

Use of Radioactive Krypton and Cardio-Green Dilution Curves in the Detection of Experimental Portal-Systemic Venous Shunts *

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INDICATOR-DILUTION technics are now important and well-recognized tools in the characterization of the circulatory shunts which occur in patients with congenital heart disease.⁷ More recently, the use of solutions of radioactive krypton gas (Kr^{85}) has further improved and simplified the detection and precise localization of such circulatory abnormalities.^{1-4, 6} The recognition of functional communications between the portal and systemic venous systems of patients with hepatic disease, or with abnormalities of the portal circulation, may be impossible without the application of percutaneous or operative portal venography, major and sometimes hazardous roentgenographic procedures. It therefore appeared desirable to evaluate the usefulness of injections of Kr^{85} and indicator dyes in the detection of experimentally-produced portal-systemic venous shunts.

Materials and Methods

Communications between the portal and systemic venous systems were established by the creation of portacaval shunts in nine mongrel dogs weighing from 10 to 20 kg. Anesthesia was induced with sodium thiopental; a cuffed endotracheal tube was inserted and positive pressure respiration was maintained with 100 per cent oxygen. The abdomen was entered through a right subcostal incision. The inferior vena cava and the portal vein were isolated approximately

1 cm. caudad to the splenic vein. Ellipses of tissue measuring approximately 1 by 2.5 cm. were excised from the walls of both vessels after partially occluding clamps had been applied and a side-to-side anastomosis was constructed. Patency of the communication was readily proved by clamping the portal vein just prior to its entrance into the liver; this maneuver resulted in rapid distension of the superior mesenteric vein and venous engorgement of the bowel when the shunt was not functioning. The portal-systemic venous shunt was also occluded or opened at will with another clamp. The indicators were injected into the splenic pulp, the portal vein, or into a branch of the superior mesenteric vein. Both indicators were also injected into the femoral vein.

One μc . of Kr^{85} dissolved in 1 ml. saline solution was used for each injection. It was detected in the expired air by means of a thin-window Geiger-Mueller tube ** inserted into the airway, used in conjunction with a rate-count meter † and a direct-writing recorder. The gas is relatively insoluble and comes out of solution almost completely at the air-blood interface in the pulmonary capillary bed. It has been shown elsewhere,¹⁻⁴ that Kr^{85} appears in expired air immediately after its arrival in the pulmonary artery.

Approximately 0.60 mg. tricarbo-cyanine dye (cardio-green) was injected with the

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** Tracerlab, model TGC-2.

† Nuclear-Chicago Corporation, model 1615-B.

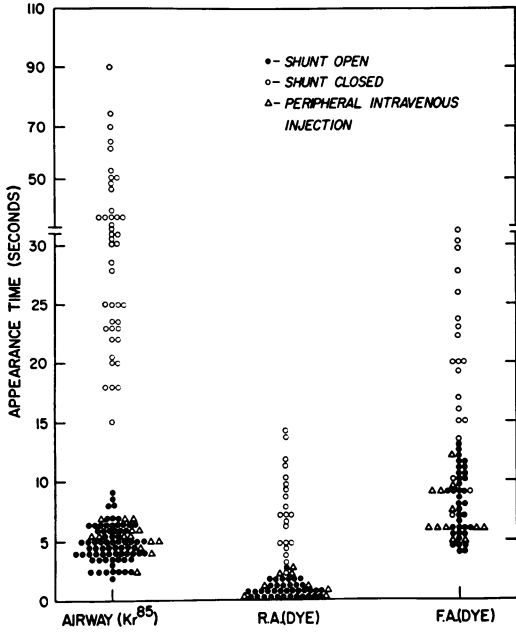


FIG. 1. Appearance time of Kr⁸⁵ in the expired air (left), of cardio-green in the right atrium (center) and in the femoral artery (right) following injections into the portal venous system (circles) and into the femoral vein (triangles).

