curred: streptokinase had already completed the activation of plasminogen and was no longer available for inhibition by tyrothricin. Since there is no inhibition of the proteolytic activity of the plasmin, tyrothricin must act on streptokinase, preventing the activation of the plasminogen.

A study also has been made of the effect of several antibiotics and chemotherapeutic agents on the activation of plasminogen by streptokinase, and on the lysis of the fibrin clot by plasmin. The compounds examined included penicillin, dihydrostreptomycin, polymyxin B, bacitracin, and sulfamerazine. All were tested at several concentrations of the active agent. No inhibition of either reaction was apparent with any of these compounds.

Summary. 1. Tyrothricin, or one or more of its components, reacts with streptokinase to prevent the activation of plasminogen and formation of plasmin. 2. Treatment of plasminogen with tyrothricin does not inhibit the activation of plasminogen by streptokinase. Plasminogen probably reacts with tyrothricin, preventing the inhibition of the added streptokinase by the antibiotic. 3. Tyrothricin does not inhibit the fibrinolytic activity of plasmin. 4. Penicillin, dihydrostreptomycin, polymyxin B, bacitracin, and sulfamerazine did not inhibit the activation of plasminogen by streptokinase nor the fibrinolytic activity of the plasmin.

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Toxicity of Mono Methyl Ether of Dipropylene Glycol (Dowanol 50B) in Studies on Auricular Fibrillation. (19699)

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A reliable method for the production of auricular fibrillation in intact animals would be useful in certain investigations. A recent report(1) on the consistent ability of the mono methyl ether of dipropylene glycol (Dowanol 50B) to provoke this arrhythmia in acute experiments on the anesthetized dog led us to inquire whether this compound could be used as a fibrillating agent in experiments repeated in a given dog on different days. The oral lethal dose was reported to be about 7.5 ml/kg (intravenous lethal dose not given) and the fibrillating dose 0.6 ml/kg intravenously or higher. Since recovery from sublethal dose administration was said to be complete, it seemed probable that Dowanol 50B could be used repeatedly as desired. We injected Dowanol 50B intravenously into 4 normal dogs in an attempt to determine whether the minimal dose producing auricular fibrillation in a given animal remains constant on different days. Such constancy of minimal dose has been reported to exist for repeated trials in acute experiments on a single day(1).

Methods. Five experiments were performed in 4 dogs. The animals each received 30 mg/kg pentobarbital sodium intravenously, and a tracheal catheter was inserted. Injections of Dowanol 50B were given rapidly into a foreleg vein while continuous recording of lead 2 was made with a direct writing electrocardiograph. Intervals of 10 to 20 minutes were allowed between injections. Because Dowanol 50B depresses respiration, dogs 1 and 2 were maintained on gentle positive blast respiration throughout, while dogs 3 and 4 were so maintained only after each injection, and were allowed to return to spontaneous respiration before a next injection was given.

Results. We found Dowanol 50B too lethal

for use in repeated experiments. Dog 1 (9.2 kg) was given 2 injections of 0.6 ml/kg each, without the production of fibrillation. With artificial respiration continued, 2 mg of methacholine chloride were given intravenously 17 minutes after the second injection, resulting in the appearance of auricular fibrillation with prolonged A-V block and later of markedly abnormal ventricular complexes. Death followed in about 5 minutes. A dose of 2 mg of methacholine chloride is rarely fatal in otherwise untreated dogs under pentobarbital anesthesia. Dog 2 (11.2 kg) received 5 injections totalling 3.0 ml/kg, the largest being 1.0 ml/kg without production of fibrillation. Two subsequent doses of 1.2 ml/kg each produced fibrillation. Death resulted after the respirator was disconnected one minute after the last injection. In dog 3 (12.7 kg) given 0.70, 0.75 and 0.70 ml/kg successively, fibrillation resulted after the second dose only. The animal died 15½ hours later and at necropsy showed gastric dilatation, pulmonary congestion and marked intestinal hemorrhage. In dog 4 (5.8 kg) administration successively of 0.17, 0.35, 0.69 and 0.52 ml/kg resulted in the production of auricular fibrillation only with the last 2 doses. The animal remained anesthetized for about 36 hours and thereafter had marked ataxia and cough for a week. In a second experiment 16 days later the minimal fibrillating dose was 1.1 ml/kg, determined after a total of 3.5 ml/kg had previously been given and after a dose of 1.0 ml/kg had failed to produce fibrillation. The animal died 2 days later without recovering from Dowanol anesthesia, 4.6 ml/kg total having been given during the last experiment.

Summary and conclusions. When administered intravenously to dogs anesthetized with pentobarbital, Dowanol 50B in adequate dosage produces auricular fibrillation, but in 4 dogs was found unsuitable for use in repeated experiments on different days, since it caused respiratory depression, prolonged anesthesia, disturbances of gait, intestinal hemorrhages and death. One animal surviving a first experiment required a significantly higher single dose and higher cumulative dose for production of fibrillation during a second experiment and succumbed following the latter.

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Effect of Liver Ischemia on Plasma in the Dog, as Measured by Electrophoretic Analysis.* (19700)

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Early attempts to study changes in the plasma proteins of dogs after hepatectomy were hampered by the short survival time of the prepared animals. Munroe and Avery(1) found no significant changes in the electrophoretic pattern of dog plasma, in periods up to 7 hours after hepatectomy. Lewis, Page, and Reinhard(2) were able to obtain plasma samples up to 16 hours after the operation. They reported but small changes. The total plasma protein fell, and a decrease in the β-globulin accounted for much of this change. We know of no reports of electrophoretic studies on plasmas of dogs with reduced hepatic circulation. Although Eck fistula dogs have been studied from a hematological viewpoint, there is little known about the electrophoretic patterns of their plasmas.

Our studies have been made on dogs which, strictly, were not Eck fistula dogs, although a portal-caval anastomosis and ligation of the portal stem close to the liver had been carried out in all of them. To obtain a maximum reduction of circulation in their livers, the dogs were subjected to a 3-stage operation in which, ultimately, all of the named vessels