has not been compensated for in a material fashion by androgens derived from extragonadal sources. That the titers of these urinary hormones would reflect such androgenic stimulation as was present, was indicated when at a later date these men received daily intramuscular injections of 20 mg of testosterone propionate in one cc of peanut oil. With this treatment, which appears to provide only a minimal degree of replacement therapy (Hamilton;[18] Catchpole, Hamilton, and Hubert[11]), the quantities of urinary androgens and estrogens were increased to lie within the range found in normal men (Hamilton, Dorfman, and Hubert[7]) and the amounts of urinary gonadotropins were reduced to normal or subnormal limits (Catchpole, Hamilton, and Hubert[11]).

Comment. Two men who had been completely castrate for 13 and 18 years, respectively, had a marked capacity for penile erection, as observed during physical examinations and as tabulated in records kept daily for a year. Statements as to the interest and ability in intercourse exhibited by one of these men who was married were corroborated by his wife. Low titers of urinary androgens and clinical and laboratory evidence of testicular insufficiency, including supranormal values for urinary gonadotropins, provide assurance that there was no considerable androgenic secretion derived from extragonadal sources.

It would appear, then, that a marked capacity for penile erection may continue for many years subsequent to castration and that this phenomenon is not the result of stimulation by androgens derived from extragonadal sources because it may occur in individuals with definitely subnormal titers of androgens in the bodily tissues and fluids. It is not suggested that this phenomenon is typical of the majority of castrate men.

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Anesthesia: XI. The Anesthetic Action of Propenyl Ethyl Ether.*

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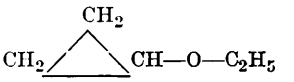
In former studies[1] the authors showed that cyclopropyl ethyl ether (cypreth ether) was an anesthetic agent in many species of animals. Attempts to induce surgical anesthesia in man with this agent were not satisfactory.[2] In man, the concentration of the vapors of cypreth ether required to induce anesthesia were irrespirable. It occurred to us to prepare an isomer of this true hybrid molecule between cyclopropane and ethyl ether.

$CH_3 \cdot CH : CH \cdot O \cdot C_2H_5$
Propenyl Ethyl Ether



Cypreth Ether

Propenyl ethyl ether is a volatile, colorless liquid, with a characteristic ethereal odor; it boils at 69°C and has a specific gravity of 0.774 at 20°C. At 25°C, 0.5 cc of this ether dissolves in 100 cc of water and the compound is not hydrolyzed at pH 7.4 in a phosphate buffer. Concentrations of the vapors of propenyl ethyl ether sufficient to produce

* The expense of this investigation was defrayed in part by a grant from the Ohio Chemical and Manufacturing Co. of Cleveland, Ohio.

1 Krantz, J. C., Jr., Carr, C. J., Forman, S. E., Evans, W. E., Jr., and Wollenweber, H. L., *J. Pharm. and Exp. Therap.*, 1941, **72**, 233.

2 Kilborn, M. G., Forman, S. E., Evans, W. E., Jr., and Krantz, J. C., Jr., *Anesthesiology*, 1942, **3**, 414.

incipient narcosis were found to be irritating to man.

Observation Anesthesias (monkey). Two large Rhesus monkeys were each anesthetized twice with propenyl ethyl ether. The induction period was short and uneventful. During induction and also during the period of surgical anesthesia much mucus accumulated in the bronchial tree. Relaxation of the musculature of the abdomen and extremities was complete under surgical anesthesia. The recovery period was prompt.

Anesthetic Index (dog). The general plan of administering the anesthetic was the same as that described previously.[3] The number of cubic centimeters per kilogram required to produce surgical anesthesia was divided into the volume per kilogram required to produce respiratory arrest and the quotient designated as the anesthetic index. In 10 dogs, the mean value per kg required to induce anesthesia was 0.45 cc while 1.43 cc per kg produced respiratory failure. The mean anesthetic index was determined to be 3.18. Two animals failed to recover when artificial respiration was instituted. There was sneezing, coughing, and much mucus produced in most of the dogs.

Blood Pressure Studies (dog). In two animals the blood pressure fell to about three-quarters of its preanesthetic value and remained at that level until approaching respiratory failure. After respiratory arrest the heart continued to beat several minutes. Under anesthesia with propenyl ethyl ether 4 dogs were cardioscoped and electrocardiograms made in the light and deep planes of surgical anesthesia. In this series of dogs, not any animal revealed any significant differences in rate, form, or regularity of the E.C.G. The dilution of the compound in Howell-Ringer's solution which produced the liminal effect on the frog's heart within one minute was determined to be approximately 0.02 molar.

Concentration Required for Anesthesia (mouse). The concentration of propenyl ethyl ether required to induce anesthesia was determined by typical partial pressure experiments described previously.[3] In 48 mice, 50% of the animals were anesthetized at a partial pressure of 2.5%, while 3% partial pressure produced anesthesia in all animals. With ethyl ether, in former studies 4% partial pressure did not produce anesthesia and 5% anesthetized 40% of the animals.