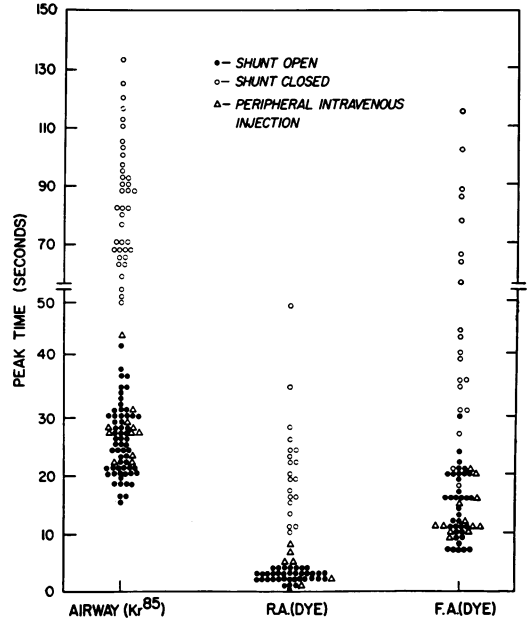


FIG. 2. Peak concentration time of Kr⁸⁵ in the expired air (left), of cardio-green in the right atrium (center) and in the femoral artery (right) following injections into the portal venous system (circles) and into the femoral vein (triangles).

Kr⁸⁵ for the recording of dye-dilution curves simultaneous with the expiratory Kr⁸⁵ curves. These curves were recorded by sampling blood from the right atrium (through a catheter introduced through the jugular vein) as well as from a femoral artery cannula. The blood was withdrawn at a constant rate through a cuvette densitometer †† by means of a mercury-filled gravity suction device. A second direct-writing instrument was utilized for the continuous recording of the concentration of cardio-green. Appearance and peak concentration times were corrected for delays in the sampling system.

Results

A total of 75 curves was obtained following splanchnic injection of Kr⁸⁵ with the portacaval shunt patent, and 46 with the shunt clamped. Fourteen Kr⁸⁵ curves were recorded following systemic venous injection. Eighty-three cardio-green curves were

obtained by sampling either in the right atrium or femoral artery from splanchnic injections with the shunt patent, and 48 with the shunt occluded. Twenty cardio-green curves were recorded following intravenous injections. The results are presented in Figures 1-3, and summarized in Tables 1 and 2.

It was observed that in the presence of a functioning portal-systemic venous communication the indicator reached the right atrium, expired gas, and femoral artery more rapidly than when the shunt was clamped (Figs. 4, 5). The injection of indicator into a peripheral vein resulted in an appearance time which was approximately equal to that resulting from injections into the portal bed in the presence of a patent shunt.

The appearance times of Kr⁸⁵ in expired air following splanchnic injections in the absence of a shunt, always exceeded the appearance times following injections either

†† Gilford Corporation, Elyria, Ohio.

