blood flow(4,12) probably accounts for the reduction in the skin(12), renal(3,4,11,13) and splanchnic blood flow.

Summary. The effect on splanchnic circulation of a constant infusion of angiotensin was investigated on 8 normal subjects and 7 cirrhotic patients with portal hypertension. The rate of angiotensin infusion was varied to obtain a rise in mean arterial pressure of 50% and ranged from 0.3 to 0.5 γ/kg/min. Both cardiac output and estimated hepatic blood flow were reduced, respectively, by 17.5 and 23.9%. Portal venous pressure remained unchanged. Splanchnic resistances increased by 118.3%. These effects were present in the subjects of both groups.

1. Page, J. H., Bumpus, F. M., *Physiol. Rev.*, 1961, v41, 331.

2. Abell, R. G., Page, I. H., *J. Exp. Med.*, 1942, v75, 305.

3. Barer, G. R., *J. Physiol.*, 1961, v156, 49.

4. Mandel, J. M., Sapirstein, L. A., *Circulation Res.*, 1962, v10, 807.

5. Caesar, J., Shaldon, S., Chiandussi, L., Guevara, L., Sherlock, S., *Clin. Sci.*, 1961, v21, 43.

6. Shaldon, S., Dolle, W., Guevara, L., Iber, F. L., Sherlock, S., *Circulation*, 1961, v24, 797.

7. Taylor, R. D., Page, I., *Am. J. Med. Sci.*, 1943, v205, 66.

8. Wilkins, R. W., Duncan, C. N., *J. Clin. Invest.*, 1941, v20, 721.

9. Bradley, S. E., Parker, B., *ibid.*, 1941, v20, 715.

10. Cournand, A., Ranges, H. A., Riley, R. L., *ibid.*, 1942, v21, 287.

11. Finnerty, F. A., Jr., Massaro, G. D., Chupkovich, V., Tuckman, J., *Circulation Res.*, 1961, v9, 256.

12. Bock, K. D., Krecke, H. J., Kuhn, H. M., *Klin. Wchnschr.*, 1958, v36, 254.

13. Assali, N. S., Westersten, A., *Circulation Res.*, 1961, v9, 189.

Received September 17, 1962. P.S.E.B.M., 1963, v112.

Effect of Drug Infusion on Splanchnic Circulation. II. Serotonin Infusion In Normal and Cirrhotic Subjects. (28031)

L. CHIANDUSSI, F. GRECO, D. INDOVINA, L. CESANO, A. VACCARINO AND F. MURATORI
(Introduced by S. Sherlock)
Institute of Medical Pathology, University of Turin, Turin, Italy

The 5-hydroxy-tryptamine or serotonin is a very recently discovered and isolated hormone(1) and its physiological properties are not yet well known. Small amounts of 5-HT (2-8 γ/kg) can produce, besides a raised pulse rate, a slight rise or a slight fall in blood pressure or even a biphasic reaction(2): larger amounts (10-100 γ/kg) are usually hypertensive(3). Andrews and Butterworth (4), on histological grounds, suggested that serotonin may constrict the hepatic vascular bed. Gibertini(5), by single injections of serotonin (100 γ/kg) into a peripheral vein or directly into the portal vein of dogs, could observe, 30-40 seconds after the injection, a rise in portal pressure, lasting 3-4 minutes. Recently a raised blood level of serotonin was found in 28 patients with portal hypertension(6). It seemed that these two findings might be related. Hence the present studies of the effect of serotonin intravenous infusion on the splanchnic hemodynamics in normal and cirrhotic subjects were undertaken.

Material and procedure. The subjects were divided into 2 groups. Group I consisted of 8 subjects without liver and cardiovascular disease. Group II consisted of 8 patients with liver cirrhosis and portal hypertension.

After catheterization of a main right hepatic vein, hepatic blood flow (EHBF) was measured by a constant infusion of Indocyanine Green, following the Fick principle (5). At least 4 pairs of arterious and hepatic venous blood samples were obtained for estimation of basal hepatic blood flow.

