synthesize the protein portion of ceruloplasmin. In a few patients malabsorption of copper may be a contributing factor.

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Observations on Blood Flow During Spontaneously Occurring Traube-Hering Waves. (24118)

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Rhythmic fluctuations in blood pressure which are slower than the respiratory rate and on which respiratory and cardiac waves are superimposed are commonly designated by the names of several or all of the authors describing them in the latter part of the last century; Traube(1), Hering(2), and Mayer(3). These investigators agreed that the waves in blood pressure were probably due to rhythmic changes in peripheral resistance secondary to rhythmic impulses conveyed from the central nervous system *via* the sympathetic nerves. Hering, further, felt on the basis of his studies that the respiratory center was the source of the rhythmic impulses which acted on the vasomotor center by way of its connections with the latter. More recently evidence has been reported indicating that chemo- and baro-receptors may be the ultimate starting point of the rhythmic impulses(6,7). Much evidence has since accumulated to support the view that rhythmic alterations in peripheral resistance account for blood pressure fluctuations. Thus it has been shown that the diameter of arteries in the ear of rabbits and dogs fluctuate rhythmically in time but opposite in direction to the rhythmic changes in arterial pressure(4). Blood flow as estimated by the hot-wire anemometer technic fluctuates similarly when measured in the leg muscles of the cat(5). Recent studies in humans using plethysmograph technics have shown similar findings and, moreover, indicate that the Traube-Hering waves are commonly seen in normal, unanesthetized subjects(8-11). Direct measurements of blood flow during the

occurrence of Traube-Hering waves seem to be almost entirely lacking in the literature, only one report being found in publications of the past 20 years. This communication(12) concerned the finding of rhythmic changes in blood flow to the hind limb of a dog, the flow changes being synchronous with but in the opposite direction to the variations in systemic artery pressure. The present communication reports briefly 2 additional instances in which direct measurements of blood flow were made during spontaneous occurrence of Traube-Hering waves in the dog.

Material and methods. Blood flow and blood pressure recordings were made in 2 separate groups of experiments on 6 dogs each. In one group the blood flow in the saphenous artery (a small branch of the femoral artery supplying the skin mainly) was measured by the differential pressure technic employing a differential strain gauge to record pressures above and below a constricted area in a plastic tube the distal end of which was inserted into the distal end of the saphenous artery near its origin. Blood was withdrawn from the opposite femoral artery and pumped through this tubing into the saphenous artery at a pressure determined by a Starling resistor which allowed shunting of blood above a fixed pressure head. Pulsatile pressure approximating normal values was employed. Thus the flow of blood through the vascular bed under study was the flow under a controlled pressure and variations in flow are inversely related to the vascular resistance. In the second group of experiments blood flow into the distal vertebral arteries was measured with electrically recording rotameters which were incorporated into the arterial side of a DeWall-Lillehei pump oxygenator, the venous return being obtained from the femoral veins. The perfusion pressure was controlled as in the first series. The carotid arteries were ligated and the soft tissues of neck tightly compressed with a metal band save for the trachea, the external jugular veins, the carotid arteries and the vagosympathetic nerve trunks. Anesthesia was induced with chloralose, 100 mg/kg, intravenously. The femoral artery blood pressure was recorded *via* a Statham strain gauge on a Sanborn polyviso recorder along with the blood flow.

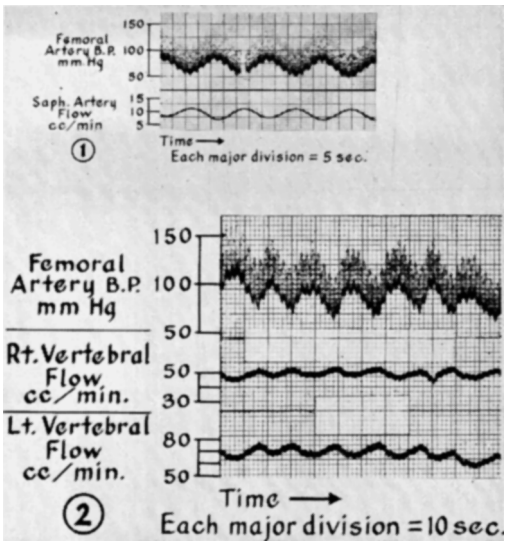

FIG. 1 and 2. Relationship between blood flow and femoral artery pressure observed in 2 instances in which Traube-Hering waves spontaneously occurred during an experiment.

Results. One of 6 animals in each of the 2 experimental groups spontaneously developed slow rhythmic fluctuations in blood pressure which had a period of about 18 to 20 seconds. Both animals were in good general condition when this occurred and remained so for a considerable period of time thereafter. The variations in blood flow under independently controlled pressure (Fig. 1,2) are seen to be exactly synchronous in time but opposite in direction to the fluctuations in systemic blood pressure. This finding indicates that in the absence of changes in perfusion pressure there is an increase in regional vascular bed resistance synchronous with the systemic blood pressure rise. This confirms the conventional view that the Traube-Hering waves are due at least in large part to centrally mediated changes in vasomotor tone. This report is being made primarily because in previous studies which have come to our attention with one exception the perfusion pressures in regional beds under study had not been controlled.

Summary. Two experiments are reported in which regional blood flow under controlled perfusion pressure was being measured by direct means along with systemic blood pressure and in which Traube-Hering waves were

seen to occur. Rhythmic changes in the regional blood flow were observed which were synchronous with but opposite in direction to the changes in systemic blood pressure. This agrees with the conventional view that changes in blood pressure in this situation are secondary to changes in peripheral resistance.

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Effect of Dicumarol on Bleeding Time.* (24119)

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Roskam(1) reported that heparin has only a slight effect on bleeding time. This observation has been confirmed many times clinically. It is also evident from simple clinical observation that the newer indirect anticoagulants such as dicumarol have little effect on normal bleeding. However, there has not been any recent investigation of the effect of dicumarol on bleeding time. Roskam showed that the effect of heparin on bleeding time depended on technical details of method used. In our study, we used the original method of Roskam and Pauwen(2). Link(3) reported that a certain number of normal rabbits fail to show increase in prothrombin time with dicumarol (non-reactors). This provides a useful control in many experiments on dicumarol (4). As reported separately(5), administration of ACTH to rabbits results in rabbits previously refractory to dicumarol showing elevated prothrombin times with the drug. One series of our rabbits were therefore treated with ACTH in addition to dicumarol.

Methods. Bleeding times were determined on ear of rabbit by the method of Roskam and Pauwen(2). The ear was shaved, the rabbit immobilized. Ten cuts were made on each ear and the ears bathed with distilled water at 30°C and pH 7.0. Time for bleeding to stop from each cut was recorded and mean bleeding time with standard deviation calculated. Prothrombin times were done by the usual Quick procedure using rabbit brain thromboplastin. Dicumarol was given orally as a single dose of 5 mg/kg. ACTH was given to some rabbits as a single intramuscular dose of 5 mg/kg at the same time as dicumarol.

Results. Eighteen rabbits were given dicumarol and prothrombin times and bleeding times determined before (day 0) and on the third day. Five rabbits were similarly treated and prothrombin times and bleeding times determined before and on the fifth day. Eleven rabbits received both dicumarol and ACTH and prothrombin times and bleeding times determined before and on fifth day. The results are shown in Table I. P values are for value of mean bleeding time compared to the same value on day 0. Comparing bleeding time on third day with that at beginning of experiment, the average of mean bleeding times for the 18 rabbits showed a slight but significant increase. Eight of the 18 rabbits gave a sig-

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