change was slight, although at the same time it was more than that seen in normal dogs.

Little change was noted in any of the organs at the end of from 30 to 60 days, and the dogs killed after the administration of cinchophen for from 100 to 630 days had normal-appearing organs both grossly and microscopically. At no time was jaundice seen, and at no time was cirrhosis produced or the structural framework of the liver altered. In the kidneys of dogs fed cinchophen there was no more evidenced nephritis than in the kidneys of control animals, although during the acute toxic stage there was slightly more tubular degeneration in the kidneys of these dogs than was seen in the kidneys of the control animals. Pancreatitis was not noted at any time, and the gallbladder, adrenal glands, lungs, and spleen were consistently normal.

8893 P

Blood Electrolyte Studies in Experimental Acute Liver Injury Produced by Arsphenamine in Dogs.*

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In the present investigation we have attempted to determine changes in the blood electrolytes following the production of hepatic parenchymal damage with arsphenamine. The studies included determinations of the blood non-protein-nitrogen, urea, sugar, CO_2 content, sodium, chloride, potassium calcium, phosphorus, magnesium, total proteins, and lactic acid, as well as complete hematologic studies.

Liver damage was produced in 6 dogs by injection of arsphenamine intravenously. Animals were kept on a diet of raw meat to which was added 2 gm. of salt daily for 2 weeks before the experiment was started. Arterial blood for determination of various electrolytes was collected anaerobically before injection of arsphenamine. Forty to 80 mg. per kilo of body weight of freshly prepared arsphenamine was then injected intravenously. About 30 minutes later this was followed by vomiting which lasted for a few minutes before subsiding entirely. In 2 animals, a single injection

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of the drug was adequate to produce icterus. Four of the 6 animals required subsequent injections of arsphenamine to produce jaundice. Death followed in all animals about 20 to 24 hours after the last injection of the drug. Arterial blood samples for electrolytes were again collected when the animal appeared definitely icteric. Six to 8 hours after appearance of jaundice the dogs became comatose and died. At no time were there convulsive seizures.

Upon death a necropsy was performed and sections of liver, kidneys, and intestines were removed for microscopic study. In 2 instances considerable congestion of the small intestine and rectum was found. The kidneys appeared grossly normal in all instances. The livers felt firm, but had a distinctly mottled appearance. The lobules were well outlined and were surrounded by punctate hemorrhages. The remaining organs appeared grossly normal. Microscopically the liver showed the most pronounced changes. Extensive central necrosis was present in all instances. The degree of the destructive process varied in the animals and it was estimated that from one-third to well over three-quarters of the individual liver lobules was destroyed. There were some well preserved cells around the periportal spaces, but even here some necrosis was present. In many areas the necrosis extended to the portal vein. The cellular structure of the lobule was entirely destroyed. The kidneys showed much less marked changes. Many of the glomerular capsules showed the presence of coagulated fluid. There was no actual damage, however, to the glomeruli. There was occasional necrosis of some of the cells of the tubular epithelium.

Results. Five of the 6 dogs developed icterus. The blood bilirubin varied from 2.0 to 16.0 mg. %, while the qualitative Van den Bergh reaction varied from a delayed biphasic to a direct reaction. The one animal that failed to develop icterus did have considerable hepatic parenchymal destruction, which was less, however, than was present in the other animals. The blood electrolyte pattern in this dog showed the characteristic alterations to be described, although to a lesser extent than in the animals in which the liver was more extensively damaged.

In all cases there occurred a marked hemoconcentration as determined by hematocrit studies. The reduction of plasma volume varied from 13.8 to 32.0%. This was associated with a proportionate increase in the number of red blood cells, but with no changes in the intrinsic character of these cells. Mean corpuscular volume, mean corpuscular hemoglobin, and the hemoglobin concentration remained unaltered throughout the experiments.

TABLE I.
Serum Electrolyte Studies in Acute Hepatic Parenchymal Damage.

