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Concerning the Naturally Acquired Resistance of the Livers of Certain Senile Dogs to Alcohol and to Chloroform.*

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In the preceding report[1] the observation was made that when dogs recovered from an intoxication by uranium nitrate with the development in the liver of a morphologically altered flattened type of epithelium, the liver acquired a variable amount of protection to a secondary intoxication from this substance and also a resistance to the toxic action of chloroform when used as an anesthetic. Of the 161 dogs referred to in this report, 21 may be classified as senile, varying in age from 9 years and 2 months to 14 years and 4 months. Liver tissue removed from 15 of these 21 animals for purposes of control before any type of intoxication had been commenced, other than a light ether anesthesia, has shown a liver injury of unknown cause characterized by a change in the morphology of the liver cells from the normal polyhedral type to an atypical, flattened type with proportionately large, deeply staining nuclei. The capillary spaces between the cords of flattened liver cells are of such a diameter as to resemble venous sinuses. There has been no connective tissue overgrowth. The 15 dogs with this type of altered liver epithelium have shown when contrasted with senile animals with a normal liver epithelium a higher initial plasma concentration of phenoltetrachlorphthalein and a retention of the dye in the plasma for a longer period than animals with a normal epithelium.

Eight of the senile animals with the atypical type of flattened epithelium have been intoxicated by the use of 20 cc. of a 40% solution of ethyl alcohol per kilo for periods varying from 8 to 12 hours. The remaining 7 animals after a 2-day period of starvation have been anesthetized by chloroform for 2 hours. The result of such intoxications has been controlled by 10 normal dogs subjected to the same experimental procedure. The normal control animals intoxicated with alcohol have developed an edema of the liver cells which commences in the periphery and involves the outer one-third to one-half of the lobules. The use of chloroform in such normal control

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[1] MacNider, Wm. deB., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 78.

animals after a period of starvation has induced a central necrosis of the liver lobules which has varied in extent. The initial concentration and percentage retention of phenoltetrachlorphthalein has been extremely variable, apparently depending upon the extent of the liver injury.

The 8 dogs which were demonstrated to have acquired a morphologically altered type of liver epithelium and later intoxicated by alcohol, and the 7 animals with a similar type of liver cell anesthetized with chloroform, showed both anatomically and functionally a resistance to these poisons. All of the animals which received alcohol as an intoxicant failed to show the characteristic injury commencing at the periphery of the lobules and extending toward the central vein. Five of the dogs anesthetized with chloroform failed to develop a central necrosis of the liver lobules. The 2 remaining animals showed an early injury to this part of the lobules.

The functional expression of this lack of injury to the morphologically altered liver epithelium by ethyl alcohol and chloroform has consisted in a lower initial concentration of phenoltetrachlorphthalein in the plasma and a more rapid disappearance of the dye from the plasma than was the case with the control animals in which the liver epithelium was susceptible to injury from ethyl alcohol and chloroform.

The number of senile dogs with a naturally acquired, morphologically altered type of liver epithelium is insufficient to permit final deductions concerning the resistance of such epithelium to intoxication by ethyl alcohol and chloroform.

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Acquired Resistance of Altered Type of Liver Epithelium to Uranium Nitrate and to Chloroform.*

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During the past nine years, studies in this laboratory were concerned with the type of liver injury induced in dogs by uranium nitrate and other chemical substances, with the mechanism of repair to the liver lobules and the influence of secondary intoxications by

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