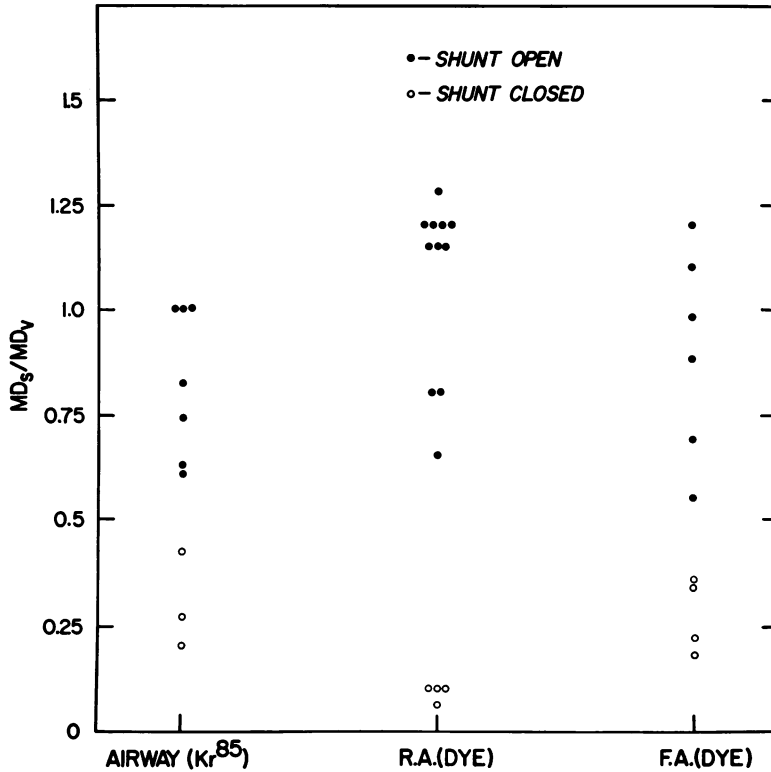


FIG. 3. Ratio of the maximum deflections after splanchnic injections of indicator (MD_s) to the maximum deflections after systemic venous injection (MD_v). Identical quantities of indicator and sensitivity of recording apparatus were used for both curves in each instance.

into the splanchnic bed with a patent shunt or into the femoral vein. Some overlap of values occurred, however, with the cardio-green curves (Fig. 1). Following injection into the splanchnic bed with a patent portal-systemic shunt, cardio-green dye appeared immediately in the right atrium;

slightly later, Kr^{85} appeared in the expired gas and even later dye was detected in the femoral artery (Table 1). However, following injection into the splanchnic bed without a patent shunt, the mean observed appearance time of Kr^{85} in the expired gas (35.7 seconds) exceeded the mean observed ap-

TABLE 1. Appearance Times (in Seconds) of Kr^{85} and Cardio-Green After Injections into the Splanchnic and Peripheral Venous Systems

	Splanchnic Injection		Fem. Vein Inj.
	Shunt Closed	Shunt Open	
Kr^{85} injection	15.7-90.7 35.7	3.2-9.7 5.6	3.2-7.7 6.1
Cardio-green injection Right atrial sampling	2.3-14.2 7.1	0.2-1.8 1.0	0.4-2.4 1.2
Cardio-green injection Femoral arterial sampling	7.7-35.7 20.7	5.2-12.2 8.7	5.7-12.7 8.0

In each instance the top numbers represent the range of appearance times, with the mean appearance times indicated beneath.

