ferent from AP in its effect on maintaining pregnancy in ovariectomized rats and also by displaying other gonadal hormonal activities(9).

Oral activity was potentiated to a greater extent than parenteral activity when measured by endometrial proliferation. This has also been reported to occur when carbonic anhydrase or G/M ratio is used as an end point (2), but not to the same degree as when endometrial proliferation is used. This marked increase in oral potency is similar to that of AP over progesterone(2,10,11). This indicates that either intestinal absorption or metabolism of progesterone is markedly altered by addition of the 17α-acetoxy group and this increase of oral activity was further altered by addition of the 6α-methyl group.

Summary. 1) 6α-methyl-17α-acetoxyprogesterone is a highly active progestin based on its ability to promote a secretory endometrium and to prevent ovulation in rabbits. 2) Subcutaneously, 6α-methyl-17α-acetoxyprogesterone is 6 to 8 times and orally 60 to 75 times as active as 17α-acetoxyprogesterone in the McPhail assay. The ability of the 6-methyl compound to inhibit ovulation in rabbits is at least 20 times as great as that of progesterone subcutaneously, while 17α-acetoxyprogesterone is 7 times as active as progesterone.

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Pressure-Volume Changes in Human Forearm Veins after Atropine Administration.* (24790)

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Atropine has been used clinically and experimentally to produce cardiac acceleration (1). Recent studies suggest that the drug may have additional major effects on the cardiovascular system(2,3). Berry and coworkers reported a fall in central venous pressure and stroke volume after atropine administration(3). These observations were interpreted to indicate pooling of blood in the veins. Such an interpretation implies reduction in venous tone since venous pressure falls after the drug is given. The experiments reported here were done to examine the tone of the forearm veins after atropine administration.

Methods. The subjects were 18 healthy male medical students. All studies were done with subjects supine. Venous pressure was measured in the antecubital vein of the dependent left arm with a Statham 0 to 5 cm Hg strain gauge. Venous tone was measured in the right forearm by the plethysmographic method previously described(4,5). Observations were made intermittently for at least 30 minutes before and after injection of 2.0 mg of atropine sulfate into an ankle vein. In

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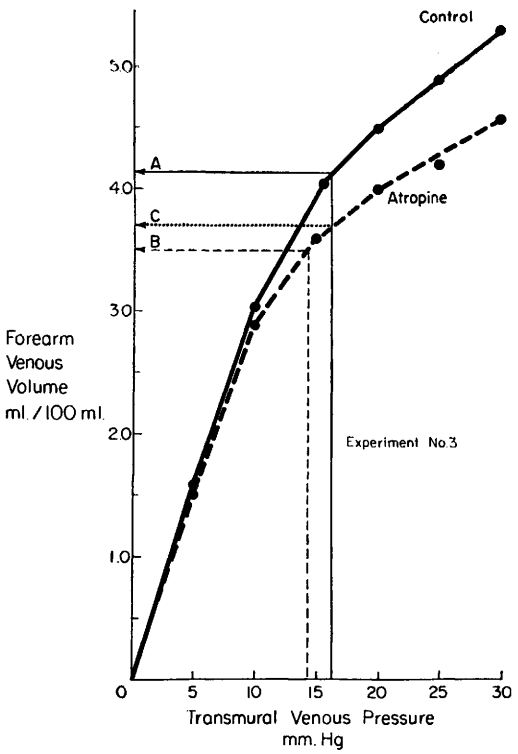

FIG. 1. A is forearm venous volume during control period. B is volume after atropine administration. C is volume which would have existed after atropine if there had been only venous constriction and no change in venous pressure.

