

failures, etc. These cases could be excluded, although the fact that their inclusion introduces no significant in-out difference indicates that random rather than systematic errors are involved.

The second group of data, the selected series, consisting of clearance periods chosen on the basis of plasma equilibrium and technical perfection, but, of course, without regard to mannitol recovery, contains 30 periods from 16 tests on 12 patients.[§]

This series contains only periods preceded and followed by determinations of plasma concentration that did not differ by more than 3.5 mg%, a value within the error of the method (standard deviation = ± 2.5 mg%). An actual difference of this magnitude, in 2 specimens drawn 30 minutes apart, would represent, on the basis of an average normal mannitol space of 15 liters,³ a gain or loss of 17.5 mg/min. and thus might obscure a very large extra renal loss. To determine whether equilibrium had been obtained in these periods, they are further subdivided into 3 subgroups: those periods with bracketing plasma levels differing by less than 1 mg%, those with levels falling 1 to 3.5 mg%, and those rising 1 to 3.5 mg%. If equilibrium had not been established one would expect an excessive urinary recovery in the periods with falling levels and a deficient recovery in those

with rising levels. Eighteen periods were bracketed by levels differing by less than 1 mg% and the mean out-in ratio of these is 0.990. There were 8 periods in the falling group with a mean ratio of 0.995 and 4 in the rising group with a mean ratio of 0.970. Since, if these values represented actual differences in plasma concentration, the ratios would be 117 and 0.82 for the falling and rising groups respectively we feel that equilibrium had been established. In these selected periods, an average of 99.3 mg of mannitol was excreted for every 100 mg injected (range 87-114). This small series has a standard deviation of 6.0 with a standard error of the mean of 1.1, giving for the difference 100.0-99.3 a *t* value of 0.64, thus failing to establish a difference between the urinary recovery of mannitol and the amount injected.

Summary and Conclusions. 1. In 92 unselected clearance periods in 29 tests on 22 patients 100.4 mg of mannitol were recovered in the urine for every 100 mg injected.

2. In 30 periods in 16 tests on 12 patients selected on the basis of plasma equilibrium and technical adequacy 99.3 mg of mannitol were recovered for every 100 mg injected.

3. These data reveal no significant extra-renal disposal of mannitol.

16649

Twelve-hour Nocturnal Gastric Secretion in Uncomplicated Duodenal Ulcer Patients: Before and After Healing.

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A recent study^{1,2} demonstrated that the volume, concentration, and output of acid in the nocturnal gastric secretion are usually

higher in patients with duodenal ulcer than in normal healthy individuals. The patients had been admitted to the hospital because of ulcer distress. Several observers have suggested that the presence of symptoms may be a contributing factor in causing hypersecretion in duodenal ulcer patients. It

¹ Levin, E., Kirsner, J. B., Palmer, W. L., and Butler, C., *Arch. Surg.*, 1948, **46**, 345.

² Levin, E., Kirsner, J. B., Palmer, W. L., and Butler, C., *Gastroenterology*, 1948, **10**, 952.

TABLE I.
Twelve-Hour Continuous Nocturnal Gastric Secretion in Patients with Duodenal Ulcer Before and After Healing.

Case	Uncomplicated active duodenal ulcer				Uncomplicated healed duodenal ulcer				% change	
	Vol. (cc)	Free acid (Cl units)	Free HCl (mg)	Time interval (mo.)	Vol. (cc)	Free acid (Cl units)	Free HCl (mg)	Vol.	Free acid (Cl units)	Free HCl (mg)
1	1104	53	2130	6½	857	22	689	0	-40	0
	737	51	1348		979	39	1375			
2	581	49	1035	4½	770	42	1163	+44	—	+
		52	933			35	991			
3	1466	103	5481	3	1324	82	3954	0	—	—
	1102	115	4606		1128	94	3869			
4		13	333	3		18	536	+	0	+ 27
	680	21	504		720	20	524			
5	1398	57	2887	3	1430	60	3123	0	0	+
		67	2657		1358	75	3707			
6	643	55	1290	3	349	25	320	-52	-44	- 74
	614	52	1162		258	34	317			
7	675	62	1523	30	1019	47	1726	+53	0	+110
	630	40	917		1164	74	3122			
8		40	1223	9	1623	64	3787	0	0	0
	1800	65	4259							
	1700	55	3403							
	1650	62	3724							
	1600	48	2795							
	1560	57	3237							
9	940	112	3828	1½ yr	1176	92	3933	0	0	0
	1396	97	4921		1108	75	3044			
	1262	70	3211							
10	1200	58	2533	2¾ yr	1344	56	2726	0	0	0
	1400	55	2803		1394	63	3033			
	1500	61	3330							
	2000	34	2476							
11	543	42	830	2 yr	731	47	1251	+	+	+ 28
	621	50	1130		654	53	1262			
12	525	34	650	2½ yr	1039	16	618	+74	0	0
	650	20	473		897	23	767			
	500	6	109							
13	939	45	1553	7	1109	37	1515	+	—	0
					1032	42	1584			

