jected penicillin in mice experimentally infected with Type I pneumococci. 2. When equal oral doses of these adjuncts are given, 'Benemid' had at least two to three times the duration of action of carinamide. 3. Plasma concentration studies show that 'Benemid' disappears from the blood stream at a somewhat slower rate than does carinamide. 4. Plasma concentration studies, combined with a consideration of the protection test data, suggest that 'Benemid' has about twice the intrinsic activity of carinamide. 5. The combined data indicate that the prolonged effectiveness of 'Benemid' in mice is the result not only of its slower rate of disappearance from the blood stream but also of its greater intrinsic activity.

1. Beyer, K. H., *Science*, 1947, v105, 94.
2. Crosson, J. W., Boger, W. P., Shaw, C. C., and Miller, A. K., *J. Am. Med. Assn.*, 1947, v134, 1528.
3. Verwey, W. F., and Miller, A. K., PROC. SOC. EXP. BIOL. AND MED., 1947, v65, 222.
4. Eisman, S. H., Kay, C. F., Norris, R. F., and Boger, W. P., *Am. J. Med. Sci.*, 1949, v217, 62.
5. Beyer, K. H., Russo, H. F., Tillson, E. K., Miller, A. K., Verwey, W. F., and Gass, S. R., *Am. J. Physiol.*, 1951, v166, 625.
6. Reed, L. J., and Muench, H., *Am. J. Hyg.*, 1938, v27, 493.
7. Brodie, B. B., Levy, B., and Bernstein, E., *J. Pharm. and Exp. Ther.*, 1947, v91, 246.
8. Tillson, E. K., Russo, H. F., Schuchardt, G. S., Gass, S. R., and Beyer, K. H., 1952, to be published.
9. Boger, W. P., Gallagher, M. E., and Pitts, F. W., *J. Phila. Gen. Hosp.*, 1950, v1, 51.
10. Boger, W. P., Personal communication.

Received February 20, 1952. P.S.E.B.M., 1952, v79.

Comparative Study of Anabolic Effects of Three Androgenic Steroids.* (19425)

W. DEAN WARREN AND MARK A. HAYES. (Introduced by R. L. Kahn.)
From the Department of Surgery, University of Michigan Medical School, Ann Arbor, Mich.

It has been reported(1) that testosterone cyclopentylpropionate (hereafter referred to as TCP) has greater anabolic and androgenic activity in rats than testosterone propionate (TP) or methylandrostenediol (MA). Studies in man(2) have shown that TCP has a more effective androgenic action than has TP. As a result of recent clinical experiments(3), it seemed desirable to attempt a comparative evaluation of the anabolic potency in man of these 3 steroidal preparations.

Method. A 56-year-old white man in good nutrition with a gastrostomy for a benign stricture of the esophagus was placed on a constant daily tube diet supplying: protein 70 g (11.2 g nitrogen), carbohydrate 98 g, 1730 calories; sodium 55.5 meq, potassium 70.7 meq, and adequate vitamin supplements all in a volume of 3050 cc. Twenty-four-hour urine specimens were collected and were measured carefully for volume and analyzed for total nitrogen (Koch-McMeekin method), carbohydrate (Nelson-Somogyi method), sodium and potassium (Perkin-Elmer flame photometer). Periodic determinations were made of the 24-hour urinary excretion of 17-ketosteroids (Robbie and Gibson method). Fecal nitrogen was not measured and was assumed to be constant(4). After a 7-day control observation period, and at 7-day intervals, the patient was given an intramuscular injection with equivalent contents of testosterone (2) of each of the 3 steroids in the following order: TP (300 mg), MA (300 mg), and TCP (353 mg).

Results. Fig. 1 presents the metabolic data of the entire experiment graphed according to the method of Reifenstein, Albright, and Wells(5). The apparent nitrogen retention manifested during the control period is accounted for in the calculated but unmeasured fecal losses. The dotted line extending through the experimental periods is the average excretion level of each substance calculated from

* Supported by the Lawrence J. Montgomery Research Fund.

