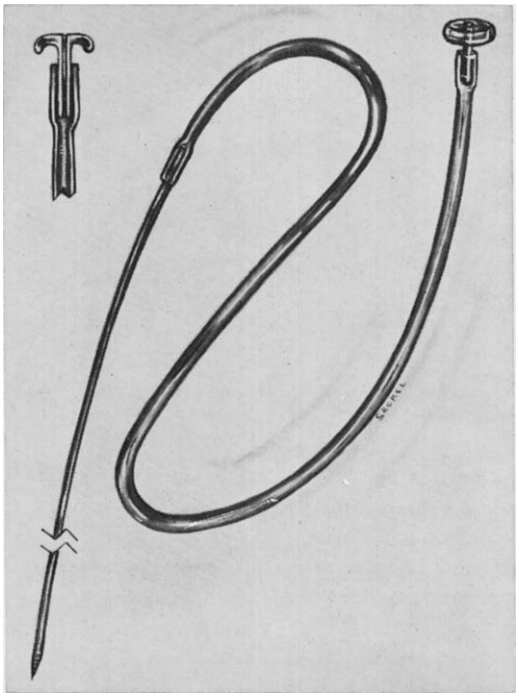

FIG. 2. Illustrates polyvinyl catheter attached to flanged segment of surflene tubing and malleable stainless steel obturator. Upper left cross-sectional view shows flanged tip.

puncture the sinus wall in the center of the mattress stitch, and the opening was enlarged to a diameter which permitted inserting the flanged lip of the catheter by gently spreading with iris scissors. The catheter which was filled with heparin (10 mg/cc) and sealed with the blunt end of the malleable silver obturator (Fig. 2), was inserted. The opposing loop was released, and the previously placed hitch was tightened as the tube was maneuvered to place the flange snugly against the overlying sinus wall. The tie was then completed with a square knot around the groove. Great care was taken to maintain the proper 90 degree angulation of the catheter with respect to the posterior surface of the coronary sinus. The obturated end of the catheter was passed through the right chest *via* a small incision made in the posterior lateral pericardium, and was then passed through the left chest wall at the 5th intercostal space adjacent to the vertebral column.

After removing the obturator, the catheter was connected to the special stopcock (Fig. 3), aspirated, and then flushed at the sampling outlet with a syringe filled with saline to remove any air bubbles. Heparin (10 mg/cc) was injected to fill the catheter while the control valve was being closed. The skin incision was slightly enlarged to position the base of the stopcock beneath the skin. The free edges of the skin were approximated over the base and were held in place by the retaining nut. Each day the catheter was tested for patency and refilled with heparin.

Results. It was important to determine whether right atrial blood could be aspirated into the coronary sinus orifice and be withdrawn through the coronary sinus catheter at the highest rates of withdrawal (25 cc/min). To test that possibility, the following procedures were performed in closed-chest dogs: (1) 20 cc of 35% diodrast was injected into the inferior vena cava under fluoroscopic observation while blood was sampled from the coronary sinus catheter at the maximum rate of withdrawal, and (2) Evans Blue dye was injected into the right atrium while measurement of changes in the density of blood was determined from the right atrium and coronary sinus. These tests gave no evidence that atrial blood was refluxed into the coronary sinus.

Since metabolic and hemodynamic studies

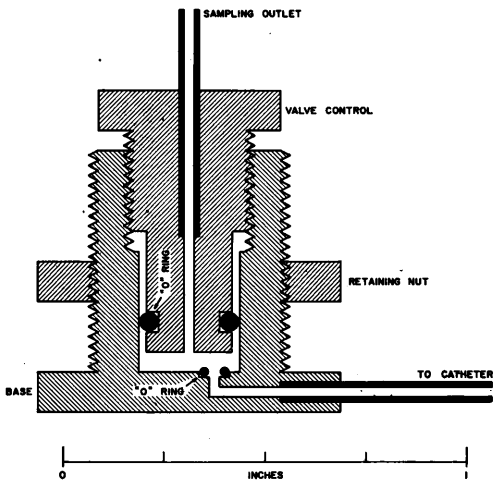

FIG. 3. Cross-sectional drawing of the specially constructed stopcock which replaces the obturator after completion of the catheterization. It is made of nylon. The inlet from the catheter and outlet to the sampling device are made from 18-gauge thin wall needle tubing.

TABLE I. Postoperative Data.

No. of dogs	Duration of patency (days)	Cause of death	Autopsy findings	Comments
3	3, 7 & 11	Ruptured aorta	Coronary sinus normal	Catheter patent
2	4 & 7	Occluded coronary artery	*Idem*	4th day survival patent 7th day survival occluded—thrombus in catheter tip
1	5	Clot in cerebral artery	"	Catheter patent
5	5, 7, 9, 12, 15	Sacrificed—drift in transducer	"	*Idem*
2	6 & 9	Dog struggled, catheter accidentally withdrawn	"	"
1	8	Sacrificed—wound infection	"	"
5	14	Sacrificed	"	"
2	14 & 26	"	Endothelial overgrowth at catheter tip	Catheter tip occluded, patent only to infusion
1	15	"	Coronary sinus normal	Catheter patent
1	17	"	*Idem*	Catheter occluded—thrombus in catheter tip
3	28	"	Partial endothelial overgrowth around flange of catheter	Catheter patent

would involve A-V oxygen differences, coronary flow measurements, and, in some cases, cardiac output, the coronary sinus catheterization technique was worked out in dogs undergoing surgery for implantation of electromagnetic flow transducers. Hence, the number of days of patency for the coronary sinus tube is minimal for those dogs in which the experiment had to be terminated because of flow transducer or other difficulties.