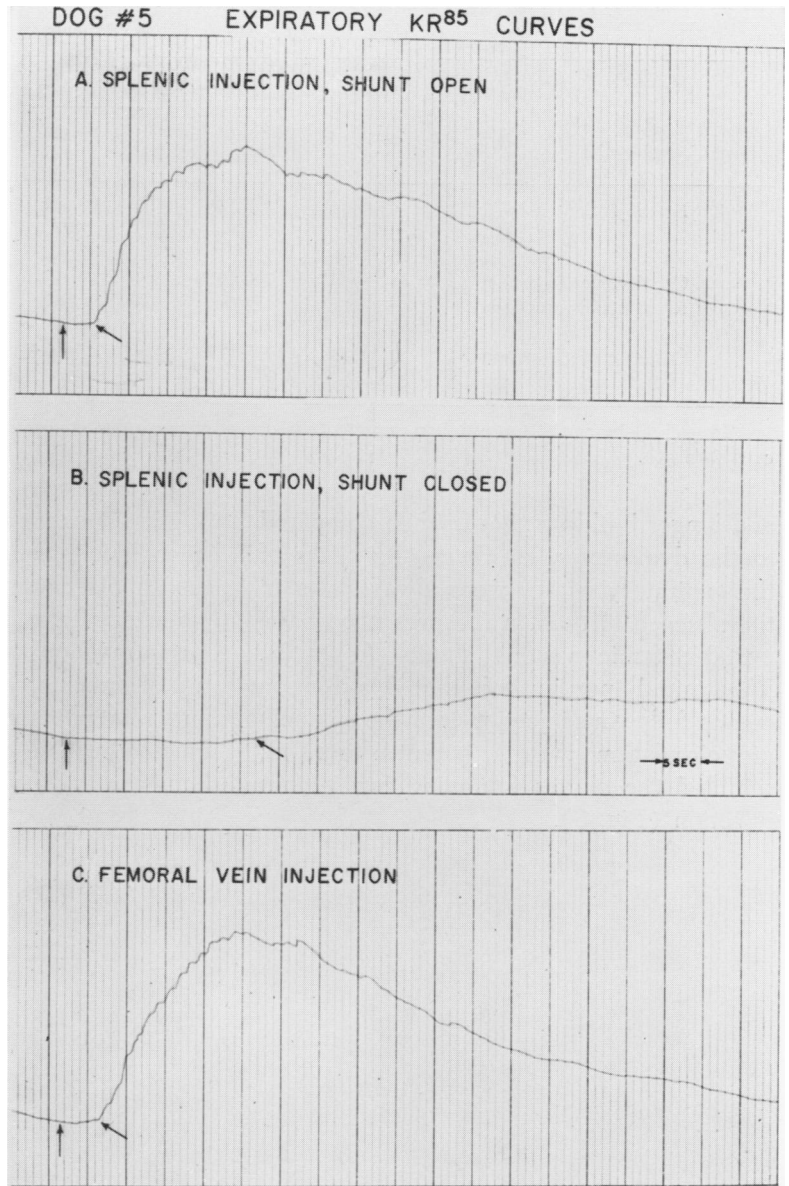


FIG. 4. Expiratory Kr⁸⁵ curves obtained after injections into the spleen with the portacaval shunt patent (A), clamped (B), and after injection into the femoral vein (C). Vertical arrows indicate time of injection. Oblique arrows indicate appearance time. Heavy vertical lines are 5 seconds apart. The quantity of Kr⁸⁵ and the sensitivity of the recording apparatus were identical for all three curves.

pearance time of cardio-green in the femoral artery (20.7 seconds). In the presence of a portal-systemic shunt the difference between the average of the right atrial and of the expired gas observed appearance times was only 4.6 seconds. However, when all of the injected indicator traversed the liver, this difference between the average of the right atrial and the expired gas observed appearance times increased to 28.6

seconds. These observations suggest that the Kr⁸⁵ does not traverse the hepatic capillary bed, directly. Presumably a portion diffuses out of the blood stream and then returns to it; thus, its appearance in expired air is delayed.

Since Kr⁸⁵ is diluted in the lungs and bronchial tree and its rate of elimination is a function of the ventilatory exchange, the expired air curves demonstrated later peak

TABLE 2. Peak Concentration Times (in Seconds) of Kr^{85} and Cardio-Green After Injections into the Splanchnic and Systemic Venous Systems

	Splanchnic Injection		Fem. Vein Inj.
	Shunt Closed	Shunt Open	
Kr^{85} injection	51.0-135 89	15.7-43 26.7	24.2-44.7 28.7
Cardio-green injection Right atrial sampling	9.8-49.2 21.0	0.7-4.4 2.8	1.4-6.4 4.3
Cardio-green injection Femoral arterial sampling	19.7-117 54	7.7-31.7 16	9.7-22.2 13.7

In each instance the top numbers represent the range of maximum concentration times, with the mean indicated beneath.

and longer build-up times, when compared to the dye curves. However, the peaks of the expiratory curves were always later in the absence of than in the presence of the portal-systemic venous shunts (Fig. 2). The initial portion of the dye-dilution curves following injection into the splanchnic circulation with a patent shunt, resembled the curves following intravenous injection (Fig. 5).

The peak concentration, following splanchnic injection of either substance with the shunts clamped, ranged from 4 to 43 per cent of the peak concentration following intravenous injection of the same quantity of indicator (Fig. 3). This reflected the larger volume of fluid into which the indicator became diluted as it traversed the hepatic capillary bed. In contrast, in the presence of a patent portal-systemic venous

