corpus luteum. No evidence of this change in the blood has been found in a study of some 2000 patients. Another explanation is a possible variability in kidney permeability at different periods of the cycle. Such evidence as we have collected in substantiation of this hypothesis has been published previously.[2]

3. *Can the kidney permeability be influenced or excretion stimulated?* The experiments of Smith and Smith[3] lead them to believe that progestin stimulates the excretion of the female sex hormone.

Repetition of their experiments, using Antuitrin (Parke, Davis & Co.) as well as progestin supplied through the kindness of Dr. George Van S. Smith, gave negative results.

In our series, both the urine and feces were extracted and titered. Two normal isolated rabbits and one spayed female were used for the Antuitrin experiments, 900 M. U. of female sex hormone being injected. Two castrated adult females were used in the progestin experiments, the dose of female sex hormone being 1800 M. U. These experiments failed to confirm the results obtained by Smith and Smith. These results might indicate a rapid destruction or fixation of the female sex hormone in some non-assayable form but other interpretations cannot be excluded.

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Effect of Digitalis and Rest on Pulmonary and Peripheral Circulation in Patients with Circulatory Failure Caused by Heart Disease.

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This study was undertaken to shed further light on the mechanism of circulatory failure caused by heart disease and on the circulatory changes that follow administration of large therapeutic doses of digitalis, and rest. Weiss and Ellis[1] observed the effect of digitalis on the volume and velocity of blood flow and other aspects of the circulation after repeated control observations in patients with

[2] Frank, R. T., and Goldberger, M. A., Proc. 2nd Int. Cong. for Sex Res., 1930, 378.

[3] Smith, G. Van S., and Smith, O. W., *Am. J. Physiol.*, 1931, **98**, 578.

[1] Weiss, Soma, and Ellis, L. B., *J. Clin. Invest.*, 1930, **8**, 435.

rheumatic heart disease and with compensated circulation at rest. In this study such repeated control observations on the aspects of the circulation measured, because of the clinical condition of the patients and of the methods used, were not feasible. A definite separation of the changes due to digitalis effect and rest between determinations, therefore, cannot be made, but the arrangement of the observations was similar to those used in the treatment of cardiac patients. To ascertain a possible correlation between the pulmonary circulation and ventilatory function, in some of the cases measurements of different components of the lung volume were also performed simultaneously with the circulatory observations. The following aspects of the circulation were studied simultaneously before and after digitalis: (1) electrocardiogram; (2) the degree of orthopnea; (3) arterial blood pressure; (4) venous pressure with the method of Moritz and Tabora[2]; (5) cardiac minute volume output with the method of Moore, Kinsman, Hamilton, and Spurling[3]; (6) the peripheral and pulmonary velocity of the blood flow according to the method of Weiss and Robb[4]; (7) blood volume according to the method of Keith, Rowntree and Geraghty[5]; (8) lung volume with the method of Van Slyke and Binger[6]; (9) oxygen and carbon dioxide content of the blood samples obtained from the femoral artery and vein.

The patients were given powder of digitalis corresponding to 2 gr. or more per 10 lb. of body weight within 24 hours. A maintenance dose of 2 to 3 gr. was given daily thereafter. All 12 patients exhibited clinical evidence of circulatory failure at rest, but according to certain clinical manifestations and laboratory findings they were divided in 3 groups.

Group A comprised 4 patients with dyspnea and orthopnea and regular cardiac rhythm. As judged from the normal peripheral venous blood flow and the normal venous pressure, the normal oxygen difference between the femoral artery and vein and the absence of peripheral edema or enlargement of the liver, no obvious congestion or circulatory disturbance existed in the peripheral circulation. The dyspnea, orthopnea, rales over the bases of the lungs prolonged mean pulmonary velocity of the blood flow, low vital

[2] Moritz, F., and Tabora, D. V., *Deutsch. Arch. f. klin. Med.*, 1910, **98**, 475.

[3] Moore, J. W., Kinsman, J. M., Hamilton, W. F., and Spurling, R. G., *Am. J. Physiol.*, 1929, **89**, 331.

[4] Weiss, Soma, and Robb, G. P., unpublished study.

[5] Keith, N. M., Rowntree, W. G., and Geraghty, G. T., *Arch. Int. Med.*, 1915, **16**, 547.

[6] Van Slyke, D. D., and Binger, C. C., *J. Exp. Med.*, 1923, **37**, 457.

capacity, decreased ratio between the vital capacity and the residual air space of the lungs, indicate a disturbance of the pulmonary circulation as well as of the physiological state of the alveolar function.

Group B comprised 4 cases with regular cardiac rhythm, which, however, from the clinical observations and the above-mentioned measurements in addition to the pulmonary congestion, exhibited also congestion of the peripheral circulation.

Group C included 4 cases with auricular fibrillation, who similarly to the cases of Group B in addition to pulmonary congestion, also showed congestion of the periphery.

Conclusions. (1) The pulmonary circulation in certain types of heart disease and in certain stages of circulatory failure may show severe disturbance with a simultaneous normal state of the peripheral circulation. (2) Orthopnea and dyspnea may be present with congestive disturbances of the pulmonary circulation alone and with normal peripheral venous pressure. (3) Auricular fibrillation with the same degree of increased venous pressure had a tendency to be associated with lower cardiac output than heart disease with regular rhythm. (4) Digitalis and rest may improve patients with orthopnea and pulmonary congestion without *necessarily* changing the cardiac output. In such cases it has been observed that the mean pulmonary velocity of blood flow increased even if the maximal velocity was unaltered. Notwithstanding the lack of essential change in cardiac output, the distribution curve of the dye in the pulmonary circuit assumed a steeper, narrower, and more symmetrical character, indicating a more normal pressure relation in the pulmonary circuit even in the presence of unaltered cardiac output. (5) In the group of patients with auricular fibrillation with low cardiac output, the increase in the volume and velocity of blood flow following digitalis and rest was particularly prominent. (6) Simultaneously with the improvement of the mean velocity of the blood flow in the pulmonary circulation, there is a decrease in the residual air and an increase in the vital capacity, indicating a dependence of the proper function of the pulmonary alveoli on the state of the pulmonary circulation. (7) These observations are in accord with the concept of the mechanism of circulatory failure expressed in a previous communication.[7]

[7] Weiss, Soma, *Ann. Int. Med.*, 1931, **5**, 100.