TABLE II.
Repeated Titrations of Anticoagulase of Control Sera.

Serum	Anticoagulase titer										
1	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
2	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25	<25
3	278	417	278	278	278	179	179	417	417	278	417
4	278	278	278	278	278	179	278	417	417	278	278
A	179	125	179	125	179	—	125	—	—	—	—
B	900	900	900	900	900	1400	900	900	900	900	900
C	278	278	417	278	417	417	278	278	278	—	—
D	417	278	417	278	417	417	417	—	—	—	—

Anticoagulase titers of sera 1, 2, 3, and 4 were determined on different days between 7/15/48 and 8/2/48.

Sera A, B, C, and D were used as controls between 8/26/48 and 1/29/49.

sera be employed in the antibody titration within 24 hours since within 48 hours small amounts of activator may again be detected.

The system used for measuring inhibitor to coagulase employs 0.5 ml of fibrinogen containing 1:1000 activator, whereas in the titration of coagulase, 1.0 ml of fibrinogen containing a dilution of 1:3500 activator is used. This procedure of increasing the activator concentration in the antibody titrations was employed so that technical variations in the amounts of coagulase or activator added, or residual amounts of activator remaining in the serum being tested, would not alter the end-point appreciably. The present test, as compared to that devised by Lominski and Roberts,[6] controls the concentration of activator in the fibrinogen and therefore more reproducible results should be obtained.

The stability of the various reagents used in this test is not definitely known. The fibrinogen solutions should be employed within a few hours of preparation. When stored at –20° or 4°C in sealed ampules, coagulase retains most of its activity over a period of a year or more, but repeated standardizations are best performed at monthly intervals. Tryptose broth is added as a diluent to the coagulase because it appears to stabilize its action so that results are reproducible. Activator, when stored in sealed ampules at –20°C or –4°C or at 4°C in rubber stoppered flasks for over a year, appeared to have lost little activity. When stored at room temperature, however, a loss of activity was observed.

Summary. A satisfactory serological test for the titration of anticoagulase in human and animal sera has been devised by controlling the various factors which enter into the coagulase-anticoagulase reaction.

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Effect of Dibuline* on Nocturnal Gastric Secretion in Man. (17383)

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It has been shown[1-5] that dibuline (dibutyl urethane of dimethyl ethyl-B-hydroxyethyl ammonium sulfate, Merck) has a qualitative effect similar to that of atropine.

* Supplied by Dr. M. I. Grossman, University of Illinois, Chicago, Ill.

1 Swan, K. C., and White, N. G., *J. Pharm. and Exp. Therap.*, 1944, **80**, 285.

2 Featherstone, R. M., and White, N. G., *J. Pharm. and Exp. Therap.*, 1945, **84**, 105.

3 Peterson, C. G., and Peterson, D. R., *J. Pharm. and Exp. Therap.*, 1945, **84**, 236.

It possesses both a smooth muscle-inhibiting and an antiacetylcholine action. Marquardt, Case, Cummins, and Grossman[6] have reported a temporary decrease in the gastric secretory rate in dogs and humans given 10 mg subcutaneously; the effect was of short duration, the secretion returning to control levels within an hour. The purpose of this paper is to summarize a study of the effect of dibuline on the nocturnal gastric secretion of 14 patients with duodenal ulcer and one with functional bowel distress.

Method of study. The group consisted of 14 males and one female (14 with duodenal ulcer and one with functional bowel distress).

I. *The effect of a single injection* of dibuline was determined in 45 studies in fasting individuals. After a control period of 6 hours from 2:30 to 8:30 p.m., dibuline was given intramuscularly in a dose of 10 mg and its effect noted in the subsequent 4 hours. The gastric contents were aspirated continuously throughout the entire period of observation, the collection bottles being replaced at hourly intervals. The volume, concentration and total output of free hydrochloric acid were measured for each hour. A depressant effect on gastric secretion was considered significant if the reduction was greater than 25% and it was sustained for as long as 2 hours.

II. *Data on the total nocturnal gastric secretion* were obtained in a series of 15 experiments. The conditions of study were identical in all. All studies were made between 9:30 p.m. and 9:30 a.m. The gastric contents were aspirated continuously, the containers being replaced at hourly intervals. The volume, concentration of free hydrochloric acid, and total output of free hydrochloric of each hourly sample were determined by the usual method. Control hourly values for the 12-hour nocturnal gastric secretion were obtained for one night prior to the use of dibuline. During the second night, 10 mg of dibuline in 1.0 cc of water were given intramuscularly at 9:30 p.m., 1:30 a.m. and 4:30 a.m. The patients did not experience any pain at the site of the injection. No effect was considered significant unless a change of 25% or more was obtained.

TABLE I.
Effect of 10 mg Dibuline I.M. on Gastric Secretion in Man.

