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## Attempts at Treatment of Hemorrhagic Diathesis by Injections of Snake Venom.

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In 1930 the author attempted to produce a Shwartzman phenomenon (local hemorrhagic necrosis following local and intravenous injections of bacterial toxic filtrates with fungus extracts). These efforts were unsuccessful. In the hope that previous local injections of a vascular poison might render the reaction site more sensitive to hypothetical toxic substances in fungus cultures, snake venom was employed. This again proved unsuccessful. Later, in collaboration with Dr. Harry Sobotka,[1] the author showed that if 14 days to one month were allowed to elapse between the time of injecting of rabbits with snake venom and the elicitation of a Shwartzman phenomenon, a large number of the animals became refractory to the latter. Since no circulating antibodies could be demonstrated to explain the refractory state, and since antivenin had no effect on the course of the Shwartzman phenomenon, the induced refractory state was thought to be due to some change in the vessel walls which made them resistant to toxic filtrates and this prevented the hemorrhage. With this possibility in mind, the author then treated with snake venom diseases which can be grouped under hemorrhagic diatheses. Patients showing certain allergic phenomena such as urticaria, neurodermitis, as well as asthma and hay fever were also treated.

Clinical trial was made in 44 cases which can be divided roughly into 3 groups:

Group I consists of 3 cases of thrombocytopenic purpura,* one case of Henoch-Schönleins syndrome (Frank's capillary toxicosis), and 2 cases of hemophilia. The hemorrhagic purpura cases had such symptoms as epistaxis and purpura; and in 2 of them there was a history of prolonged and profuse menstrual periods. Two of this group have been under treatment with snake venom for 9 months, and one for 6 months. The 3 patients showed definite clinical improvement with a marked decrease in purpura and epistaxis, and a decrease in the duration and profuseness of the men-

[1] Peck, S. M., and Sobotka, H., *J. Exp. Med.*, 1931, **54**, 407.

* Since submitting this report for publication two additional cases of thrombocytopenic purpura have been treated with similarly good results.

strual flow. In one patient the platelet count is now 220,000, while in the other 2 it is still below 60,000.

The 2 hemophiliacs have been under observation by Dr. N. Rosenthal for a number of years. They have now been under snake venom treatment for 5 months with what appears to be encouraging results.

The patient with Henoch-Schönleins syndrome had recurrent purpura, hematuria and a history of prolonged and profuse menstrual periods. The menstrual period which came on after she had received treatment with snake venom for several weeks was shorter and markedly less profuse. Her hematuria has disappeared and she has been free from purpuric manifestations for over a month.

Group II, in which the best results have been observed, consists of a case of epistaxis (idiopathic) present for more than a year in a 7-year-old boy, and 5 cases of functional uterine bleeding also of long duration. Very soon after treatment was begun these cases showed a definite improvement in the form of a reduction in duration and amount of bleeding. It is impossible as yet to determine whether the results are permanent. These cases will be reported in detail with Dr. M. Goldberger.

Group III includes 32 allergic cases of the type previously mentioned. In the majority of them the results have not been satisfactory. In a few cases, however, very definite clinical improvement seemed to follow the treatment.

*Method.* The venom used was that of the moccasin snake *(Ancistrodon piscivorus)*. The standard dose for an adult was 0.2 cc. of a 1:3000 solution in physiological saline given intradermally. This was increased in most cases to 2 injections of 0.2 cc. each in different sites. The injections were given once or twice weekly, and the duration of the treatment varied with the cases.

*Comment.* The clinical results in cases with such varied etiologic factors seem to substantiate the theory that the venom achieves its results by acting directly on the blood vessels. This viewpoint is strengthened when we consider that there was a marked beneficial effect on the tendency to hemorrhage in 2 of the cases of thrombocytopenic purpura, although the platelet count did not rise appreciably.

Stockton and Franklin[2] have reported good results with antivenin in a case of purpura. Antivenin has had no therapeutic effect in one of the author's cases of thrombocytopenic purpura.

Experiments in rabbits seem to show that in these animals anti-

[2] Stockton, M. R., and Franklin, C. H., *J. Am. Med. Assn.*, 1931, **96**.

venin plays no rôle in the production of the resistant state to bacterial toxic filtrates produced by the venom.

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## Effect of the Prolonged Use of Ethyl Alcohol on Renal Function and Pathology in the Dog.*

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Observations were previously made on the acute toxic effect for the kidney in both normal and naturally nephropathic dogs of an alcoholic distillate obtained after the fermentation by yeast of a mixture of corn meal and sugar or corn meal and molasses.[1] It was later demonstrated[2] that such distillates were able to induce a type of chronic nephropathy in the dog which was largely confined to the endothelium of the glomerular capillaries. The animals in the 2 groups of experiments were given 10 cc. per kg. of the distillate. Normal dogs were used as controls and received 10 cc. per kg. of a 40% solution of ethyl alcohol. The experiments lasted from 6 weeks to 3 months. The animals receiving the alcoholic distillate as well as the control animals were then sacrificed. Both the normal and naturally nephropathic dogs which received the alcoholic distillate showed definite evidence both functionally and anatomically of renal injury. The control dogs gave but slight evidence in so far as renal function was concerned of any departure from the normal. Similar observations of the relative nontoxicity of ethyl alcohol for pigeons have recently been made by Hanzlik.[3]

The present investigation is concerned with the effect of ethyl alcohol on renal function and pathology in the dog when taken over long periods in the amount of 10 cc. per kg. of a 40% solution. The experiments have lasted from 6 months to 2 years and 2 months. Twenty-three adult dogs have been used. The animals were kept in metabolism cages and allowed an unrestricted amount of water except on the days set aside for observation. They were fed on bread, scraps of meat, a small amount of butter and milk.

* This investigation was made possible by the Edward N. Gibbs Prize Fund of the New York Academy of Medicine.

1 MacNider, Wm. deB., *J. Pharm. and Exp. Therap.*, 1925, **26**, 97.

2 MacNider, Wm. deB., PROC. SOC. EXP. BIOL. AND MED., 1925, **22**, 52.

3 Hanzlik, P. J., *J. Pharm. and Exp. Therap.*, 1931, **43**, 339.