lish the method there with comparable results.

Summary. 1. A modified technic for the determination of the antistreptolysin titer of serum has been described which involves the use of a concentrated lysin reduced to the active form at the time of use.

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Effect of Heparin and Dicoumarol on Thrombosis Induced in the Presence of Venous Stasis.*

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The effect of heparin[1,2,3] and more recently dicoumarol[4,5,6] on the course of experimentally induced venous thrombosis has been extensively studied. However, the methods of producing intravascular thrombi used have not always been uniformly successful. For the evaluation of the effect of anticoagulants upon thrombosis a method of consistently producing thrombi is essential. In a preliminary report[7] the author states that he found stasis a prerequisite for the consistent production of occluding thrombosis by the insertion of intravascular foreign bodies. Rabinovitch and Pines[3] also found it necessary to add stasis (by partial ligature of the vein) to the intimal damage produced by stretching the vein to insure thrombosis. In view of the effect of stasis on experimental intravascular thrombosis[7,8] and the generally held clinical opinion as to stasis in the pathogenesis of thrombosis,[9] the antithrombotic action of heparin and dicoumarol [3,3'-methylenebis (4-hydroxycoumarin)] was studied in the presence of venous stasis.

Methods. Rabbits were used as the experimental animal. Prothrombin concentrations were estimated by the method of Quick[11] using rabbit brain thromboplastin in both whole and 16% plasma.[10,12] Coagulation times were determined by the capillary tube method using free-flowing venous blood. In preliminary experiments[7] various sclerosing agents and the intravascular insertion of darning cotton and wool yarn failed to consistently induce thrombosis in the absence of stasis and congestion. Soaking the wool yarn in defibrinated blood was found to augment thrombus formation to some degree. In the method of producing thrombosis finally adopted white wool knitting yarn was soaked in defibrinated dog's blood, thoroughly dried, and all gross masses of dried blood removed by gently pulling the yarn between the fingers. It was then unraveled into single strands; 2 strands loosely wound together were used as an intravascular foreign body. The neck of rabbits anesthetized

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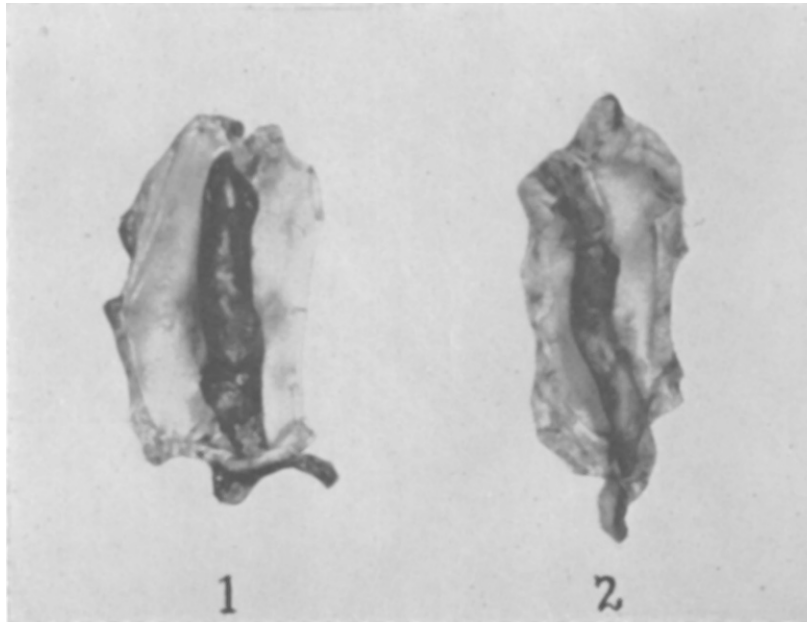

FIG. 1.
Thrombi produced in the jugular vein of rabbits by the insertion of blood-soaked wool yarn in the presence of stasis.

with nembutal intravenously, was shaved and a midline incision made to expose both jugular veins. The fascia was gently removed from these vessels from low in the neck to well above their bifurcation. A double strand of the blood-impregnated wool was threaded via a straight needle through 2 or 3 cm of the lumen. Temporary pressure with cotton sponges was used to control oozing following the venepuncture. A small (2 x 10 mm) metal clip was placed about the lower end of the exposed vein in such a manner that 3 or 4 respiratory cycles occurred before the vein emptied when it was digitally compressed above the foreign body. Great care was taken to insure the patency of the vein at this point. The wound was closed with a continuous cutaneous cotton suture. No dressing was applied, thus avoiding external compression of the vein.