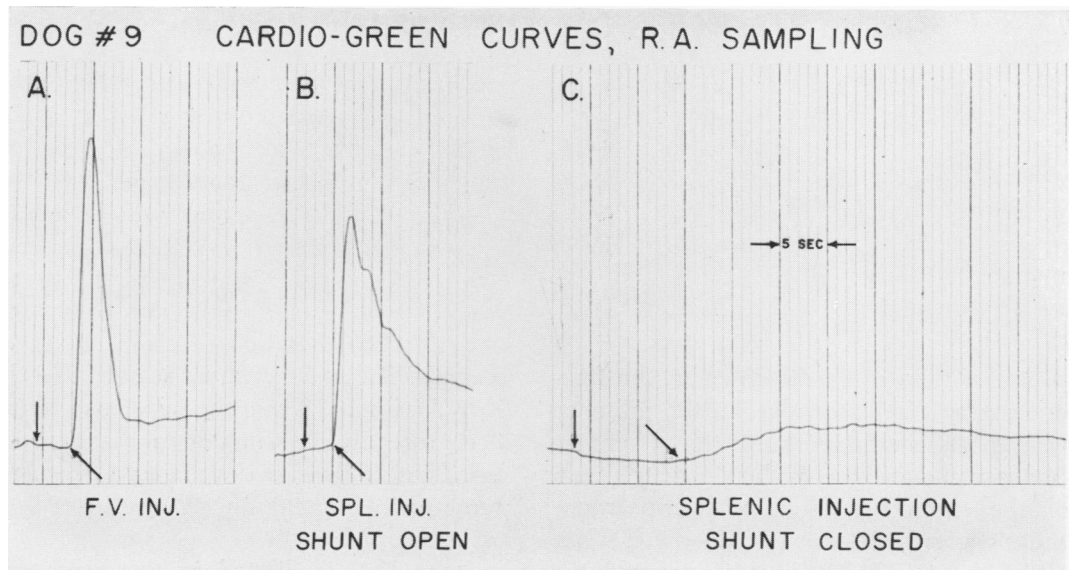


FIG. 5. Dye-dilution curves obtained by right atrial sampling. Cardio-green was injected into the femoral vein (A), into the spleen with the portacaval shunt open (B) and closed (C). Vertical arrows indicate time of injection. Oblique arrows indicate appearance time. An identical amount of cardio-green was employed for each curve.

shunt, the peak concentration of indicator ranged from 55 to 128 per cent of the peak concentration following intravenous injection.

Comment

The present study demonstrates that indicator-dilution technics can be used to detect shunts between the portal and systemic venous systems. When cardio-green dye and Kr^{85} were injected into the spleen or into the portal venous system the characteristics of the resultant dilution curves were modified by the presence of a functioning communication between the portal and systemic veins. The appearance and peak times of indicator in the right atrium, expired gas (pulmonary capillary bed) and femoral artery occurred earlier in the presence of than in the absence of such a shunt. Comparison of curves resulting from portal venous and systemic venous injections into one animal, under constant hemodynamic conditions, permitted each dog to act as its own control. Thus, the values for the appearance time, peak time and peak concentration of indicator in all three sampling sites, resembled those obtained following systemic venous injections only when the portal-systemic venous shunt was patent.

The detection of Kr^{85} in expired air appears to be the most sensitive of the three methods studied; the separation of values obtained with and without shunts was more complete than when cardio-green dye was employed. Further advantages of the use of Kr^{85} over cardio-green are that right atrial catheterization or arterial cannulation are obviated and no blood is required. In the absence of a portal-systemic venous shunt, all of the injected Kr^{85} must traverse the hepatic capillary bed; the diffusion of Kr^{85} out of the hepatic vascular bed delays its appearance in the expired gas.

