temic artery. The samples were analyzed for their radioactivity. The diagnosis of a shunt could be made when the ratio of radioactivity in right heart or pulmonary artery samples to that in systemic artery samples exceeded 10%. The apparent advantages of the method and the possible usefulness of other radioactive gases are discussed.

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Detection of Circulatory Shunts by Use of a Radioactive Gas.* (23630)

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The most widely used technic for detection of left-to-right circulatory shunts requires the demonstration of a sudden increase in oxygen content at or past the site of the shunt. The widely varying flow rates and oxygen contents of blood entering the right atrium from the superior vena cava, inferior vena cava, azygous vein, and coronary sinus sometimes make it difficult to estimate the mixed venous oxygen content before the site of the shunt is reached. The oxygen contents of the cavae, which constitute the major part of the venous return, may differ by as much as 4 vol. %, and usually have a difference of one to 1½ vol. %(1). The comparative flow rates in the cavae, usually taken as a 2:1 ratio, are merely an estimate in any patient. Attempts to circumvent these problems have been made by the introduction of a foreign substance into the circulation. Swan and Wood(2) injected dye into the right side of the circulation and recorded dye dilution curves with an earpiece oximeter. Use of a foreign gas, nitrous oxide, was suggested by Callaway† and has been utilized in a large series of patients by Morrow, Sanders and Braunwald (1). They were able to detect 41 out of 43 shunts by taking an integrated one minute sample simultaneously from an intracardiac catheter and a peripheral artery during the inhalation of 15-25% nitrous oxide. However, the shunt was missed in 11 of these 43 patients by use of the oxygen "step-up" method. The superiority of the nitrous oxide method is evident, but there are disadvantages. Analyses of nitrous oxide samples are difficult and time consuming. A high blank value is always present, and it may sometimes be difficult to achieve a significant arterial level. The use of an innocuous foreign gas which is easily absorbed and analyzed would simplify the situation. Dr. Louis Dotti of this hospital suggested a radioactive gas. This paper describes our experiences with ethyl iodide, containing radioactive I^{131}. This gas (without the I^{131}) was used extensively 32 years ago in human cardiac output determination(3) and was proved to be without ill effects. Analysis of blood containing radioactive ethyl iodide is achieved simply by placing a one half or one cc sample in a well counter for one or 2 minutes. The I^{131} half life of 8 days provides a safety factor and facilitates easy handling.

Method. Dogs weighing from 10 to 20 kg were anesthetized with pentobarbital, and a Cournand catheter was inserted (under fluoroscopic guidance) into the pulmonary artery via the jugular vein. This position was confirmed by pressure traces before and after each ethyl iodide administration and by withdrawal pressure tracings. Catheters were also

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† Unpublished data.

inserted (under fluoroscopy) into the superior or inferior vena cava and into the femoral artery. Each catheter and stop-cock system contained a dead space of 1.5 cc. An endotracheal tube with an inflatable cuff was inserted into the trachea. The ampule containing the radioactive gas was placed in a piece of polyvinyl tubing and both ends clamped. This was connected to a one-way respiratory valve attached to the endotracheal tube. The ampule was crushed with a hammer and the clamps removed. Exhaust from the valve was collected in a large polyvinyl bag, or a series of bottles containing ethyl alcohol which absorbs the radioactive gas. A by-pass allowed the animal to breath until the clamps were removed from the tubing containing the radioactive gas. Blood samples were taken simultaneously from the pulmonary artery, femoral artery, and vena cava at approximately 5 second intervals by withdrawing 1.5 cc into a syringe through a 3-way stop cock and ejecting into test tubes containing heparin as an anticoagulant. One or one half cc samples were pipetted from the collection tubes into lusteroid counting tubes, and radioactive content was measured in a standard well counter with a scintillation detector. Atrial septal defects were prepared by right thoracotomy, venous inflow occlusion, and removal of a piece of interatrial septum 7 to 20 mm in diameter under direct vision. Circulation was restored, the atrium sutured, and the chest closed. Ethyl iodide was then administered, or in some cases, was given after an interval of several weeks. Radioactive ethyl iodide containing I^{131} was obtained from the Radiochemical Centre, Amersham, England. It contains a specific activity of 5 millicuries per mmole. Ampules used contained 11 to 137 microcuries.