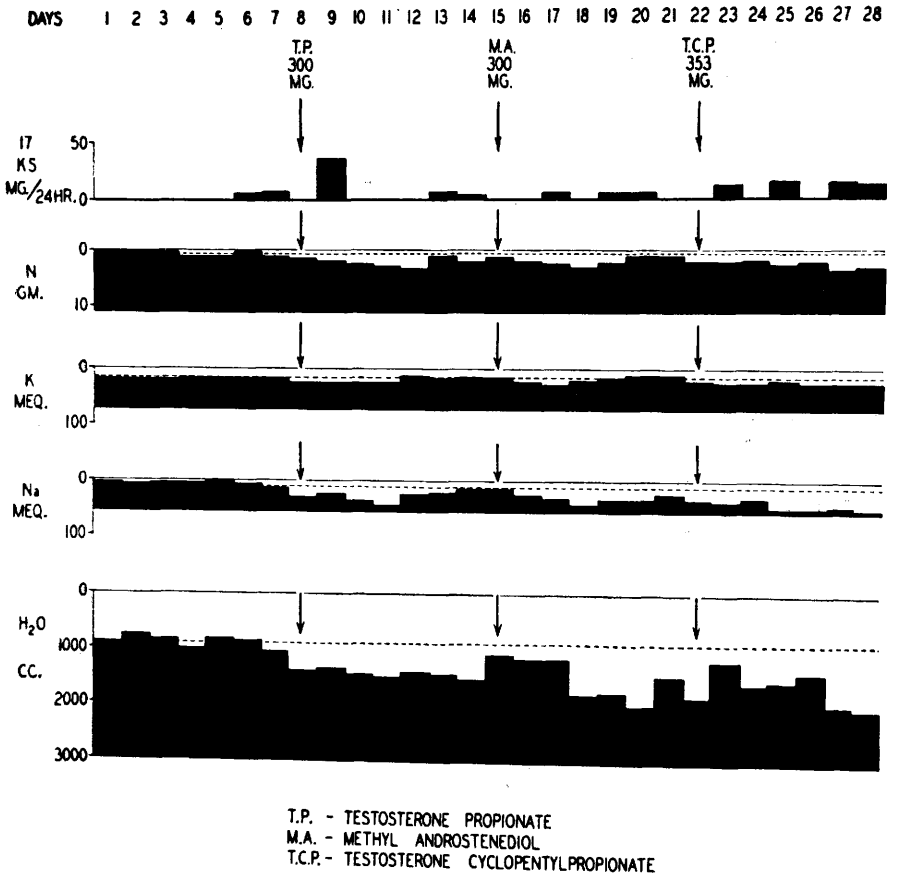

FIG. 1. Daily metabolic data illustrating the effects of the 3 androgenic drugs. The arrow indicates the day of administration of the drug. Data charted according to Reifenstein, Albright and Wells(5).

the control period and shows the absolute retentions produced by the 3 steroid preparations. Table I presents both the daily average excretory levels and the cumulative balances of water, nitrogen, sodium and potassium as effected by the 3 individual steroids compared with the control period. The anticipated retention of water, nitrogen, sodium and potassium(6,7) occurred following the injection of each of the preparations. It is readily apparent, however, (Table I) that the most profound effect followed the administration of TCP, when the comparable 7-day period cumulative retention of nitrogen was significantly greater by almost a factor of 2 and the 24-hour urinary excretion of 17-ketosteroids still indicated available steroid. The cumulative retentions of nitrogen, water and electrolytes with both TP and MA were essentially the same with equivalent dosages and were of much shorter duration, though the 17-ketosteroid excretion is reliable only in evaluating the duration of activity of TP, since MA is not metabolized and excreted as a

TABLE I. Daily Average Excretory Values and Cumulative Balances for Sodium, Potassium, Nitrogen as Influenced by the 3 Androgenic Agents.

Period, days (incl.)		Water, cc	N, g	Na, meq	K, meq
		Avg daily urinary excretion			
Control	1-7	2150	10.3	44.5	54.6
TP	8-14	1640	9.1	25.9	50.8
MA	15-21	1590	9.2	23.8	50.3
TCP	22-28	1440	8.2	11.5	48.7
		Cumulative retention			
Control	1-7	—	—	—	—
TP	8-14	3700	8.2	150.3	16.8
MA	15-21	3910	7.7	165.1	20
TCP	22-28	4990	14.1	251.4	31.1

17-ketosteroid.

