

split into geometric figures whose areas can be obtained by multiplication of their heights and widths according to the rules of arithmetic.

Results. The morphological changes induced may be summarized as follows: 1. Dilatation of the central veins and neighboring capillaries. 2. Engorgement of the central veins and neighboring capillaries with r.b.c. and granular eosinophilic debris. 3. Formation of conglutination thrombi in the central veins. 4. Areas of focal necrosis about the thrombosed central veins. 5. In some cases, a generalized, but slight, infiltration of the tissue with polymorphs. 6. Degenerative changes in the cells about the central veins, a. narrowing of cells; b. loss of characteristic cord-like structures, piling up of cells with ill-defined borders and fragmentation of cells; c. loss of staining affinity, both by nucleus and by cytoplasm; d. increased and coarse granular appearance of cytoplasm; e. vacuolization of cytoplasm; f. hemosiderm pigmentation; g. decrease in number of nuclei; h. degenerative changes in nuclei, pyknosis, karyolysis. 7. Hyperplasia of portal canals. 8. Edema of portal canals. 9. Slight degenerative changes in cells surrounding the portal canals. 10. In those slides studied for quantitative changes, as much as 90% to 94% of the tissue has been damaged.

The production of areas of focal necrosis is particularly interesting, for this apparently bears out Mallory's⁶ hypothesis as to the origin of focal necrosis in the liver in typhoid. That focal necrosis is caused by the plugging of capillaries by enlarged Von K pfer cells, or the proliferation of endothelium, has been doubted by later workers.

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Cinchophen Poisoning.*

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Cinchophen is usually given in therapeutic doses of $7\frac{1}{2}$ grains 3 times a day. Considering 150 pounds as the normal or average weight, this is a dose of 22 mg. per kilo.

In order to produce cinchophen poisoning quickly 3 dogs were

⁶ Mallory, F. B., *J. Exp. Med.*, 1898, **3**, 611.

* This work was aided by a grant from the American Medical Association. We wish to thank Dr. H. R. Fishback for donating the dogs with kidney damage.

given 27 times the therapeutic dose, *i. e.*, 595 mg. per kilo mixed with their food. Every 3 or 4 days the blood sugar, urea nitrogen and Van den Bergh were determined. In this group the dogs refused to eat after from 8 to 10 doses of the drug. The urea nitrogen showed a marked rise, then a depression followed by death. Dog 1 lived 10 days, Dog 4, 17 days, and Dog 2, 20 days. At autopsy these dogs showed from one to 3 acute gastric ulcers and a number of yellowish areas over the surface of the liver. On microscopic examination the liver showed varying degrees of liver necrosis from small areas of coagulation necrosis just beneath the capsule, as in Dog 1, to complete disappearance of liver cells in small areas, as in Dog 4.

Dogs 5 and 6 were given the same dose of cinchophen per kilo. The blood sugar, blood urea nitrogen and bromsulphalein retention determinations were made. Dog 6 ate 2 doses, refused to eat more, and died 9 days later. The urea nitrogen increased at first, then decreased in amount. When the urea nitrogen decreased the bromsulphalein test showed increased retention of the dye. Dog 5 ate 3 doses of the drug, then refused to eat. The changes in blood determinations were similar in that the urea nitrogen was slightly increased in amount, then decreased, while the bromsulphalein was retained. After fasting the bromsulphalein retention subsided and the urea nitrogen increased in amount. At this time the dog ate another dose of the medicine and a more marked retention of bromsulphalein resulted. The urea nitrogen was again decreased in amount. After the retention had become less the same results were seen after another 2 doses given by stomach pump. The autopsy on Dog 5 revealed a diverticulum of the duodenum and yellowish areas over the liver. Dog 6 showed no gastric ulcers but showed slightly opaque areas over the liver surface. Microscopic examination revealed areas of coagulation necrosis.

In another 2 dogs kidney damage was produced by a method of clamping the renal artery devised by Dr. Ivy and his coworkers.¹ After recovery (11 months later) these dogs were fed the normal dose of cinchophen, *i. e.*, 22 mg. per kilo of weight. The same determinations were made as in the preceding series. Dog 8 serves as a good example for these 2. The urea nitrogen shows a slight rise, then a slight decrease as the bromsulphalein retention is increased. The bromsulphalein shows an increasing retention with fluctuation in degree until two feedings were missed and a drop occurs. These dogs are still living.

¹ McEnery, Meyer and Ivy, *J. Lab. and Clin. Med.*, 1927, **12**, 349.