Results. Ethyl iodide was administered 19 different times. Five of these experiments were considered to be technically unsatisfactory and are excluded from the data. There are 8 studies in normal dogs and 6 on dogs with atrial septal defects. An additional element of control was present in that 4 of the 6 atrial defect dogs had ethyl iodide studies prior to the preparation of the defect.

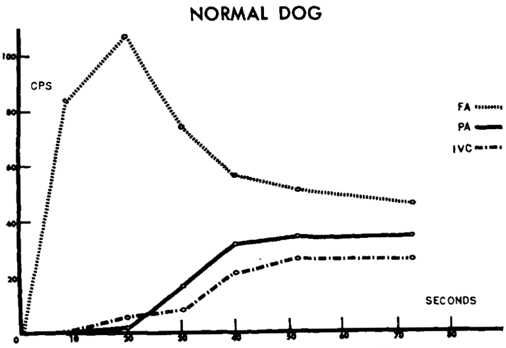

FIG. 1. CPS represents radioactivity in counts per sec. FA, PA, and IVC represent radioactivity in femoral artery, pulmonary artery, and inferior vena cava, respectively.

Normal dogs. Results in a typical normal dog are seen in Fig. 1, where the radioactivity in counts per second is plotted against the time of sampling. Radioactivity in femoral arterial samples is seen to rise rapidly to a high value and then to fall off toward an equilibrium value. Measurable concentrations appear in the pulmonary artery at 20 seconds and continue to rise as arterial values fall. The concentration in the inferior vena cava is initially higher than in the pulmonary artery, but then falls below it. Samples were also taken up to several hours, but equilibrium was reached in 5 to 8 minutes with all 3 values identical. They fell off slowly thereafter. It should be noted that significant levels were easily reached in this 15 kg dog using the low dose of 35 microcuries.

Although femoral artery and pulmonary artery curves followed the same pattern in all normal dogs, venous curves varied depending on the sampling site. Inferior vena cava values were at times slightly higher than pulmonary artery values for the first 25 seconds. Inferior vena cava samples were usually higher than superior vena cava or femoral vein samples.

Atrial defect dogs. Fig. 2 shows the results of administering 32 microcuries of ethyl iodide to a 20 kg dog in which an atrial septal defect had been prepared 4 months previously. The pulmonary artery radioactivity is at a high level in the first sample and remains high throughout the sampling period. Inferior vena cava values are similar to those in the

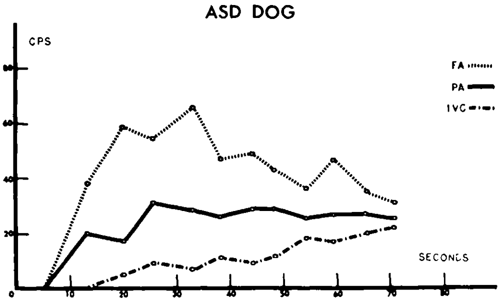

FIG. 2. Symbols similar to those in Fig. 1.

normal dog of Fig. 1. Autopsy of this dog demonstrated a well healed atrial septal defect 12 mm in diameter. The rapid rise of pulmonary arterial values is clear evidence of a left-to-right shunt. In 2 of the atrial septal defect dogs, the first pulmonary artery sample is higher than the corresponding arterial sample. This is to be expected if the samples are taken early enough following the inhalation of ethyl iodide.

In all dogs with an acute or chronic atrial septal defect, the results were similar to those in Fig. 2 during the first 20 seconds. However, the caval sample after 20 seconds was sometimes seen to rise above the pulmonary arterial level, especially where arterial levels were seen to fall off rapidly after a high initial value. Presumably recirculation causes the high venous level.

In the shunt dogs, pulmonary artery values usually fell with a rapidly falling arterial content, whereas in the normals, pulmonary artery values continued to rise.

In 2 dogs, catheters were placed in the pulmonary artery, femoral artery, and the vena cava as described above. Normal studies were performed, an atrial defect was made, the chest closed, and a second ampule of ethyl iodide was administered. The first ampule gave typically normal results. Results from the second ampule were similar to those of the atrial defect dogs, with the addition of a high base line.