Summary. Comparative anabolic evaluations after a single equivalent dose injection of testosterone propionate, methylandrostenediol and testosterone cyclopentylpropionate indicate that TP and MA are about equal in anabolic potency, while TCP is twice as effective over a comparable period of time. TCP is also effective for a greater period of time, undetermined in this study.

The authors are indebted to many people for their assistance in this investigation: B. S. Dobbie, H. Bergene, and their staff on the surgical wards, University Hospital; J. P. Chandler, Consulting Biochemist, University Hospital; H. F. Hailman, the Upjohn Co., Kalamazoo, Mich., for the oral fat emulsion (Lipomul) and the testosterone cyclopentylpropionate; F. E. Houghton, of Ciba, Summit, N. J. for the testosterone propionate; M. W. Amster, Schering Corporation, Bloomfield, N. J., for the methylandrostenediol (Methostan).

1. Sakamoto, W., Gordon, G. S., and Eisenberg, E., PROC. SOC. EXP. BIOL. AND MED., 1951, v76, 406.
2. Hailman, H. F., personal communication.
3. Hayes, M. A., Hodgson, P. E., and Coller, F. A., *Ann. Surg.*, in press.
4. Albright, F., Forbes, A. P., Bartter, F. C., Reifenstein, E. C., Jr., Bryant, D., Cox, L. D., and Dempsey, E. F., in Symposia on Nutrition, Vol. II *Plasma Proteins*, J. B. Youmans, edit., C. C. Thomas, Springfield, 1950.
5. Reifenstein, E. C., Jr., Albright, F., and Wells, S., *J. Clin. Endocrinol.*, 1945, v5, 367.
6. Kenyon, A. T., Knowlton, A., Sandiford, I., Koch, F. C., Lown, G., *Endocrinol.*, 1940, v26, 26:
7. Hayes, M. A., *Univ. Mich. Med. Bull.*, 1951, v17, 83.

Received February 21, 1952. P.S.E.B.M., 1952, v79.

Effect of Follicle-Stimulating Hormone on Gonads of Immature C57 Black Mice.* (19426)

HENRY D. MOON AND CHOH HAO LI.
From the Division of Pathology, School of Medicine, and the Department of Biochemistry, University of California, San Francisco and Berkeley.

While mice have been utilized extensively for the bioassay of urinary gonadotropins, there have been no reliable data on the effects of highly purified follicle-stimulating hormone in mice. This study was performed with the purpose of determining the responsiveness of mice of the C57 black strain to a highly purified follicle-stimulating hormone (FSH) preparation isolated from sheep pituitary glands (1,2). Female C57 black mice, 20 to 24 days old, were injected daily with FSH for 5 days and autopsied 24 hours after the final injection. Groups of 6 mice were used for each level of FSH. At autopsy the ovaries and uteri were dissected, weighed and fixed in formalin. Paraffin sections of the uteri and the ovaries, stained with hematoxylin and eosin, were prepared.

A right orchidectomy was performed on male mice 21 to 27 days old of the C57 black strain; the right testis was weighed and fixed in formalin. Immediately following orchidectomy, FSH was injected daily for 5 days. The animals were sacrificed on the 6th day following orchidectomy, 24 hours after the final injection. The left testis was weighed and fixed in formalin. Microscopic sections of both testes were prepared. Controls of both sexes of similar age range were not injected.

Results. Female mice. The ovaries showed no morphologic changes at 0.05 and 0.10 mg levels. The uteri of all mice showed endometrial and myometrial stimulation characteristic of that produced by estrogens. The uninjected controls showed infantile ovaries and uteri (Table I). With total doses of 0.25 mg or more the ovaries showed some follicular development. A 5 mg total dose produced occasional follicular hemorrhages and early thecal luteinization.

Male mice. The uninjected controls showed

* Aided in part by grants from the University of California Cancer Grant, the Eli Lilly Laboratories, Merck and Co., and the Armour Laboratories.