

Iodine-131 Labeled Cholografin Studies in Dogs with Normal and Abnormal Liver Physiology. (23728)

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Langecker(3) first described a new chemical compound 2,4,6-Tri Iodo-3-acetylamino Benzoic acid. In the same year Frommhold (1) and Hornykiewytch(2) demonstrated the value of the sodium salt of this new compound (cholografin) as an intravenous cholangiographic agent. Frommhold in his early paper suggested that this compound might be useful as a liver function test. More recent work(4) has shown a correlation between failure of opacification of the biliary tree after the intravenous injection of cholografin and liver diseases. Inasmuch as cholografin is readily tagged with I^{131} and the excretion of such a compound could be easily followed, it was thought that cholografin tagged with I^{131} warranted a study to determine if it might be used as a liver function test. This study reports the build-up of radioactivity over various organs, clearance rate of the radioactivity from the blood, and excretion of radioactivity in the urine following intravenous injection of cholografin tagged with I^{131} in normal dogs and in dogs in which liver physiology had been altered.

Method. Four normal dogs, a dog in which the common bile duct had been ligated, and a dog in which a portal-caval shunt had been performed were studied after being fasted and dehydrated for 12 hours. Following the injection of 12 microcuries of cholografin* labeled with I^{131} , the radioactivity was determined anteriorly over the heart, liver, and bladder using a scintillation detector with a count rate meter. The clearance rate from the blood was determined by counting blood samples drawn at intervals in a well scintillation counter. When possible the dogs were catheterized and the radioactivity of the urine determined. The tagged cholo-

grafin was diluted with untagged sodium cholografin† to a total dose of one half ml/kg of body weight. A dog on which normal values had been determined was explored and the common bile duct was ligated. Subsequent studies with tagged cholografin were repeated. A second dog was anesthetized a number of times with carbon tetrachloride. After each anesthesia, the study was repeated. Thyroid uptake studies were done on a number of dogs to determine if any free iodine had been concentrated by this organ.

Results. On the 4 normal dogs it was found that the approximate time to clear one-half the radioactivity from the blood stream averaged 74 minutes with a range of 71 to 80 minutes. The time required to clear the blood of one-half the radioactivity in dogs in which the common duct had been ligated was significantly increased to 108 minutes or greater as shown in Fig. 1 and 2. No significant change in the clearance rate was observed whether the dogs were hydrated or dehydrated.

Fig. 3 shows the change in clearance rate of radioactivity from the blood produced by carbon tetrachloride anesthesia. The time necessary to clear one-half the radioactivity from the blood was increased from 71 minutes before administering carbon tetrachloride anesthesia to a value in excess of 120 minutes after the second and third anesthesia.

Following a portal-caval shunt the clearance of radioactivity from the blood was similarly delayed as shown in Fig. 4.

When the radioactivity was monitored over various organs no differences were noted whether the dogs were hydrated or dehydrated except for possibly a slightly higher radioactivity over the bladder in the hydrated dogs. Unfortunately sufficient urine samples could not be obtained to substantiate this.

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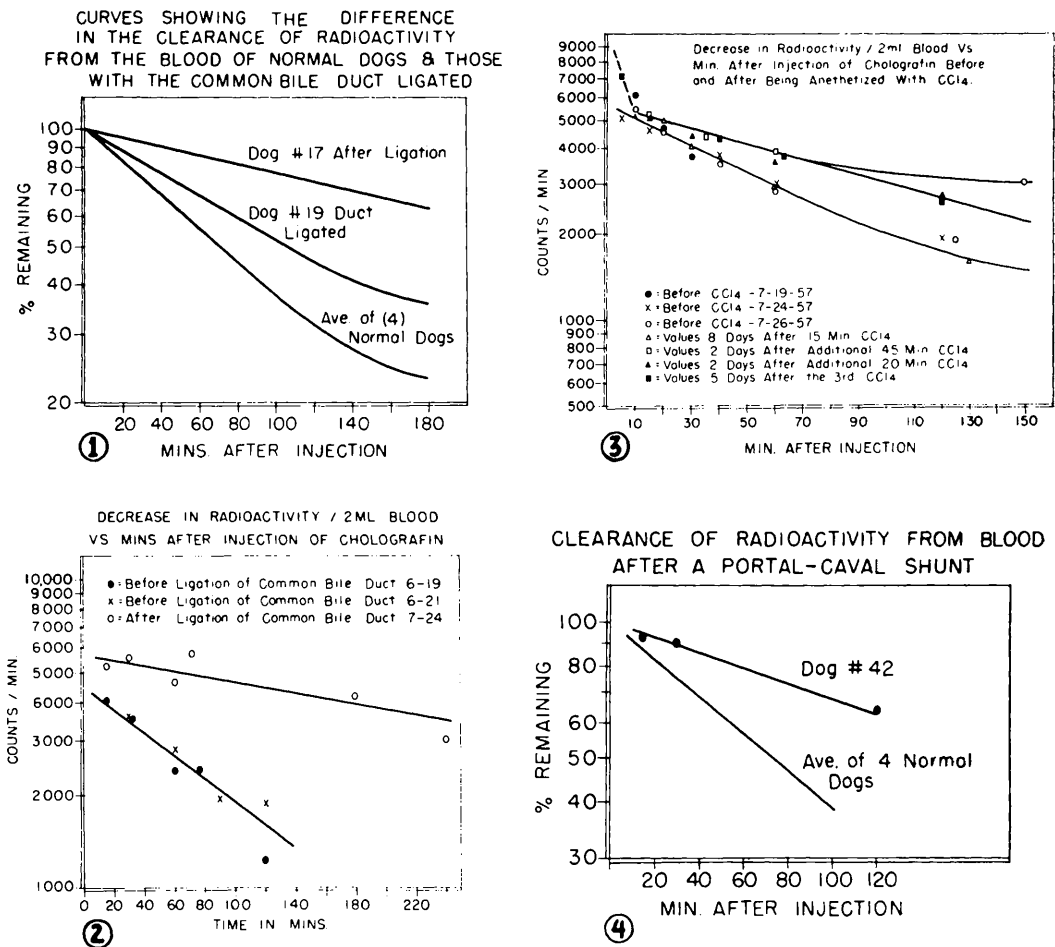