Control Animals. In 6 animals 2 strands of blood-impregnated wool yarn were inserted on each side, and metal clips were placed about both jugular veins. In all of the 6 rabbits bilateral occluding red thrombi were found in 48 hours. (Fig. 1 and 2.) In 6 other rabbits the wool yarn was inserted bilaterally but the metal clips to slow the flow of blood were placed on only one side. Occluding red thrombi were present in 48 hours in all the veins constricted by a clip but in only 3 of the 6 veins to which no clip had been applied. The consistent occurrence of occluding thrombosis in veins treated in this manner in the presence of stasis and congestion and the failure of thrombosis to occur in one-half of the veins in which no stasis was induced emphasizes the importance of stasis in the production of experimental thrombosis by this method.

Heparinized Animals. Heparin was administered as the sodium salt intravenously in 10 mg doses twice daily to all animals in this series. Six rabbits received the first injection of heparin immediately before the bilateral jugular insertion of the wool yarn. Prior to heparin administration the coagulation time of all animals (from 3 to 5 minutes) was recorded twice daily for 2 days. Coagulation times obtained 6 hours after the last previous injection of heparin were consistently over 60 minutes. Of the 6 animals in this series one died of spontaneous hemorrhage 24 hours and one 36 hours after operation. At autopsy both animals showed gross gastrointestinal and

intraperitoneal hemorrhage. The jugular veins in both animals contained firm red thrombi. The 4 remaining animals were autopsied 48 hours after operation; both jugular veins were found to be occluded by firm thrombi in every case. In 2 additional rabbits blood-impregnated wool yarn was inserted into both jugular veins, but partial constriction of the vein by a metal clip was omitted. Determination of coagulation times and the administration of 10 mg of heparin intravenously twice daily as noted were also carried out in these animals. After 48 hours the jugular veins of both animals contained small thrombi with the colorless characteristics of "white thrombi."[1]

Dicoumarolized Animals. Seven rabbits were used in this series of experiments. Control prothrombin and coagulation times were established in each animal on 2 successive days. Following this a single excessive dose of dicoumarol† (100 mg) was administered by mouth. Prothrombin times were determined daily until the animal died or was killed. When the prothrombin concentration reached 20% or less of the control value (usually within 48 hours) insertion of a double strand of wool yarn as described above was carried out. In 3 of this group of animals a metal clip was placed on only one jugular vein; in the other 4 animals metal clips were placed bilaterally using the precautions to insure incomplete obstruction outlined above. Three of the animals died within 36-48 hours after operation from generalized hemorrhage. All the remaining animals were examined 48 hours after operation. All the jugular veins that had been constricted with a metal clip contained red thrombi indistinguishable from those in the untreated control animals. Of the 3 veins which had not been constricted by a clip, 2 contained thrombi distinctly smaller than those of the untreated controls; the third vein contained a thrombus the same size as in the controls.

Summary and Conclusions. 1. A method for the consistent production of experimental intravascular thrombosis is described. 2. The important role of stasis in the pathogenesis of thrombosis is emphasized. 3. The results show that the administration of heparin and dicoumarol in adequate doses to delay coagulation was not sufficient to prevent the development of experimental intravascular thrombosis in the presence of stasis of the venous circulation as induced in these experiments.

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Increased Resistance of Carrot-Fed Rats to Carbon Tetrachloride.

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The increased resistance of carrot-fed rats to acute anoxia has been reported by Campbell[1,2,3] and later confirmed by Nelson *et al.*[4] Since there is considerable evidence suggesting that the necrosis of the liver which follows the administration of carbon tetrachloride may be due to tissue anoxia, rather than to a direct toxic effect of the halogen hydrocarbon on the liver cells, it was decided to determine if a carrot diet would increase the resistance of rats to carbon tetrachloride. The possible protective action of charcoal was also studied as Campbell had shown that a high charcoal diet also increased the resistance of rats to acute anoxia.

Rats weighing from 150 to 250 g were used for all of the experimental work. In each individual experiment animals of the same sex

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