Comparison of ASD and normal dogs. The best indication of a left-to-right shunt seems to appear in the early part of the curves before recirculation plays an important part in the pulmonary arterial concentration of radioactivity. Comparison of pulmonary artery and arterial concentration at identical times after administration of ethyl iodide would be the best indication of the presence of a shunt. However, the intermittent sampling technic and the fact that ethyl iodide was inhaled rather than injected does not allow measurement of the exact time radioactivity reaches the pulmonary veins. Therefore, the time chosen for comparison was at the highest arterial level reached within the first 14 seconds after radioactivity was first noticed in the arterial blood. This eliminated the problem of recirculation and also the complication of a falling arterial level.

Table I presents results of the comparison of pulmonary artery and femoral artery values at the times indicated. This shows in the normals a range of 0% to 4.9%, with an average value of 1.6%, whereas the atrial defect dogs had a range of 20.0% to 60.6%, with an average of 43.9%.

In addition, samples compared at any time earlier than that shown in Table I always showed an even lower pulmonary artery to femoral artery ratio. Earlier comparison in the atrial defect dogs nearly always showed a higher ratio than that indicated in Table I, with pulmonary artery sometimes exceeding femoral artery.

The metabolism of ethyl iodide is being studied, but indications are that radioactivity

TABLE I.* Radioactivity in Pulmonary and Femoral Arteries during Inhalation of Radioactive Ethyl Iodide in Dogs.

	Time after 1st arterial radioactivity, sec.	PA (counts/sec.)	FA (counts/sec.)	PA/FA, %
Normal	10	1.5	107	1.4
	12	0	153	0
	15	0	121	0
	7	0	7.5	0
	6	15	305	4.9
	11	0	45	0
	10	9	185	4.8
Avg				1.6
Atrial septal defect	13	31	55	56.4
	8	7	18.8	37.2
	12	53	92	57.6
	13	40	200	20
	11	97	160	60.6
	9	39	152	25.7
Avg				42.9

* Background counts averaged 3.9 counts/sec.

is rapidly excreted in the urine and expired air. Studies on the uptake of the thyroid gland are also in progress.

Discussion. Use of the radioactive gas as described gives a clear indication of the presence of an atrial septal defect and the technic presumably will also apply in ventricular septal defect, anomalous pulmonary venous drainage, patent ductus arteriosus, and other types of left-to-right shunts. In view of the low amount of radioactivity, and lack of toxicity of ethyl iodide, the method would seem applicable in human diagnostic procedures. It would have the added feature of rapid, accurate analysis, so that the presence of a shunt might be known within a few minutes, while the catheter is still in position. Additional ampules may be administered for more exact localization of the defect.

It would also seem possible to calculate the amount of left-to-right shunt by a simple mixing formula.

The ratio of shunt flow to pulmonary flow should be determined by the following formula:

$$\frac{Q_s}{Q_{pf}} = \frac{C_{pa} - C_{cav}}{C_a - C_{cav}}$$

Where: Q_s —amount of shunt flow
Q_{pf} —amount of pulmonary flow
C_{pa} —conc. of radioactivity in the pulmonary artery
C_{cav}—conc. of radioactivity in the cavae
C_a —conc. of radioactivity in the femoral artery

The validity of the above formula is now under investigation. It may be possible to use values before the onset of recirculation, in which case concentration in the cavae will not be a factor. The use of mean values as obtained in an integrated sample, or by use of the area under the curves will be necessary. Measurement of coronary flow simply by pulmonary arterial catheterization may be possible by use of these formulae and a gas which is not absorbed by the tissue. Coronary sinus blood would then have the same concentration as arterial blood. A radioactive gas, krypton 85, has been used by Hansen(4) to replace nitrous oxide when measuring coronary flow by the method of Kety and Schmidt (5) using coronary sinus catheterization. Krypton 85 has a half life of 9.4 years, and it would seem that ethyl iodide with a half life of 8 days would be safer and more convenient for this purpose.

The possibility of using this gas for pulmonary diffusion problems should also be considered.

Summary. A radioactive gas, ethyl iodide, containing I^{131}, has been administered to normal dogs and dogs with atrial septal defects. Simultaneous samples taken in the pulmonary artery and femoral artery give a clear indication of the presence of the shunt. Its use in human diagnostic procedures is suggested.

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