Data are presented in Table I showing the course of 26 dogs included in this series. In all dogs, the lining of the coronary sinus was normal and showed no evidence of trauma, distortion, or formation of thrombi. When obstruction occurred, the cause was either an endothelial overgrowth at the tip of the catheter (2 dogs—14th and 26th postoperative day), or formation of thrombi within the catheter tip (2 dogs—7th and 17th postoperative day).

Long range patency was not determined because in most cases the experiments were terminated for reasons other than coronary sinus tube obstruction. The time of sacrifice of 22 dogs with patent tubes varied from 3 to 28 days. Viewed in this light, this surgical technique has yielded a somewhat shorter period of maximum patency than that reported by Galla(3) (28 compared to 37 days), but it obviates the formation of intraluminal thrombi.

Discussion. The criteria for successful catheterization of the coronary sinus were (1) evidence that the blood sample derived from the coronary sinus was not contaminated by blood from the right atrium at the maximum rates of withdrawal, (2) the rate of sampling could be maintained constant over any predetermined period and was not limited by the chronotropic and inotropic activity of the heart or the position of the body at rest, standing, or during treadmill exercise, (3) sampling could be performed without causing discomfort to the dog, or producing excitement, (4) catheter patency was of sufficient duration to ensure normal postoperative recovery prior to experimentation, (5) no thrombus formation or obstruction occurred in the coronary sinus. Results obtained in 17 preliminary experiments (not reported here), contraindicated the use of catheters of small diameter (I.D. .027 in., O.D. .055 in.) which yielded shorter term patencies.

This method has been used over a period

of 18 months. Reproducible results have been obtained by 3 different research groups in this laboratory, yielding a maximum patency of 4 weeks.

Summary. A technique is described for chronic catheterization of the coronary sinus in dogs, permitting a constant rate of sampling coronary sinus blood in states of normalcy and stress. This method, in combination with arterial blood samples and left coronary inflow, permits quantitative measurement of changes in left ventricular metabolism in chronic unanesthetized dogs.

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Received May 10, 1963. P.S.E.B.M., 1963, v113.

Submaxillary Gland Hypertrophy in Rats Fed Proteolytic Enzymes.* (28518)

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Previous studies(1) indicate that raw pancreas contains an orally active, heat-labile factor whose ingestion resulted in a marked hypertrophy of the submaxillary glands of rats. In this report data are presented indicating that a number of proteolytic enzymes of both animal and vegetable origin can induce a similar effect.

Procedure and results. Ninety male rats of the Long-Evans strain and 42 male rats of the Holtzman strain ranging between 50 and 62 g in body weight were divided into comparable groups of 6 animals each. One group of each strain was fed a basal natural food stock ration.† The remaining groups were fed the stock ration plus the various supplements indicated in Table I. Supplements were added in place of an equal amount of stock ration. Rats were placed in metal cages with raised screen bottoms (3 animals per cage) and were provided the various test diets and water *ad libitum*. Animals were sacrificed after 12 days of feeding and the submaxillary glands were removed and weighed. The latter were placed immediately thereafter in 10% neutral formalin solution, prepared for paraffin embedding in the routine manner, sectioned at 7 μ in thickness and stained with the periodic acid-Schiff technique and with hematoxylin and triosin. Data on body and submaxillary gland weights are summarized in Table I. In agreement with previous findings(1) desiccated and defatted raw pancreas at levels of 5% and 10% of the diet resulted in a highly significant increment in submaxillary gland weight. Papain and Protease P-6, enzyme preparations obtained from *Carica papaya* were also active in this regard, the former at levels of 5% and 10% of the diet and the latter at levels of 2½% and 5% of the ration. Crystalline chymotrypsin at levels of 0.2% and 0.5% of the diet and crystalline trypsin at levels of 0.1% and 0.2% of the ration also induced a marked increment in submaxillary gland weights. The parotid glands of rats fed the above supplements, however, did not differ significantly in weight from those of animals fed the unsupplemented stock ration. In contrast to findings with the proteolytic enzymes indicated above, pepsin when incorporated at levels of 2½% and 5% in the diet was without significant effect on submaxillary gland weight. In general supplements which induced a hypertrophy of the submaxillary glands also resulted in a reduction in body weight, degree of

* This investigation was supported in part by a research grant from Nat. Inst. of Dental Research, P.H.S., N.I.H.

† Staley's Rockland Rat Diet in Meal Form, A. E. Staley Manufacturing Co., Decatur, Ill.