	Vol., %	Conc. free HCl, %	Free HCl mg, %
Increase > 25%	31	26	33
No significant change	43	34	27
Decrease > 25%	26	40	40

Results. Effect of a single injection of dibuline (Table I). The hourly volume was higher than the control values in 31% of the studies and did not change in 43%. A decrease of 25% or more from the control values was noted in 26% of the studies. Both the concentration and the output of free hydrochloric acid were lower in 40% of the studies. On the other hand, values greater than the control occurred during the administration of dibuline in 26 and 33%, respectively.

Effect on the 12-hour nocturnal gastric secretion. (Table II). In 3 individuals, the volume exceeded the control values. It was not affected significantly in 8 studies; lower volume was noted in 4 studies. In 3 of the latter, the concentration and output of free hydrochloric acid were diminished simultaneously. In 4 additional patients the concentration of free hydrochloric acid diminished although the volume of gastric secretion was unaffected. The total output of free hydrochloric acid (mg) was unchanged in 4 studies, considerably higher than the control values in 5, and lower in 6.

Discussion. The present results indicate that the effect of dibuline on gastric secretion in man is variable and similar to that obtained with atropine sulfate.[7] Both increases and decreases in secretion, as compared with the control period, were observed. The decreases particularly seem to be of sufficient magnitude to be of some significance. The recommended dose of dibuline (10

[4] Peterson, C. G., and Peterson, D. R., *Gastroenterology*, 1945, **5**, 169.

[5] Cummins, G. M., Marquardt, G. H., and Grossman, M. I., *Gastroenterology*, 1947, **8**, 205.

[6] Marquardt, G. H., Case, J. T., Cummins, G. M., and Grossman, M. I., *Am. J. Med. Sci.*, 1948, **216**, 203.

[7] Levin, E., Kirsner, J. B., and Palmer, W. L., to be published.

TABLE II.
Effect of Dibuline (10 mg I.M. at 9:30 p.m., 1:30 and 5:30 a.m.) on 12-Hour Nocturnal Gastric Secretion in Man.

	Control			During Dibuline			% change		
Case	Vol. (cc)	Free HCl (Cl units)	Free HCl (mg)	Vol. (cc)	Free HCl (Cl units)	Free HCl (mg)	Vol.	Free HCl (conc.)	Total output HCl
1	435	75	1191	744	54	1456	+71	—28	+
2	998	89	3200	1456	79	4170	+46	—	+30
3	401	49	719	506	34	624	+26	—30	—
4	1188	42	1833	1047	69	2616	—	+64	+43
5	553	67	1352	671	76	1851	+	+	+37
6	922	59	1988	1103	65	2593	+	+	+30
7	583	60	1282	671	72	1761	+	+	+37
8	1188	90	3892	1074	94	3690	—	+	—
9	1026	83	3103	1207	78	3416	+	—	+
10	598	56	1211	616	35	790	+	—38	—35
11	740	58	1556	622	39	885	—	—33	—43
12	1008	33	1208	757	14	387	—25	—58	—68
13	1232	63	2802	726	33	878	—41	—48	—69
14	1098	48	1908	591	33	491	—55	—31	—74
15	572	42	875	214	68	526	—63	+64	—40

mg) seems comparable to 1.0 to 2.0 mg of atropine. The decrease in gastric secretion, when it occurs, persists usually for 2 to 3 hours only. The repeated administration of the drug 4 hours after the initial dose is no more effective than the initial injection.

Dibuline is tolerated better than atropine. The parenteral injection of the latter in 1.0 mg doses every 4 hours, very frequently produces marked dryness of the mouth, blurring of vision, and tachycardia. Repeated injections of 10 mg of dibuline every 4 hours very seldom produce side effects; when they do occur, however, the symptoms are mild and of brief duration.

Conclusions. The effect of dibuline on gastric secretion is variable, transitory, and unpredictable. Further trial of the drug in the treatment of peptic ulcer seems to us unwarranted.

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Possible Sources of the Androgenic Factor in Cow Manure. (17384)

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The bacterial flora of the stomach of a ruminant is known to synthesize a number of compounds: proteins from urea;[1] vitamin B complexes,[2,3] etc. It was felt desirable to determine changes in 17-ketosteroids on incubated feces.

Turner[4] finds an androgenic factor in fecal material of pregnant cattle and goats. Longwell and Gassner[5] report increased size of comb when chicks are fed dried fecal material as part of their diet. They have made some attempt at characterization of the compound but have not reached a definite conclusion as to its chemical nature.

It seems desirable to investigate two pos-

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4 Turner, C. W., *J. Dairy Science*, 1947, **30**, 1.

5 Longwell, Bernard B., and Gassner, F. X., *Fed. Proc.*, 1947, **6**, 272.