Perhaps the principal advantage of this method of determining blood fibrin is its simplicity. The major difficulty is in obtaining the venom. However, since only a minute amount is required for each test, a small supply will last for a very long time. Even the quantities used in the present study (0.06 mg. of the dried venom per test) were far greater than necessary.

We wish to express our indebtedness to Dr. C. H. Kellaway, Director of the Walter and Eliza Hall Institute of Melbourne, Australia, who supplied us with the venom used in this investigation.

7863 P

Acquired Resistance of Liver Cells to the Toxic Action of Uranium Nitrate.*

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A statement has been made previously concerning the type, distribution and severity of the injury to the liver by the use through subcutaneous injection of a solution of uranium nitrate.[1, 2] In addition, observations were recorded[2] concerning the types of repair processes developing in the liver as a result of the reaction of the liver to this hepatoxic agent, and the resistance or lack of resistance which such processes manifested when the liver was subjected to the toxic action of chloroform, administered by inhalation.

The present series of experiments are concerned with the injury induced to hepatic epithelium by the subcutaneous use of uranium nitrate in the amount of either 2 or 4 mg. per kilogram, the type of repair process which is inaugurated by such injuries and the resistance which certain cells in such areas of repair may acquire to secondary intoxications by uranium. During the course of the experiments biopsy material has been obtained from the liver for cytological study and at such periods tests of hepatic function have been made by the use of phenoltetrachlorphthalein according to the technique devised by Rosenthal.[3]

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1 MacNider, Wm. deB., PROC. SOC. EXP. BIOL. AND MED., 1919, **16**, 82.

2 MacNider, Wm. deB., *Trans. Assn. Am. Physicians*, 1934, **49**, 14.

3 Rosenthal, S. M., *Bull. Johns Hopkins Hosp.*, 1922, **33**, 432.

Sixty-three dogs have been used in the experiments. Twenty-nine of the dogs were intoxicated with 2 mg. of uranium nitrate per kilogram. Ten of the animals failed to survive the intoxication In the remaining 19 dogs there was an initial increase in the plasma concentration of phenoltetrachlorphthalein at the height of the intoxication which did not exceed 18%. In 8 of these animals the plasma was free from the dye in half an hour. In the remaining 11 dogs the removal of the dye was delayed. Biopsy material removed from the livers of such animals showed an increase in stainable lipoid material in the hepatic epithelium, and edema, but rarely vacuolation or necrosis of the cells. The vascular tissue of the liver failed to show any evidence of injury. An injury of this diffuse type and severity was followed by changes of repair which were usually complete within 9-20 days, and consisted in the formation of an essentially normal type of hepatic epithelium with a return of liver function to the normal as indicated by the use of phenoltetrachlorphthalein. When such animals were reintoxicated by the same amount of uranium nitrate there was no cytological evidence of epithelial resistance on the part of the liver and hepatic function as indicated by the use of the above mentioned dye as imperfectly as it indicates such function was depressed.

Thirty-four animals were intoxicated by the subcutaneous injection of 4 mg. of uranium nitrate per kilogram. Eighteen of these animals effected a survival and form the basis for the following observations. In this group the evidence of a disturbance in hepatic function was greater than that in the previous group. The initial plasma concentration of the dye was of a higher percentage, attaining a maximum of 24% in 2 of the dogs. The dye persisted in the plasma for as long as 2 hours. At such a stage of functional depression biopsy material removed from the livers showed an advanced edema, vacuolation and in areas necrosis of the epithelium. In less damaged cells lipoid material was present as large droplets or fused masses. Within 4 to 10 weeks in animals which have survived such a degree of liver injury there occurs an improvement in hepatic function, usually without its return to the normal. Biopsy material obtained from the liver at such a stage of recuperation has shown the repair process to the epithelium to have taken place through the formation of an atypical, flattened type of cell with proportionately large, deeply staining nuclei. The newly formed epithelium may be syncytial in structure. When such animals are reintoxicated with 4 mg. of uranium nitrate per kilogram it has been observed that the change in the type of cell in the liver develop-

ing as a process of repair has imparted resistance to the liver against this hepatoxic agent. There occurs but slight evidence of epithelial injury and hepatic function as indicated by the use of phenoltetrachlorphthalein may or may not be depressed from the pathological normal established by the liver as a result of an atypical type of fixed cell repair.

7864 C

Effects of a General Anesthetic (Sodium Amytal) on the Erythrocyte Count Following Hemorrhage.

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Although it is generally agreed that there is a reduction of the erythrocyte count after hemorrhage due presumably to a dilution of the circulating blood nearly all of the evidence of this phenomenon has been obtained some hours, *i. e.*, 24 or more, after bleeding. The behavior of the red blood count within a few hours after hemorrhage has not been extensively investigated, and among observers there is considerable disagreement, some finding an increase in the cell count indicating concentration and others finding a decrease indicating dilution.*

During other experiments it was noticed that the effect of general anesthesia seemed to have a very marked influence on the behavior of the red blood count after hemorrhage. A series of experiments were then undertaken, 13 in all. In 6 of them the blood was removed from the circulation from the femoral artery under local (novocaine) anesthesia, in the others after the induction of general anesthesia by means of the injection of sodium amytal intravenously. The amount of drug given did not exceed 50 mg. per kilogram of body weight in any case. However, many dogs received less than this amount for the injection was given slowly and discontinued as soon as the animal was deeply asleep. A single bleeding was done in each case amounting to from 3 to 4% of the body weight. Preliminary observations of the red blood cell count, venous, capillary and arterial, with the animal under general as well as without

*Lack of space precludes discussion of these observations.