

It was thought that increase in oxygen consumption thus produced by redox indicators might be used to combat the effects of HCN or CO on mammals. Previous workers have confined their attention to the effects of methylene blue used in conjunction with cyanide. Among other things it was found empirically that methylene blue favored the recovery of animals poisoned by cyanide<sup>6, 7</sup>. Since CO has long been known to resemble CN in its effects on respiration it was thought of interest to see whether methylene blue also favored recovery in animals subjected to CO.

Experiments were carried out using rats which were placed one at a time in a chamber containing HCN gas or CO (about 1%). The time to unconsciousness was noted. As soon as an animal became unconscious it was removed from the chamber and given an intraperitoneal injection of methylene blue. The time required for recovery was determined using as a criterion of recovery the ability to run straight forward. Eighty rats were used; 40 controls and 40 dye-treated.

It was found that the use of methylene blue shortened the time required for recovery from HCN poisoning to about  $\frac{1}{3}$ , and that from CO to about  $\frac{1}{2}$  of that for untreated animals.

These results suggest that there is an activation of oxygen by methylene blue which manifests itself when aerobic oxidation is interfered with.

It is suggested that methylene blue injections could be used advantageously in cases of HCN or CO poisoning.

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### Utilization and Excretion of the Female Sex Hormone.

ROBERT T. FRANK, MORRIS A. GOLDBERGER AND FRANK SPIELMAN.

*From the Gynecological Service and the Laboratories, Mount Sinai Hospital, New York City.*

Of importance are answers to the question of (1) what happens to the female sex hormone after injection, (2) how is it excreted, (3) can the excretion be stimulated?

1. *What happens to the female sex hormone after injection?*  
Half hourly blood samples taken from isolated adult rabbits in

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<sup>6</sup> Sahlin, Bo, *Skand. Arch. Physiol.*, 1926, **47**, 284.

<sup>7</sup> Eddy, N. B., *J. Pharm. and Exp. Ther.*, 1931, **41**, 449.

whom 2000 M. U. of female sex hormone had been injected intravenously in one dose, showed that only 1 M. U. could be recovered from 4 cc. of serum during the first hour, and none thereafter. After subcutaneous injection, 5 cc. showed this reaction during the first hour. Twenty-four hours later the blood of a rabbit injected with 3000 M. U. and killed 24 hours later by bleeding, showed less than 1 M. U. in 40 cc. of blood, one-half of the total blood volume. From another rabbit given 3000 M. U. and killed 24 hours later, extracts made from the total skeletal musculature, the lungs, brain and liver were assayed. With the exception of the liver, the total extract of the organ proved negative. The extract corresponding to one-half the total liver contained but 1 M. U.

This series of experiments shows that large amounts of female sex hormone given intravenously or subcutaneously in the rabbit, rapidly disappear from the circulation and cannot be recovered from the internal organs 24 hours after injection. These results do not show whether the hormone is destroyed or so changed within the body fluids or tissues as to be no longer demonstrable by the Allen and Doisy reaction.

2. *How is the female sex hormone excreted?* Allen<sup>1</sup> found that female sex hormone was excreted almost quantitatively when injected into monkeys. We injected 2 African green monkeys, a male and female, each with 1500 M. U. of the hormone subcutaneously. Careful titer of the total urine for the next succeeding 2 days showed an excretion of approximately one-fifth of the amount of hormone injected.

An assay of the total amount of female sex hormone excreted in the urine of a normal fertile, normally menstruating woman, over one period was compared with the succeeding month during which time the individual received 5000 M. U. subcutaneously on the 9th, 15th and 26th day of the cycle. The differences in excretion of the entire amount during the month, as well as a comparison of the day before, during and after the injection, showed no appreciable changes.

Based on the observation of a large number of normal women, it is noted that although the blood samples during the first 3 weeks of the cycle show no variation, an increased excretion of female sex hormone in the urine occurs between the 9th and 11th day and again from the 24th to the 28th day. This might be interpreted as a short transitory flooding of the circulation with large quantities of female sex hormone suddenly elaborated by the follicle and

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<sup>1</sup> Allen, E., personal communication.

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.<sup>2</sup>

3. *Can the kidney permeability be influenced or excretion stimulated?* The experiments of Smith and Smith<sup>3</sup> 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.

GEORGE P. ROBB AND SOMA WEISS.

*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) of the Boston City Hospital, and the Department of Medicine, Harvard Medical School.*

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<sup>1</sup> 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

<sup>2</sup> Frank, R. T., and Goldberger, M. A., Proc. 2nd Int. Cong. for Sex Res., 1930, 378.

<sup>3</sup> Smith, G. Van S., and Smith, O. W., *Am. J. Physiol.*, 1931, **98**, 578.

<sup>1</sup> Weiss, Soma, and Ellis, L. B., *J. Clin. Invest.*, 1930, **8**, 435.