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Relationship Between Acute Liver Injury Induced by Alcohol, Retention in Plasma of Phenoltetrachlorphthalein and Elimination of Phenolsulphonephthalein.*

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The observation was made that dogs acutely intoxicated by ethyl alcohol in a certain number of experiments showed an increase over the normal in the elimination of phenolsulphonephthalein by the kidneys.[1] Such an increase was transitory, developing within 3 hours after the use of the alcohol and decreasing if the alcohol was withheld from 48 to 72 hours. The increase in the output of phenolsulphonephthalein by this group of dogs was associated with an edema and fatty infiltration of the liver lobules which commenced at their periphery and involved from one-half to two-thirds of their substance. The conclusion was made that the increase in the elimination of this dye was due to the liver failing to destroy a portion of it which would increase the amount available for elimination by the kidney. Similar observations have been made by Hanner and Whipple[2] on the relationship between a liver necrosis induced by chloroform and an increase in the elimination of this dye.

In the present preliminary study 12 dogs have been employed to ascertain the relationship, if any, during an acute liver injury from alcohol between the percentage retention and rate of disappearance from the plasma of phenoltetrachlorphthalein and the percentage elimination of phenolsulphonephthalein by the kidneys. Four of the animals were not given alcohol. These serve as controls. The dogs were starved for 2 days. No restriction was made on the water intake. The control dogs were then lightly anesthetized by a morphine-ether anesthesia and liver tissue removed for histological study. The remaining 8 animals were given 10 to 15 cc. of a 40% solution of ethyl alcohol by stomach tube and kept in a state of semialcoholic anesthesia by repeating the alcohol for 12 hours. At the end of such periods they were also lightly anesthetized with a similar anesthetic and liver tissue obtained for study.

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[1] MacNider, Wm. deB., and Donnelly, G. L., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 586.

[2] Hanner, J. P., and Whipple, G. H., *Arch. Int. Med.*, 1931, **48**, 598.

The use of phenoltetrachlorphthalein as a test for liver function was conducted according to the technique devised by Rosenthal,[3] while the phenolsulphonephthalein elimination was estimated according to the method of Rountree and Geraghty.[4] The phenoltetrachlorphthalein estimations were made immediately following the short period of anesthesia and also at the expiration of one hour following the introduction of the dye. The phenolsulphonephthalein determinations were made 2 hours later and represent the total output of this dye in a 2 hour period. The course of the following experiments, 2 from the control group and 2 from the animals intoxicated by alcohol, are characteristic for the 2 groups.

Control Animals. The dog of Exp. 1 showed a concentration of phenoltetrachlorphthalein in the plasma of 8%. At the end of an hour the plasma was negative for the dye. The elimination of phenolsulphonephthalein by the kidneys was 66%. The control animal of Exp. 4 had a plasma concentration of phenoltetrachlorphthalein of only 6.6% with a disappearance of the dye from the plasma within an hour. The elimination of phenolsulphonephthalein was 54%.

The livers of these animals were normal. There was no edema or necrosis of the liver cells. The nuclei stained normally. Fine dust like particles of lipoid material could be detected in the cells when such tissue was fixed in formaline and stained with Scharlach R. by Hersheimer's method.

Animals Intoxicated with Alcohol. The dog of Exp. 3, after an alcoholic intoxication lasting for 12 hours showed a phenoltetrachlorphthalein concentration in the plasma of 16% and a retention of the dye of 7% at the end of one hour. The elimination of phenolsulphonephthalein by this animal was 83%. The dog of Exp. 11 gave a plasma concentration of 27.8% with a retention at the end of an hour of 17.3%. In this animal there occurred an elimination of phenolsulphonephthalein in a 2 hour period of 93%.

The livers of the dogs intoxicated by alcohol have shown a reaction similar to that previously[1] described. A marked edema usually without necrosis of the cells, a failure of the nuclei to stain normally and the presence of variable amounts of stainable lipoid material. These changes commence and are most marked in the periphery of the lubules. The extent of the injury has varied from one-half to over two-thirds of a liver lobule. In those animals with

[3] Rosenthal, S. M., *J. Am. Med. Assn.*, 1922, **79**, 2151.

[4] Rountree, L. G., and Geraghty, J. T., *J. Pharm. and Exp. Therap.*, 1909, **1**, 579.

the most marked evidence of such an injury the initial concentration of phenoltetrachlorphthalein in the plasma has been higher, its presence has persisted for an hour and the elimination of phenolsulphonephthalein has been greater than in the animals with a less marked liver injury.

The use of phenoltetrachlorphthalein as a test for liver function indicates a definite relationship between the degree of liver injury and the percentage elimination of phenolsulphonephthalein by the kidneys.

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Further Studies on the Life Cycle of the Avian Tubercle Bacillus.

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The primary object of this paper is to indicate briefly that the experimental high lights of a life cycle for the tubercle bacillus have been consummated. The cycle at present consists of 4 stabilized stages which are vegetative, and 3 transition stages between them which are reproductive or gonidial—7 in all. Of the reproductive stages 2 are probably asexual, and inquiry into the *possible* sexual nature of the other will be reported in a subsequent paper.

Each important stage has been thoroughly single-celled before progression to the next stage has been induced by germination of its appropriate gonidial form; which form constitutes the cytologic mechanism for the transition. For this reason Stages 2, 4, and 6 should perhaps be designated as "phases"* except for possible confusion in the text. Stage 1 is the S form of the avian tubercle bacillus which gives rise to Stage 2, which is filterable.[1, 2, 3] It in turn germinates as Stage 3 in stabilized diplococcus form. As a transition form of Stage 3 is the large tetrad form, Stage 4, which gives rise to the stabilized diphtheroid Stage 5, which in turn yields acid-fast gonidia constituting Stage 6. These

* The term "phase" indicates an absence of detectable multiplication of such a form before its germination into a "stage", which is capable of vegetative multiplication for many "generations".

1 Mellon, Ralph R., PROC. SOC. EXP. BIOL. AND MED., 1931, **29**, 206.

2 Mellon, Ralph R., and Fisher, L. W., *J. Bact.*, 1932, **23**, 18.

3 Mellon, Ralph R., and Fisher, L. W., *J. Inf. Dis.*, 1932, **51**, 117.