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Bromsulfalein Retention in Experimental Obstructive Jaundice. (19383)

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(Introduced by P. György.)

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In a previous study, prolonged retention of bromsulfalein (BSP) was observed in patients with regurgitation jaundice(1). The present experiments were performed to study this phenomenon in the laboratory animal. The work of Snell, Greene, and Rowntree(2), and Cantarow and Wirts(3) suggested that phenoltetrachlorphthalein in the dog and bromsulfalein (phenoltetrabromphthalein) in the cat were cleared from the plasma rather rapidly despite complete biliary obstruction. These observations have been extended in the present study of BSP retention in dogs and rats with common bile duct ligation.

Material and methods. Six mongrel dogs were anesthetized with intravenous pentobarbital and the common bile duct of each was sectioned between 2 ligatures. Following complete recovery, BSP (5 mg per kilo) was injected intravenously. Tests were done at weekly intervals in each animal for an average of 3 weeks. Serum was analyzed for dye before each injection, and at ½, 24, 48 and 72 hours after the injection. The same operation was performed in 13 Sprague-Dawley rats under ether anesthesia. After recovery, 5 mg of BSP per 100 grams of body weight were injected intravenously or intraperitoneally. Serum obtained by cardiac puncture was analyzed at the same intervals as for the dogs. One test only was done in each rat. The method of Gaebler(4) using the Evelyn photoelectric colorimeter was employed in determining serum concentration of dye. Abnormal retention was considered present if the concentration exceeded 0.5 mg % in dogs(5) (equivalent to 5% retention), and 1.0 mg % in rats(6).

TABLE I. Duration of BSP Retention in Experimental Obstructive Jaundice.

	Dog*	Rat*
< 24 hr	9	0
24-48 hr	8	9†
48-72 hr	2	4‡

* No. of tests performed.
† Dye inj. intrap.
‡ " " intrav.

TABLE II. Average Daily Urinary Excretion of BSP in Experimental Obstructive Jaundice.*

Day	Dog	Rat
1	42	22
2	2	7
3	0	1
4	0	0
Total	44	30

* % of amount inj.

Results. In Table I, it will be seen that in dogs with complete biliary obstruction, with serum bilirubin values ranging from 8-12 mg %, BSP was removed from the serum within 72 hours. A similar rapid clearance was also observed in rats with common bile duct obstruction. The serum bilirubin in these animals was 5-6 mg %.

Analyses were carried out to determine how much of the retained dye was excreted. An

analysis of the feces revealed no dye. This is not surprising since its presence in the stool requires a patent biliary system. In regard to renal excretion, Table II shows that in both species studied, less than 55% of the administered dye appeared in the urine.

Discussion. It is apparent that the results obtained in dogs and rats with regurgitation jaundice differ significantly from similar observations in human subjects(1). The rapidity with which BSP disappears from the serum of these animals suggests that other mechanisms are present for removal of dye in the absence of hepatic excretory function.

Cohn, Levine and Streicher showed that BSP is removed from the serum of the hepatectomized dog(7). Our data indicate that the dye is similarly removed when normal hepatic pathways are blocked. These data, however, are not applicable to BSP removal in man(1,8).

It has been stated that the kidney is able to excrete significant amounts of BSP when the serum concentration remains elevated for prolonged periods(9). In our experiments, 30-50% of the amount of dye given was recovered in the urine. Mechanisms of removal or destruction other than renal, therefore, probably play a role when the dye is not completely excreted through normal channels. In this connection, Brauer and coworkers have demonstrated that BSP may be chemically altered by the liver(10,11).

Summary. In dogs and rats with complete biliary obstruction, the retention of BSP in the serum was of much shorter duration than that previously observed in man. Conclusions concerning mechanisms of BSP removal in man based on observations made in the dog must be questioned in the light of these data.

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Effect of Chloromycetin and Streptomycin on Embryonic Tissue Growth in *In vitro* Tissue Culture. (19384)

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In a recent survey of the literature, it was noted that few reports have been presented concerning the effects of chloromycetin and streptomycin on normal cells in *in vitro* tissue culture. Ikegaki(1) has reported on the depressive effect of streptomycin on tissue growth, while Rodkova(2), Lepine, *et al.*(3) have presented conflicting data concerning chloromycetin.

Experiments were conducted in our laboratories with the following aims: (a) To satisfy increasing interest in the action of antibiotics on normal cells, with a view toward using antibiotics to help maintain sterility in tissue cultures. (b) To attempt to confirm the few existing reports.

Methods and Materials. Chloromycetin: Test solutions of chloromycetin were made up in the Tyrode portion of the usual tissue culture media(4) which was made up to the following concentrations in the final nutrient media: 1200, 900, 600, 480, 360, 240, 120 and