FIG. 1-4.

Representative curves of radioactivity over dogs with disturbed liver function are shown the liver and heart of normal dogs and of in Fig. 5. In all the normal dogs there was

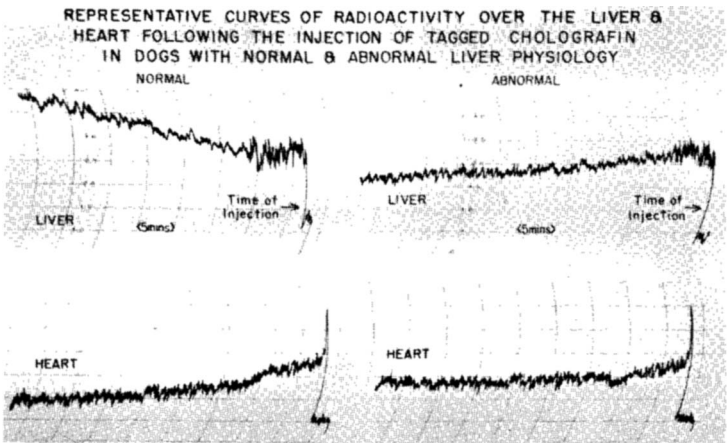


FIG. 5.

TABLE I. Percent of Total Radioactivity Excreted in Urine for Time Intervals Shown before and after CCl_4 Anesthetics.

No. of CCl_4 anesthetics	% excreted
Before any CCl_4	1.5 in 60 min.
8 days after 1st	3.1 60 "
2 " " 2nd	5.0 35 "
2 " " 3rd	6.1 30 "
5 " " 3rd	5.2 30 "

concentration of at least 20% radioactivity over the liver, whereas in dogs with disturbed liver physiology there was no concentration or an actual decrease of radioactivity over the liver. The decrease of radioactivity over the heart was similar to the clearance of radioactivity from the blood and in general the curve fell more rapidly in the normal dogs. Generally the radioactivity over the bladder rose to higher levels in the dogs with disturbed liver physiology.

No concentration of radioactivity could be detected in the thyroid glands of the dogs.

The percent of radioactivity excreted in the urine was calculated after each of the carbon tetrachloride anesthetics. A progressive increase in the amount of radioactivity excreted was found (Table I). A routine urinalysis performed 5 days after the third carbon tetrachloride anesthesia was normal.

The dog on which a portal-caval shunt had been performed showed a high urinary excretion of 11.5% in 60 minutes.

In Fig. 3 the value for clearance of radioactivity from the blood 8 days after administration of 15 minutes of anesthesia with carbon tetrachloride is the same as the normal curve. This is explained by the small amount of anesthesia given and the 8-day de-

lay which is sufficient for liver regeneration.

Frommhold in his early work stated that the iodine was very tightly bound to cholografin. The lack of radioactivity over the thyroid indicates that insignificant free iodine is present in the tagged cholografin at the time of injection or is liberated from the cholografin by the liver or other organs.

It has been shown with tagged rose bengal (5) that the ligation of the common bile duct of dogs did not alter concentration in the liver but increased concentration of radioactivity in the gall bladder. In this study, concentration of radioactivity, as determined over the anterior aspect of the liver, decreased following duct ligation.

Conclusion. 1) After injection of cholografin tagged with I^{131} in normal dogs and in dogs with altered liver function, there are sufficient differences in concentration of radioactivity in the liver to warrant further investigation of this material as a possible liver function test in human patients. Significant differences are also noted in the clearance rate of radioactivity from the blood and excretion in the urine.

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