Delayed Anesthetic Deaths (rat). Twelve male adult rats were anesthetized with propenyl ethyl ether to the surgical plane and maintained in this condition for one-half hour. Two animals were sacrificed immediately thereafter for histologic study. The remaining 10 animals lived and were in good nutritional state over a period of 28 days observation.

Histologic Studies of Viscera (dog and rat). Two of the rats used in the delayed death studies were used for histologic studies of the kidneys and liver. There were no abnormalities attributable to the anesthetic. Three dogs were anesthetized lightly with cyclopropane and liver biopsies performed. The anesthetic agent was changed to propenyl ethyl ether and anesthesia maintained for from one to 2 hours and a second hepatic biopsy performed. There were no significant abnormalities.

Hemolysis Studies (dog). Ten cc volumes of propenyl ethyl ether of varying concentrations in normal salt solution were maintained at 25°C. To each of these was added 0.1 cc of defibrinated dog's blood and the time for hemolysis observed. Concentrations of 22, 43, and 84 mg % produced no hemolysis within 12 hours. A saturated solution of the agent in normal salt solution produced hemolysis within 5 hours at 25°C.

Summary. Propenyl ethyl ether produces prompt surgical anesthesia in many species of animals upon inhalation. The anesthetic index is higher than ethyl ether and the compound appears to be without deleterious action upon the myocardium, the normal histology of the liver or kidney, or upon the red blood cell in anesthetic concentrations. However, this ether in common with its isomer, cypreth ether, produces irritation of the upper respiratory

[3] Krantz, J. C., Jr., Carr, C. J., Forman, S. E., and Evans, W. E., Jr., *J. Pharm. and Exp. Therap.*, 1940, **69**, 207.

[4] Krantz, J. C., Jr., Carr, C. J., Evans, W. E., Jr., and Forman, S. E., *J. Pharm. and Exp. Therap.*, 1943, **78**, 115.

tract in animals and especially in man. For this reason we are of the opinion that the compound is unsuited as a volatile anesthetic in man.

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The Serum Potassium in Two Cases of Sprue.

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Studies of sprue and allied conditions in recent years have shown that many elements of the diet are poorly absorbed or poorly utilized. The dietary constituents chiefly emphasized have been fat, carbohydrate, protein, calcium, phosphorus, and vitamins A, D, K, and parts of the B-complex. In some instances the defective absorption of a particular element of the diet is reflected in serum values lower than normal. This is notably true for calcium. To our knowledge no previous investigation of the values of serum potassium in sprue-like syndromes has been carried out. We have recently observed 2 cases of sprue in which the serum potassium was found to be at extraordinarily pathological levels. The blood chemical findings in these 2 patients at the time of admission to the hospital are the subject of this report. Determinations of the serum potassium were carried out by the method described by Harrison and Darrow.[1]

Case 1 was a 53-year-old Spaniard who complained of diarrhea, a sore tongue and extreme weakness for 3 weeks prior to his hospital admission. He was markedly emaciated, weighing only 37 kg (81.4 lbs), and gave the appearance of having been ill much longer than his history would indicate. His tongue was smooth and reddened. He was having 5 or 6 loose bowel movements a day, and the stools were found to contain excessive amounts of fat. The oral glucose tolerance test showed a low curve. He had achlorhydria and a severe, macrocytic, hyperchromic anemia. The blood chemical values are shown in Table I. It will be noted that the serum potassium level was 1.1 meq/L (4.3 mg/100 cc), as compared with the normal range of approximately 4.1 meq/L (16 mg/100 cc) to 5.6 meq/L (22 mg/100 cc).

Case 2 was a 44-year-old Greek woman, whose symptoms of sprue were later attributed to lymphosarcoma of the intestine and mesenteric lymph nodes. She had, during this time, 3 to 8 bulky, frothy, foul-smelling stools daily. She had had a moderate anemia which had responded somewhat to treatment with liver and transfusions, without general improvement. During her entire illness she had complained of weakness, which on admission was so severe that she could not feed herself or sit up unaided. The patient was emaciated, weighing 40 kg (88 lbs), and was extremely weak, although no true paralysis was present. She had a marked steatorrhea. The oral glucose tolerance test showed a low curve. The Chvostek and Trousseau signs were positive. The blood chemical values are shown in Table I. On admission the serum potassium was 1.3 meq/L (5.1 mg/100 cc) and 5 days later was even lower, 1.1 meq/L (4.3 mg/100 cc).

These values for the serum potassium, 1.1 and 1.3 meq/L are almost, if not quite unique. Abnormally low levels have been reported previously in several different clinical conditions. First, and most commonly, low serum potassium has been encountered in familial periodic paralysis. It was first reported by Biemond and Daniels[2] who found a level of

[1] Harrison, H. E., and Darrow, D. C., *J. Biol. Chem.*, 1937, **121**, 631.

[2] Biemond, A., and Daniels, A. P., *Brain*, 1934, **57**, 91.