5 subjects the experiment was repeated on a later day with the subject wearing a lower body anti-gravity suit inflated to 30 mm Hg. Forearm venous pressure-volume curves were constructed from the plethysmographic data (6). These curves (Fig. 1) express, in ml/100 ml of tissue, the forearm venous volume which exists at any level of transmural venous pressure between 0 and 30 mm Hg. The last point on the curve, the volume at a transmural pressure of 30 mm Hg, is designated arbitrarily as the *venous distensibility*. A high value is associated with reduced venous tone or dilatation, a low value with increased venous tone or constriction. Since venous pressure-volume characteristics are the same in both arms, the naturally occurring forearm venous volume may be determined by drawing a perpendicular line from the point on the pressure axis which corresponds to measured venous pressure, or transmural pressure, in the opposite arm. The volume coordinate of point of intersection of this line with the curve is the naturally occurring venous volume. The volume which would have existed after atropine administration if there had been only venous constriction and no change in venous pressure was estimated by applying the control venous pressure to the curve obtained following drug administration (Fig. 1). Control values are averages of at least 2 observations. Recorded values after atropine administration are single observations made at the time of maximal venous constriction. Statistical analysis of the data was done by the methods of Fisher(7).

Results. Venous pressure usually began to fall promptly after injection of atropine. Venous constriction appeared within 10 to 15 minutes and was maximal at 20 minutes.

Forearm venous pressure fell in 16 and remained unchanged in 2 experiments (Table I). The pressure averaged 14.6 $\pm$ 1.75 mm Hg during control periods and fell to an average of 12.4 $\pm$ 2.26 with atropine ($p < 0.001$). Venous constriction occurred in 17 of the 18 tests, although in 2 the change was slight. The venous volume at a transmural pressure of 30 mm Hg, *i.e.*, venous distensibility, averaged 4.0 $\pm$ 0.72 ml/100 ml of forearm tissue during control periods and fell to an average of 3.4 $\pm$ 0.57 after drug administration ($p < 0.001$). The naturally occurring forearm venous volume fell in each experiment. Volume decreased from an average of 2.6 $\pm$ 0.57 ml/100 ml during control periods to 2.0 $\pm$ 0.59 after atropine ($p < 0.001$). The venous volume which would have existed if there had been only venous constriction and no change in venous pressure averaged 2.3 $\pm$ 0.60 ml/100 ml.

The decrease in volume was caused by active venous constriction combined with fall in venous pressure. In 11 experiments venous constriction was primarily responsible for the decrease in venous volume and in 5 the decrease was caused primarily by fall in transmural pressure. In the other 2 both factors contributed equally to volume change. Although the fall in venous pressure was apparent soon after injection of the drug, the maximal change in venous distensibility appeared

TABLE I. Forearm Venous Responses to Atropine Administration.

Exp. No.	Venous pressure, mm Hg		Venous distensibility, ml/100 ml		Venous vol, ml/100 ml		Venous vol,* ml/100 ml
	Before	After	Before	After	Before	After	After
1	15.0	15.6	3.9	2.9	2.8	2.2	2.2
2	17.3	16.0	3.4	2.7	2.7	1.4	1.6
3	16.3	14.3	5.3	4.6	4.1	3.5	3.7
4	13.8	11.0	3.4	3.0	2.0	1.4	1.7
5	15.0	11.7	4.9	4.1	3.0	2.6	2.9
6	14.7	13.0	3.1	3.0	2.3	1.7	1.9
7	12.5	10.0	4.0	3.5	2.4	1.9	2.2
8	15.6	15.6	5.3	4.1	3.4	2.7	2.7
9	17.1	14.2	4.5	3.9	3.2	2.0	2.4
10	17.1	14.6	3.9	3.3	2.9	2.4	2.7
11	15.1	11.6	4.4	3.6	3.1	2.2	2.8
12	13.7	10.0	3.8	3.2	2.3	1.4	1.8
13	15.8	14.3	3.6	3.2	2.6	2.4	2.6
14	14.5	12.3	3.4	3.4	2.3	2.0	2.3
15	11.5	9.0	3.0	2.8	1.7	1.2	1.4
16	11.7	10.5	4.5	4.0	2.3	1.6	1.9
17	13.2	9.3	4.0	3.6	2.3	1.8	2.3
18	13.7	11.3	3.1	2.5	2.2	1.3	1.4
Mean	14.6	12.4	4.0	3.4	2.6	2.0	2.3
Stand. dev.	1.75	2.26	.72	.57	.57	.59	.60
Mean diff.		2.22		.56		.66	
Stand. error		.26		.07		.07	
Probability		<.001		<.001		<.001	

* Forearm venous volume after atropine if there had been only venous constriction and no change in venous pressure.

about 20 minutes later. This delayed venous constriction could result from pooling in some other vascular bed. If pooling occurred in the lower limbs or splanchnic bed, inflation of a lower body anti-gravity suit might be expected to prevent the forearm venous constriction and the fall in venous pressure. The venous responses, however, were not altered significantly in the 5 subjects in whom the experiment was repeated with the inflated anti-gravity suit (Table II).

