Clinical experience[9] has confirmed the work of Holder and MacKay, and we feel that the beneficial action of urea in combination with the sulfonamides in the treatment of infections may be due partly to the effects described in this paper.

13767 P

Distribution of Vitamin A in Experimental Liver Damage.*

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The vitamin A content of cirrhotic livers is low[1, 2, 3] but in acute human[2, 4] and experimental[5] hepatitis normal amounts are found. The blood vitamin A level in acute hepatitis, however, is low[6, 7, 4] and hemeralopia appears.[8] Histologically in human cirrhosis and hepatitis the vitamin A distribution is markedly altered; the total amount often reduced.[9] To explain these alterations the histologic vitamin A distribution in experimental liver damage was studied.

Sixty-two rats were intoxicated with various doses of carbon tetrachloride. Of these 15 were on stock diet; 15 received supplements of 800 units of vitamin A every other day; 3 each received a high fat, high protein and high carbohydrate diet respectively. Of 23 vitamin A deficient rats, 13 received one dose of 800 units of vitamin A; another 6, 8 mg carotene. The organs were examined by routine histology and for vitamin A by fluorescence micro-

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scopy.[9, 10] Some livers were also chemically examined for vitamin A.[11]

Within 24 hours after injection of 0.1 cc CCl_4 lipoid droplets with strong vitamin A fluorescence accumulate in the center of the liver lobules. These develop by gradual enlargement of the small lipoid droplets with vitamin A fluorescence which normally line the edge of liver cells. With repeated CCl_4 injections central necroses, proliferation and collapse of the connective tissue develop.[12] The central fat droplets become larger and their vitamin A fluorescence inhomogenous, the strongest fluorescence being in the immediate center. The vitamin A fluorescence disappears from the Kupffer and liver cells in the uninvolved peripheral areas and from the fatty changes of the intermediary zone. After administration of 5.6 cc CCl_4 in 27 injections within 69 days, a cirrhotic picture develops. The lobular pattern is reversed as the original centers are linked by proliferated connective tissue surrounded by liver cells with extensive fatty changes. Vitamin A fluorescence is imparted by only a few large fat droplets in the original center and by fine droplets in surrounding histiocytes. All other fat droplets which extend to the original periphery are free of fluorescence.

In rats receiving vitamin A supplements the fatty changes seem more extensive, but the connective tissue proliferation is less marked. Vitamin A fluorescence in the fatty areas is stronger, and the intact areas retain the fluorescence longer. In rats on high carbohydrate diet the fatty changes are less extensive than in those on high fat or high protein diet and the normal Kupffer and liver cells showed more fluorescence.

CCl_4 intoxication of vitamin A-deficient rats produced similar fatty changes as in normal rats but without vitamin A fluorescence of the fat. If these rats receive a dose of vitamin A or carotene, the large fat droplets in the center of the lobules acquire the fluorescence, whereas the histologically unaltered peripheral areas do not. Chemically less vitamin A is stored in the liver of the vitamin A-deficient rats with CCl_4 intoxication than in control deficient rats after feeding the vitamin. If both groups of rats are continued on vitamin A-deficient diet, the depletion of the smaller vitamin A stores in the large fat droplets of the intoxicated rats takes as long as that of the larger stores in the Kupffer and liver cells of the controls.

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The change in the histologic vitamin A distribution during CCl_4 intoxication indicates a shift of vitamin A from morphologically intact peripheral areas of the lobules to the central fatty areas. This shift exceeds the altered fat distribution since small fat droplets in the normal periphery and medium sized ones in the intermediary zone are free of vitamin A fluorescence. It is problematic whether vitamin A actually moves from the periphery to the center, or whether it is more utilized from the periphery than from the central large fat droplets. The latter take up the vitamin faster and release it slower than the intact areas as shown by the repletion and depletion experiments respectively of vitamin A-deficient rats. This supports observations that in human liver damage the blood vitamin A level is low despite occasional quantitative normal liver stores,[13] and that hemeralopia may occur. The fact that vitamin A supplements cause vitamin A storage in the intact areas after repleting the fatty ones, renders such therapy in liver damage rational. A high carbohydrate diet has a similar effect.

Intoxication of rats with phosphorus (15 rats), thyroxin (9) and bile acids (9) showed similar results.

Summary. In CCl_4 poisoning vitamin A is found in damaged but not in uninvolved liver areas. The pathologic areas take it up faster and release it slower than normal ones. High vitamin A therapy repletes the uninvolved areas.

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Sulfaguanidine in the Treatment of Infectious Enteritis in Swine.*

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The reports of Marshall, *et al.*,[1, 2] on the use of sulfaguanidine in

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