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Metabolism of Radioactive Cholografin in Normal Controls and in Patients with Known Liver Disease. (25314)

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It was shown(1) that concentration of radioactivity by liver following injection of cholografin tagged with iodine 131 was less in dogs with altered liver physiology than in normal dogs. Differences were also noted in clearance rate of radioactivity from blood and excretion of radioactivity in urine. The present study was undertaken to determine whether or not similar results would be obtained with normal controls and patients with known liver diseases.

Procedure. Twenty-five μcuries of sodium cholografin‡ tagged with iodine 131 were administered intravenously to normal controls and to patients in whom liver disease had been proven either by needle biopsy or by laboratory studies. The tagged cholografin was diluted to a volume of 1 ml/40 lb body weight with untagged sodium cholografin. This study was also performed on one patient with abdominal enlargement but negative liver function tests and needle biopsy. Individuals were fasted 12 hours preceding the test. Following intravenous injection of tagged cholografin, concentration of radioactivity over liver and bladder was determined by scintillation detectors, ratemeters, and strip chart recorders. Blood samples were drawn at intervals to determine clearance of radioactivity from blood. Two hours after injection of tagged cholografin the subjects were given 5 ounces of water. One hour later urine specimens were collected and percentage of injected radioactivity excreted in these specimens was determined in a deep-well scintillation detector and scaler. Urine and fecal specimens were collected from controls until insignificant radioactivity was present. Urine was collected from patients for 24 hours and feces for 48 hours. The percentage of original radioactivity excreted in urine and feces was calculated for these periods. Controls were 4 young healthy adults with no history or signs of liver disease and on whom serum bilirubin levels were normal.

Results. In normal subjects the level of radioactivity over the liver increased at least 30% above equilibrium level recorded immediately after complete mixing of injected cholografin in blood volume. In patients with proven liver disease there was no concentration of cholografin by the liver and in several cases there was a decrease of 60% of radioactivity over the liver in 30 minutes. Representative curves are illustrated in Fig. 1.

Concentration of radioactivity in bladders of normal subjects increased slightly over a 30 minute interval with a maximum increment of approximately 15%. In a similar period of time 3 of 5 patients with proven liver

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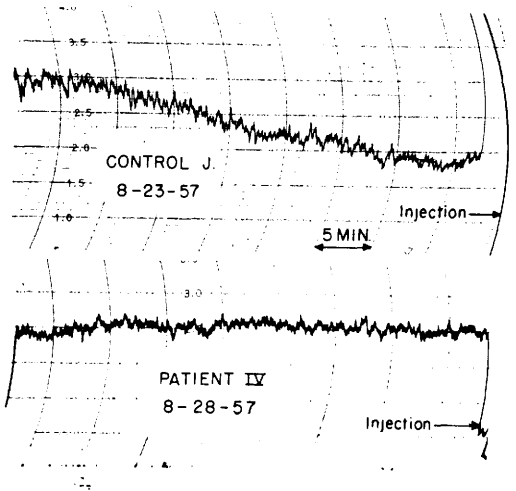

FIG. 1. Representative curves of concentration over the livers of one of the controls and one of the patients.

disease had increases in radioactivity of 40, 70, and 55% and the other 2 patients had an increase of 12%.

The time necessary to clear one-half the radioactivity from blood stream in controls varied from 80 to 150 minutes, averaging 112 minutes. In 4 patients with liver disease the time was in excess of 210 minutes; in the fifth case, 160 minutes.

The percent radioactivity in 3 hour urine specimens of controls ranged from 4.6% to 7.4%. The average was 5.9% with a standard deviation of 1.1%. The 24 hour urine specimens varied from 14.3 to 17.2% with average of 15.6% and standard deviation of 1.2%. The 3 hour urine specimens on patients with liver disease ranged from 6.1% to 19%. Two cases were within the range of normals. On 24 hour urine samples the range was 16.1 to 36%. The lowest of these was on one patient with a normal 3 hour excretion and was the only one within the normal range for 24 hours excretion.

Total radioactivity collected in feces of controls ranged from 52 to 75%. After 48 hours very little radioactivity was recovered (less than 10%). In patients with liver disease recovery of radioactivity in stool specimens for 48 hours varied from 0.45 to 11%. In one patient with obstructive jaundice there was no radioactivity in the 24 hour specimen. The patient was taken to surgery before a 48 hour specimen could be obtained.

On the patient with psychosomatic complaint of abdominal enlargement and normal liver function tests and liver biopsy the above tests were all similar to those found in the normal subjects. The results of controls are shown in Table I and those of patients with liver disease in Table II.

Discussion. The differences in results between control and patient groups closely parallel earlier results of animal work.

