have been destroyed by bacterial action, it is doubtful whether any of the galacturonic acid was absorbed.

Conclusions. Less than 10%, if any, of galacturonic acid, introduced as an isosmotic and isotonic solution, is absorbed from the canine small and large intestine and the human small intestine. Isosmotic galacturonic acid stimulates the secretion of fluid by the small intestine of unanesthetized human and canine subjects.

13204

Effect of Androgen Administration upon Pregnandiol Excretion in Cyclical Women.

UDALL J. SALMON, SAMUEL H. GEIST AND A. AUSTIN SALMON.
From the Laboratories, Mount Sinai Hospital, New York City.

There is abundant evidence in the studies of Venning and Browne[1, 2] and others,[3, 4, 5] which indicates that the progesterone which is formed in the corpus luteum of cyclical women is excreted in the form of sodium pregnandiol glucuronidate (SPG). In previous communications, we have reported that testosterone propionate, administered in sufficient amounts to cyclical women, suppresses follicle growth, ovulation and corpus luteum formation,[6] inhibits production of estrogen and progesterone by the ovary[7, 8] and, as a consequence, prevents the development of the secretory pattern of the endometrium, ultimately leading to atrophy of the endometrium[7, 8, 9] and vaginal mucosa.[10, 11]

1 Venning, E. H., and Browne, J. S. L., *Am. J. Physiol.*, 1937, **119**, 417.

2 Venning, E. H., and Browne, J. S. L., *Endocrinology*, 1937, **21**, 711.

3 Hamblen, E. C., Ashley, C., and Baptist, M., *Endocrinology*, 1939, **24**, 1.

4 Stover, R. F., and Pratt, J. P., *Endocrinology*, 1939, **24**, 29.

5 Wilson, R. B., Randall, L. M., and Osterberg, A. E., *Am. J. Obs. and Gyn.*, 1939, **37**, 59.

6 Geist, S. H., Gaines, J. A., and Salmon, U. J., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 319.

7 Geist, S. H., Salmon, U. J., Gaines, J. A., and Walter, R. I., *J. A. M. A.*, 1940, **114**, 1539.

8 Salmon, U. J., *J. of Clin. Endocrinology*, 1941, **1**, 162.

9 Gaines, J. A., Salmon, U. J., and Geist, S. H., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 779.

10 Salmon, U. J., Walter, R. I., and Geist, S. H., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 467.

11 Salmon, U. J., Geist, S. H., and Walter, R. I., *Am. J. Obs. and Gyn.*, 1939, **38**, 264.

The evidence pointing to inhibition of corpus luteum development and suppression of progesterone formation consisted of (a) the failure to find a corpus luteum in the ovaries of cyclical women treated with testosterone, at a time when one would, under normal conditions, expect to find one;[6] and (b) the failure to find a secretory pattern in the premenstrual endometrium of these women.[7, 9] As part of a series of studies of the biologic properties of androgens in the human female, we investigated the effect of androgen administration upon excretion of the pregnandiol complex.

Methods and Material. A group of 8 women with regular menstrual cycles, in whom premenstrual endometrial biopsies revealed typical secretory patterns indicative of normal estrogen-progesterone production, were given androgens. SPG determinations were performed according to the method of Venning,[12, 13] during periods of the cycle indicated in Table I. At the termination of the experimental study, 3 of these patients were operated upon and the ovaries examined grossly and microscopically for corpora lutea.

The androgens used were: (1) methyl testosterone (3 patients), given orally, in daily doses of 50 to 150 mg (total doses of 1480, 2350 and 2800 mg); (2) testosterone propionate in oil, administered intramuscularly (3 patients), in individual doses varying from 50 to 100 mg (total doses of 600, 1050, and 1175 mg); (3) testosterone (500 mg) and testosterone propionate (516.6 mg) pellet implantation (2 patients).

TABLE I.

Case No.	Androgen	Dose, mg	Route of administration	Time of administration, days of cycle	Pregnandiol excretion: Amount, mg	Pregnandiol excretion: Time of studies, days of cycle	Remarks
1	m.t.	1480	oral	1-21	0	1-40	M.P. suppressed.
2	m.t.	2350	"	1-24	0	4-24	M.P. suppressed. No c.l. found at operation.
3	m.t.	2800	"	1-30	0	6-30	M.P. suppressed.
4	t.p.	600	intramuscular	1-14	0	6-30	M.P. suppressed. No. c.l. found at operation.
5	t.p.	1050	"	1-23	0	6-34	M.P. suppressed. No c.l.
6	t.p.	1175	"	10-21	55	14-22	M.P. occurred on 24th day of cycle.
7	t.p.	516.6	pellet implantation	1	0	1-43	M.P. suppressed.
8	t.	500	" "	4	0	4-30	M.P. suppressed.

m.t.—methyl testosterone. t.p.—testosterone propionate. t.—testosterone. M.P.—menstrual period. c.l.—corpus luteum.