Mean arterial pressure (MAP) was very often recorded by a Rangoni-Battaglia electromanometer; the tracings were electrically damped.

Intrasplenic pressure (ISP) and wedged and free hepatic vein pressures (WHVP and FHVP) were, alternatively, simultaneously recorded by a couple of Rangoni-Battaglia electromanometers with zero reference point 5 cm below the sternal angle. They were repeatedly recorded before and during serotonin infusion.

Portal venous pressure (PVP) was calculated from the formula:

$$\text{PVP (mm Hg)} = \frac{\text{ISP} + \text{WHVP}}{2}$$

or was assumed to equal the WHVP.

Splanchnic resistances (SR) were calculated from the formula:

$$\text{SR (dynes/sec/cm}^{-5}) = \frac{(\text{MAP} - \text{PVP}) \times 80}{\text{EHBF (l/min)}} (6).$$

Cardiac output (CO) was measured before and during the serotonin infusion by an indicator dilution technic, using 10 μc of RISA.

Rate of intravenous infusion of serotonin* was 30 γ/kg/min. After a 20 minutes interval, 4 paired samples of blood were obtained, at 5 minute intervals, for hepatic blood flow estimation.

Results. (Fig. 1). Mean arterial pressure: The pressor effect of the drug was in both groups variable, unpredictable, and not related to basal arterial pressure. In Group I there was a reduction of 5.5%, in Group II a rise of 4.6%; the differences were not significant ($P>0.05$).

Cardiac output: No significant changes in cardiac output were noted during serotonin infusion (it was reduced by 0.1%). Only its fractions to the circulatory districts in the organism were redistributed.

Estimated hepatic blood flow: In both groups hepatic blood flow was slightly reduced. In Group I by 15.7% ($P>0.05$), and in Group II by 2.6% ($P>0.05$). The average of both groups was reduced by 9.2% ($P>0.05$) from 1289 to 1138 ml/min.

Intrasplenic and hepatic venous pressures: Both intrasplenic and wedge and free hepatic venous pressures showed a trend, similar to

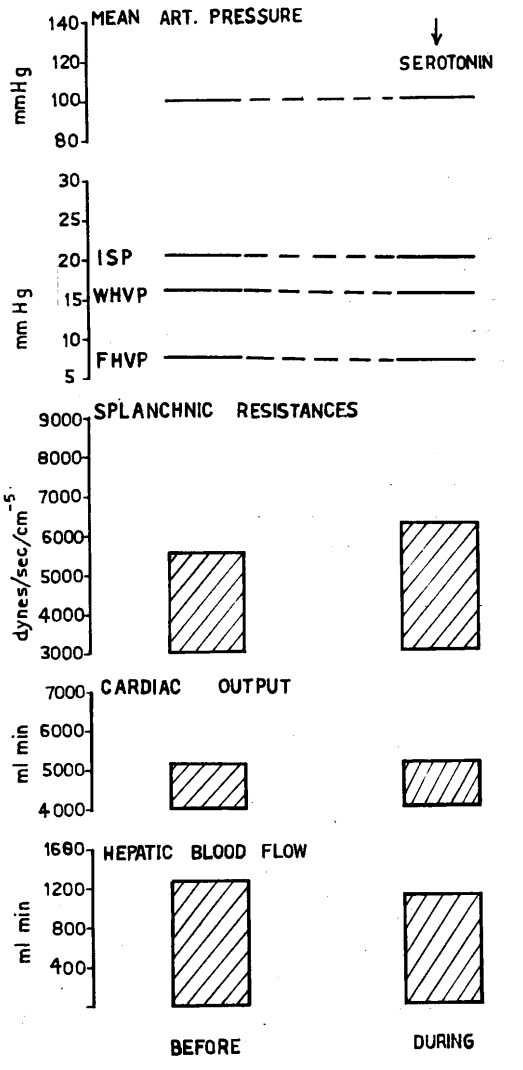

FIG. 1. Effects of serotonin infusion on parameters of splanchnic circulation.

the hepatic blood flow, to a slight reduction, more evident in Group I than in Group II. In Group I all the differences were significant ($P<0.05$). For both groups the over-all reductions were respectively 5.6%, 7.1%, and 15.2%.