Summary. 1) Observations on forearm venous distensibility, volume and pressure were made in normal subjects before and after intravenous administration of atropine sulfate. Venous pressure fell in 16, venous constriction occurred in 17 and venous volume fell in each of 18 experiments. These responses were not altered significantly in the 5 instances where experiments were repeated with a lower body anti-gravity suit inflated. 2) Atropine did not cause venous dilatation or venous pooling. Venous constriction occurred

TABLE II. Effect of Antigravity Suit on Venous Responses to Atropine Administration.

Exp. No.*	Venous pressure change, mm Hg		Venous distensibility change, ml/100 ml		Venous volume change, ml/100 ml	
	Without†	With‡	Without	With	Without	With
14	2.2	2.7	.0	.2	-.3	-.5
15	2.5	3.4	.2	.0	.5	-.5
16	1.2	2.0	.5	-.6	.7	-.6
17	3.9	3.4	.4	.5	-.5	-.7
18	2.4	.8	.6	-.6	-.9	-.9
Mean	2.4	2.5	.3	.4	.6	.6
Stand. dev.	.97	1.10	.24	.27	.23	.17
Mean diff.		-.02		-.04		-.06
Stand. error		.47		.07		.06
Probability		>.9		>.5		>.3

* Experiments 14 through 18 repeated with anti-gravity suit inflated.
† Without anti-gravity suit. ‡ With anti-gravity suit inflated to 30 mm Hg.

almost uniformly and in each instance blood shifted from the forearm.

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Mono-Substituted Vit. B_{12} Amides. I. A Microbiological Study.*† (24791)

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Smith(1) suggested that the labile amide groups of the B_{12} molecule function in enzyme reactions involving B_{12}. There are 3 of these, probably those on the propionamide chains. The amide linkages can be hydrolyzed with dilute acid or alkali. The acids can then be converted to variously substituted amides by reaction with methylamine, ethylamine, or aniline(1,2). Many substituted amides have been reported to have anti-Vit. B_{12} activity (3). Since Vit. B_{12} is essential for growth of many organisms and man, it could be supposed that a specific antagonist of Vit. B_{12} might stop cell growth. This report compares the microbiological activity of these 3 mono-substituted amides for 4 different B_{12}-requiring organisms.

Methods. The B_{12}-requiring organisms used are: *Lactobacillus leichmannii* ATCC No. 4797, *Escherichia coli* 113-3, *Euglena gracilis, Z* strain, and *Ochromonas malhamensis*. Technics for using these organisms for B_{12} assay have been reported(4,5,6). The methylamide, ethylamide, and anilide derivatives of the monocarboxylic acid of Vit. B_{12}, obtained in dry form, were dissolved in distilled water and diluted appropriately.

Results. The effect of mono-substituted amides on growth of the 4 organisms is given in Table I. As B_{12}-substitutes, the amides are practically inactive for *E. coli* and *O. malhamensis*. Their slight activity may be related to some B_{12} contamination of the amides. The amides support half-maximal growth for *L. leichmannii* in low concentrations, and almost full growth in higher concentrations. The ethylamide and methylamide do not support full growth of *E. gracilis*, but they are more than 3 times as effective as the anilide as B_{12}-substitutes. Additions of amides to various concentrations of B_{12} showed that they neither inhibited nor enhanced B_{12} utilization, since growth was unchanged from that without amide addition.

When *E. coli* is grown in the presence of the amide and suboptimal levels of methionine, the 2 are utilized synergistically; methionine and B_{12} combinations are additive (Table II). When combined with methionine, methylamide, ethylamide and anilide are respectively 30, 100, and 300 times less effective than B_{12} for growth of *E. coli*. In concentrations greater than 30 μg/ml of methionine, growth stimulation by added amide was not noticeable because adequate concentra-

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