Dog No.	N.P.N mg. %	Urea mg. %	Sugar mg. %	CO_2 Content m.eq/l	Na m.eq/l	Cl m.eq/l	K m.eq/l	Ca mg. %	Ph mg. %	Mg mg. %	Lactic Acid mg. %	Total Proteins gm. %	Qual. Van den Bergh	Quant. Van den Bergh mg. %	Icterus Index (units)	Plasma Vol.			mg./k arsphenamin intrav.
																		mg.	
1	26	11	80	24.4	144.6	114.4	4.0	9.6	3.4	—	16.4	5.6	neg.	0.5	6	50.5	11/26 - 2:30 P.M.	Control-60	76cc.
	84	53	16	12.5	145.8	107.0	13.5	9.5	12.9	—	85.0	5.4	delayed Biphasic	2.5	20	34.5	11/27 -12:10 "	Dog died	
4	36	18	85	29.5	145.3	107.5	4.1	11.8	6.6	1.6	19.5	5.5	neg.	0.5	6	56.5	12/7 -10:30 A.M.	Control-53	78cc.
	35		85										neg.				12/13 - 2:45 P.M.	-60	88cc.
																	12/18 - 8:00 "	-70	101.5cc.
	88	41	20	19.7	138.0	100.4	11.3	11.6	18.0	4.3	80.0	5.1	delayed Biphasic	3.6	56	48.1	12/20 - 8:00 A.M.	Dog died	
8	31	—	83	26.4	147.0	110.6	—	10.4	3.5	—	13.4	4.9	neg.	0.5	6	—	7/8/35 -10:00 A.M.	Control-60	56cc.
																	7/10 -10:00 "	-70	66cc.
	108	—	100	19.5	146.9	93.6	—	—	6.6	—	35.8	5.2	Direct	10.0	100+	—	7/11 - 3:30 P.M.	-80	75cc.
																	7/12 - 8:00 "	Dog died	
10	30	17	70	26.7	143.3	111.4	4.9	10.0	4.4	1.8	11.7	4.8	neg.	0.5	4.0	65.2	7/19/35-10:00 A.M.	Control-50	61cc.
																	7/20/35-10:30 "	-50	61cc.
	76	56	32	17.2	138.4	101.6	5.6	9.5	15.4	2.4	47.0	4.8	Prompt Biphasic	3.7	100	56.4	7/22/35- 4:00 P.M.	Dog died	
12	30	12	88	22.4	140.3	109.0	4.1	10.2	4.0	1.2	13.4	7.0	neg.	0.5	6.0	66.1	7/24/35-10:00 A.M.	Control-40	38cc.
																	7/25/35-10:00 "	-50	47cc.
	128	100	92	14.6	138.2	94.8	5.7	9.3	16.0	2.4	24.6	6.5	very faint delayed Biphasic	0.5	7.0	56.4	7/26/35- 8:30 "	Dog died	
14	34	18	72	27.6	143.0	104	5.9	10.2	3.3	—	10.4	6.1	neg.	0.5	5.0	62.1	7/29/35-10:00 A.M.	Control-40	45cc.
	40	25	90	23.4	139.0	99.4	—	9.8	3.8	—	29.1	5.6	Direct	5.7	60.0	57.2	7/30/35-11:00 "		
			60								40.2						7/31/35-10:15 "		
	90	75	50	21.4	137.1	83.8	7.6	10.4	11.4	—	70.0	6.1	Direct	16.0	100.0	52.4	7/31/35-11:15 "	Dog died	

Alterations in the blood electrolytes at the height of the jaundice were marked. All animals developed acidosis, reduction in the CO_2 content of the blood varying from 22 to 50%. The acidosis was due essentially to a considerable increase in lactic acid in the blood. This increase varied from twice to 7 times the control values. The increase in lactic acid was roughly proportional to the extent of liver damage. All the dogs showed a considerable drop in serum chlorides. This drop varied from 7.2 to 20.2 milli-equivalents per liter. No change occurred in the serum sodium values. The inorganic phosphorus of the serum increased from 1½ to almost 4 times the original control values, while the calcium remained remarkably constant. In 2 animals there occurred an increase in serum potassium values, and in the 3 animals in which magnesium studies were made the original control figures were doubled or trebled. An elevation of non-protein nitrogen and urea occurred in all cases. Four of the animals developed a definite hypoglycemia, the blood sugars being 16, 20, 32, and 50 mg. %. The development of hypoglycemia may be explained by the fact that following extensive injury to the liver this organ is incapable of converting lactic acid into glycogen. As a result of this incapacity there occurs an accumulation of lactic acid in the blood, and eventually a depletion of liver glycogen which is the major available source for blood sugar.

8894 C

Effect of Certain Drugs on After-Contraction.

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When voluntary muscles are put under tension against resistance through conscious effort, and then allowed to relax with the resistance removed, there follows an involuntary contraction in the original direction. Thus, as has long been known, if one stands against a wall, pushing the hand strongly against it, with the arm held stiff, on stepping away from the wall, the arm slowly rises toward a horizontal position. This phenomenon, which may be called after-contraction, has been studied by Kohnstamm, Csiky and others, who have given various explanations of its mechanism, none of which, however, seems adequate. In view of the more recent advances in the physiology of the nervous system, it seemed to us that further