Splanchnic resistances in both groups were slightly, but not significantly raised ($P>0.05$), respectively 13.5% and 13.0%.

Discussion. Serotonin intravenous infusion induced in all the subjects tachicardia, palpitations and cardiac pain. The pressor effect, variable and unpredictable, was always

* "Antemovis" Vister.

slight. The serotonin effect on the splanchnic circulation was also slight and often statistically not significant. Its infusion elicited a moderate reduction of hepatic blood flow and portal venous pressure and a slight rise of splanchnic resistances. Differences of material, dose and technic probably account for differences with the data obtained by Gibertini(5). There was no evidence that serotonin could represent, as suggested by Magdaleine *et al.*(6), a vasoconstrictor agent, able to cause or to maintain in man a portal hypertensive state.

Summary. The effect on splanchnic circulation of a serotonin constant infusion was investigated on 8 normal subjects and 8 cirrhotic patients with portal hypertension. The rate of serotonin infusion was of 30 γ/kg/min.

Mean arterial pressure, cardiac output and portal venous pressure were not significantly affected.

The estimated hepatic blood flow was reduced by 9.2% ($P<0.05$) and the splanchnic resistances were raised by 13.0% ($P<0.05$).

There was no evidence that a raised serotonin blood level in man could cause or maintain a portal hypertensive state.

1. Erspamer, V., *Pharmacol. Rev.*, 1954, v6, 425.

2. Page, I. H., McCubbin, J. W., *Circulation Res.*, 1953, v6, 354.

3. Schneider, J. A., Yonkman, F. F., *J. Pharmacol. and Exp. Therap.*, 1954, v8, 84.

4. Andrews, W. H., Butterworth, K. R., *J. Physiol.*, 1958, v141, 38.

5. Gibertini, G., Lodi, R., *Chir. e Pat. Sper.*, 1960, v8, 990.

6. Magdelaine, M., Dreux, C., Bonvarlet, A., Leger, L., *Présse Med.*, 1962, v70, 7.

Received September 17, 1962. P.S.E.B.M., 1963, v112.

Arterial Blood Acid-Base Balance in Unrestrained Waking Cats.* (28032)

B. RAYMOND FINK AND A. SCHOOLMAN (Introduced by W. S. Root)
Department of Anesthesiology and Neurosurgery, College of Physicians and Surgeons, Columbia University, New York City

Available data on the blood acid-base balance of the intact cat(1,2) refer either to venous blood or to mixed venous and arterial blood, in both cases on animals depressed by anesthesia. Because of the susceptibility of the cerebral circulation and of neural responses to changes in carbon dioxide tension, reliable reference values are needed for standardizing acid-base balance in neurophysiological experiments. Such values are reported here for animals free from experimental restraints and with an intact nervous system.

Healthy cats weighing 2.5 to 3.5 kg, observed for 2 weeks before operation, were anesthetized with pentobarbital, 35 mg/kg body weight, injected intraperitoneally. After ligation of the left common carotid artery a 17-gauge polyethylene catheter was introduced below the ligature and advanced into the aorta. The peripheral end of the catheter, mounted on an 18-gauge hypodermic needle capped with rubber, was anchored to the parietal bone. The needle hub projected through the skin, leaving the rubber cap easily accessible for sampling. Blood samples of one ml were withdrawn at intervals up to 15 days after the operation. pH was measured at 37°C. Carbon dioxide content was determined micromanometrically and pCO_2 calculated from the Henderson-Hasselbalch equation ($pK = 6.1$). In 3 animals samples of 2 ml were drawn, permitting determination of serum sodium and potassium with a Patwin flame photometer, chlorides with a Cotlove chloridimeter, packed red cell fraction by microhematocrit and hemoglobin oxygen saturation with a Beckman DU spectrophotometer and Nahas cuvette. Two ml of heparinized saline (50 mg per 1000 ml) were flushed through the catheter after each

* Supported by U.S.P.H.S. grant.