TABLE I. Values in Control Group.

Test	Controls T	J	C	B	$\bar{X}$	s
$T\frac{C^*}{2}$	150	80	100	120	112	30
$\frac{T\ 2\ hr\ \dagger}{T\ \frac{1}{2}\ hr}$	.60	.42	.43	.55	.50	.08
3 hr urine (%)	5.5	5.9	7.4	4.6	5.9	1.1
24 " " (%)	15.6	17.2	15.8	14.3	15.6	1.2
Fecal recovery (%)‡	67	72.0	52.7	52.0		
Inc. activity§ over liver (%)	30	50	88	40		
" " § " bladder (%)	15	Slight	Slight	15		

* $T\frac{C}{2}$ = Time (min.) needed for radioactivity in blood to be reduced to ½ the value immediately following inj.

† $\frac{T\ 2\ hr}{T\ \frac{1}{2}\ hr}$ = Ratio of radioactivity in the blood 2 hr after inj. of cholografin to radioactivity in blood ½ hr after inj.

‡ For 3-4 day period. After 48 hr recovery was less than 10%.

§ Areas monitored for 30 min. following inj. of radioactive cholografin.

TABLE II. Values of Liver Function Tests in Patients.

Patient	I	II	III	IV	V	VI	
Diagnosis	CA pancreas	Inf. hepatitis	Cirrhos.	Cirrhos.	Cirrhos.	Psycho-somatic	Normal values
BSP, 60 min. (%)			20	30	Neg.	<5	<5
Thymol turbidity	5.5	15.4		17.5		3.7	.4–4
Alk. phosphatase (Bodansky units)	5.4	5.2		2	3.05	1.2	1–4
Bilirubin (mg)	22.5	18.2	9.8	1.75	2.40	.75	.2–1
Total protein	7.0	6.8	5.8	8.3	6.1	7.9	6–8
Albumin	3.3	3.0	2.5	2.2		4.7	2–4
Globulin	3.7	3.8	3.3	6.1		3.2	1–2
Prothrombin (%)	90	100	60	45		100	70–100
Thymol floc.		2+		3+		0	<1
Bile in urine		4+	0	0		0	0
Cholografin studies							
Inc. activ., liver (%)	− 5	−60	− 8	0	0	+60	>+30
" " , bladder (%)	+40	+70	+12	+55	+12	+12	< 15
T C/2 (min.)	>210	>210	>210	160	>210	135	112 ± 30
T 2 hr/T ½ hr	.81	.83	.81	.65	.81	.63	.50 ± .08
3 hr urine (%)	10.6	7.3	6.1	19	6.7	4.4	5.9 ± 1.1
24 " " (%)	20.6	43.3	16.1	27.4	18.1		15.6 ± 1.2
48 " fecal (%)	0 (24 hr)	.46	11.0	9.8	3.6	64.0	>42

Of various tests performed, the sharp contrast in build-up of radioactivity over the liver between controls and patients with liver disease is the most significant and most consistent. Lack of significant concentration of cholografin by the diseased liver affords a simple method of evaluating liver function.

Determining percentage of injected radioactivity excreted in urine is no more difficult than monitoring the liver, but several patients in our small series failed to excrete in excess of the normal range. Nevertheless, the differences between means of the 2 groups are statistically significant. If this procedure is used, the added parameter of renal function must be considered. Probably correlation of specific gravity of morning urine specimen would suffice.

The differences between the 2 groups in clearance of radioactivity from blood and in excretion of radioactivity into the bowel were also significant, but not as striking as in monitoring the liver. These tests are also somewhat objectionable because of the necessity of multiple venepunctures for the former and the difficulty and unpleasantness of collecting stool specimens for the latter.

The time necessary for radioactivity of blood to decrease to one-half its original value and the ratio of radioactivity of blood at 2 hours to that at one-half hour after injection are a function of the same process. The latter procedure requires only 2 venepunctures, but the accuracy derived from multiple determinations of radioactivity is lost.

Before deciding on a routine dose of 1/40 ml of cholografin/lb of body weight, various determinations were performed on controls using .15 ml of cholografin/lb of body weight and undiluted tagged cholografin (less than .0075 ml/lb). The results were similar to these presented here, except that urinary excretion was slightly higher when greater total doses of cholografin were administered. Since 1/40 ml/lb of body weight permitted use of a supply of tagged cholografin even after it decayed to a specific activity of approximately 6 μc/ml and since this dose did not produce nausea in any of the subjects, it was subsequently used.

Conclusions. 1. Hepatic uptake, clearance of radioactivity from blood, and excretion of radioactivity into urine and feces of patients with liver disease differ signficantly from similar determinations in controls.

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