12 Venning, E. H., *J. Biol. Chem.*, 1937, **119**, 473.

13 Venning, E. H., *J. Biol. Chem.*, 1938, **126**, 595.

Results. Methyl Testosterone. No SPG was found in any of the patients during the current cycle when the androgen was being administered. In each case, the expected menstrual period was suppressed. The pregnandiol determinations were performed beyond the time when the pregnandiol complex would normally be found. In one case, the studies were conducted for 40 consecutive days. One patient of this series (Case No. 2) was operated on at the end of the experiment. The ovaries did not contain a current corpus luteum.

Testosterone Propionate. In this group, one patient was given testosterone propionate during the first 2 weeks (Case No. 4), one during the first 3 weeks (Case No. 5), and a third during the middle 10 days of the cycle (Case No. 6). In the first two, no SPG was found in the urine, whereas a total of 55 mg was recovered from the urine of the third patient. Cases No. 4 and No. 5 were both operated on and no corpus luteum was found in either.

It is noteworthy that in Case No. 6. in which 55 mg of SPG was found, the testosterone propionate was administered after the 9th day of the cycle when, presumably, the hypophyseal gonadotropic factor had already been secreted. Apparently, the administration of even so large a dose as 1175 mg of testosterone propionate could not suppress progesterone production if given during the middle of the cycle. If the testosterone is administered during the first 2 weeks of the cycle, a much smaller dose (*e. g.,* 600 mg) will prevent pregnandiol excretion (Case No. 4). This is in agreement with previous observations that 500 to 600 mg of testosterone propionate is sufficient to suppress ovulation and menstruation if administered during the first 2 weeks of the cycle, but has no such inhibitory effect on the current cycle if the same or larger doses are administered during the last 2 weeks of the cycle.[7, 8]

Androgen Implantation. In the 2 patients implanted, one with 516.6 mg of testosterone propionate on the first day of the cycle (Case No. 7) and the other with 500 mg of testosterone on the 4th day of the cycle (Case No. 8), the SPG was completely absent from the urine for 42 and 26 days, respectively, after the implantation. The testosterone propionate pellet (Case No. 7) was excised 63 days after the implantation and was found to have lost 306.6 mg representing an average daily absorption of 4.9 mg. At this rate, the patient absorbed approximately 137.0 mg during one cycle. The testosterone pellet was excised 58 days after the implantation and was found to have lost 344 mg, representing an average daily absorption of 5.9 mg. During the current cycle (24 days) this would

represent an absorption of 141.6 mg of testosterone. Previous studies have shown that, when administered intramuscularly in solution in sesame oil, the absorption is very rapid and consequently a considerable amount of the hormone is excreted before it can produce any effect.

Summary and Conclusions. Eight women with regular menstrual periods and normal cyclic estrogen and progesterone production, as evidenced by the finding of typical secretory endometria premenstrually, were treated with androgens (methyl testosterone by mouth, testosterone propionate by injection, and testosterone and testosterone propionate by implantation) in order to determine the effect of the androgens upon excretion of SPG. The results indicate that doses of androgens which have been found, in previous studies, to be suppressive (*i. e.*, to cause suppression of pituitary gonadotropic hormone excretion; inhibition of ovulation and menstruation), when administered early in the cycle, result in failure of SPG to appear in the urine during the current cycle and lead to suppression of the next expected menstrual period. In one patient (Case No. 6), 1175 mg of testosterone propionate, administered after the 9th day of the cycle, did not appear to appreciably affect the excretion of the pregnandiol complex during the current cycle.

These results are interpreted as indicating that if sufficient androgens are administered early in the cycle, before the pituitary gonadotropin has been secreted or had time to exert its effect on the ovary, progesterone production is suppressed, resulting in absence of pregnandiol from the urine during the current cycle. That absence of SPG from the urine is due to failure of progesterone formation and not to interference with the conversion of progesterone to the pregnandiol complex is proven by the absence of corpora lutea from the ovaries in the patients with no pregnandiol excretion.

13205

Some Aspects of Metabolism Following Parenteral Administration of Casein Hydrolysate.

MELVILLE SAHYUN.

From the Biochemical Research Laboratory, Frederick Stearns and Company, Detroit, Mich.

During the process of digestion of proteins, amino acids are liberated and pass unchanged into the portal circulation. A portion