Preliminary observations, in patients, indicate that these technics permit detection of the portal venous-systemic venous shunts produced by esophageal varices or sur-

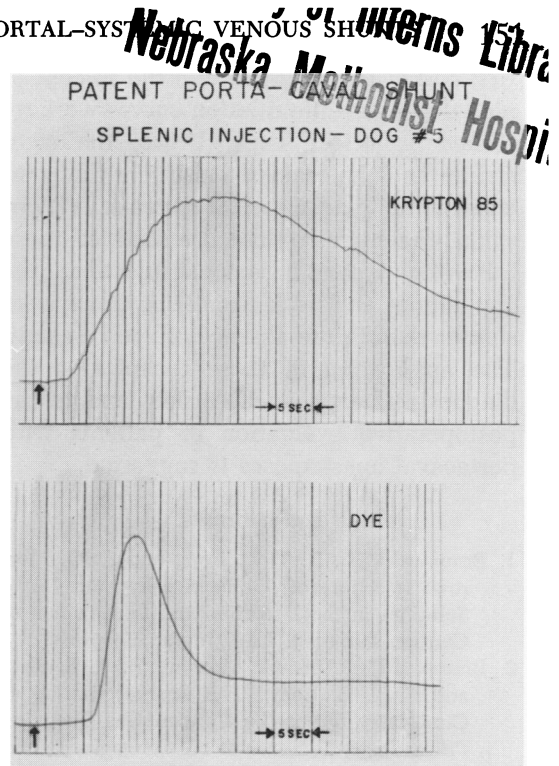


FIG. 6. The expiratory Kr^{85} curve (upper) and femoral artery cardio-green dilution curve (lower) were recorded simultaneously following the splenic injection of a mixture of these substances. The appearance time in the expired gas precedes that in the femoral artery. However, the concentration of Kr^{85} in the airway rises and falls more slowly than that of dye in arterial blood.

gically created portacaval anastomoses. The detection of patent portacaval shunts in the presence of esophageal varices also appears possible.⁵ In clinical practice percutaneous puncture of the spleen and the injection of Kr^{85} dissolved in 1 ml. saline solution through a number 23- or 25-gauge needle would appear to be preferable to the injection of much larger volumes of radio-paque solutions through larger needles. However, the relative sensitivities of the Kr^{85} and contrast roentgenographic technics for the detection of varices remain to be demonstrated.

Summary

Technics are described which permit the detection of experimentally produced portacaval shunts. Following the injection of

Kr⁸⁵ and of cardio-green into the spleens of nine dogs, multiple dilution curves were recorded from the expired gas, the right atrium and the femoral artery. In the presence of a patent portal-systemic venous shunt, the curves obtained resembled those following systemic venous injection; the appearance and peak circulation times were shorter than in the absence of such a shunt. The application of these technics to the diagnosis of esophageal varices and to the postoperative evaluation of patients with portacaval anastomoses is suggested.

References

1. Braunwald, E., R. T. L. Long and A. G. Morrow: Injections of Radioactive Krypton (Kr⁸⁵) Solutions in the Detection and Localization of Cardiac shunts. *J. Clin. Invest.*, in press.
2. Braunwald, E., A. G. Morrow, R. J. Sanders and R. T. L. Long: The Characterization of Circulatory Shunts by Foreign Gas Technics. Proceedings, Symposium on Congenital Heart Disease, Amer. Assoc. Adv. Science, Washington, D. C., Dec. 1958, in press.
3. Long, R. T. L., E. Braunwald and A. G. Morrow: The Clinical Use of Radioactive Krypton Injections in the Detection and Localization of Cardiac Shunts. To be published.
4. Long, R. T. L. and W. P. Cornell: The Use of Radioactive Gas Solutions in the Detection of Left-to-Right Circulatory Shunts: A New Method Utilizing the Counting of Expired Gas. *Proc. Soc. Exper. Biol. & Med.*, in press.
5. Long, R. T. L., C. Lombardo, E. Braunwald and A. G. Morrow: Radioactive Krypton and Cardio-green Dilution Curves in the Clinical Detection of Portal-Systemic Venous Shunts. In preparation.
6. Long, R. T. L., J. Waldhausen, W. P. Cornell and R. J. Sanders: The Detection of Right-to-Left Circulatory Shunts: A New Method Utilizing Injections of a Radioactive Gas, Kr⁸⁵. *Circulation Res.*, in press.
7. Wood, E. H., H. J. C. Swan, *et al.*: Symposium on Diagnostic Applications of Indicator-Dilution Technics. *Proc. Staff Meet. Mayo Clin.*, 32:463, 1957.