+ Slight but not significant increase.

— Slight but not significant decrease.

TABLE II.
Nocturnal Gastric Secretion: Average Volume, Free Acidity, and Output Free Hydrochloric Acid.

	Vol. (cc)	Free acid (Cl units)	Mg free HCl
Normal	581	29	661
Duodenal ulcer (series No. 1)*	1004	61	2242
Active uncomplicated duodenal ulcer (present series)	1047	58	2208
Healed uncomplicated duodenal ulcer (present series)	1002	54	1957

* For complete data see reference No. 2.

seemed desirable therefore to measure the nocturnal gastric secretion in a group of patients with uncomplicated active duodenal ulcer having distress, and to repeat the same determinations in the same individuals during a period when the ulcer was healed and symptoms were not present.

Methods. The 12-hour nocturnal gastric secretion was measured in 13 patients with duodenal ulcer during a period when their ulcer was easily demonstrable roentgenologically and when typical distress was present. The studies were repeated in the same individuals after medical treatment had led to healing of the ulcer roentgenologically and to the complete subsidence of symptoms; the latter studies were carried out $2\frac{1}{2}$ months to $2\frac{3}{4}$ years after the ulcer was known to have healed.

The methods of study were identical with those described previously,^{1,2,3} enabling a strict comparison with our earlier observations. All data were submitted to statistical analysis. Previous studies have shown² that in the same individual with duodenal ulcer the total volume of the nocturnal gastric secretion on the average varies by approximately 20% and the free acidity and output of free hydrochloric acid by approximately 25%. This spontaneous variation was taken into account in evaluating the present results.

Results. The data for total volume, free acidity and output of free hydrochloric acid in the 12-hour nocturnal gastric secretion in the same individual during the phase of active ulcer and again during the period of healed ulcer are presented in Table I. The volume was unchanged in 9, significantly greater in 3, and significantly diminished in 1 (Case 6).

The free acidity of the total volume was unchanged in 11, and diminished in 2 (Cases 1 and 6). The output of free hydrochloric acid was unchanged in 9, significantly greater in 3, and diminished in 1 (Case 6). For the entire group there were no significant differences in the average volume, free acidity and output of free hydrochloric acid before and after healing of the ulcer (Table II).

The present data, in agreement with that obtained in previous studies^{1,2,3} (Table II), indicate that the average nocturnal gastric secretion in patients with uncomplicated duodenal ulcer and also in patients with healed uncomplicated duodenal ulcer is significantly greater than that of normal healthy individuals. Furthermore, the average night secretion of patients with healed uncomplicated duodenal ulcer is not significantly different from that of patients with duodenal ulcer requiring hospitalization because of distress (Series I).^{1,3}

The hourly pattern of acid secretion after the ulcer had healed was the same as had been noted during the period of active ulcer. The secretion of acid in all individuals in this series was continuous and was maintained at a relatively higher level than is seen in normal individuals. In no instance were there periods of anacidity for as long as one hour.

The persistence of hypersecretion in the vast majority of cases after healing of duodenal ulcer emphasizes the importance of continued careful antacid therapy in such patients.

Conclusions. 1. In the same patient with duodenal ulcer the 12-hour nocturnal gastric secretion is usually unaltered with healing of the ulcer.

2. The average 12-hour nocturnal gastric secretion of patients with active ulcer is not

³ Levin, E., Kirsner, J. B., Palmer, W. L., and Butler, C., *Gastroenterology*, 1948, **10**, 939.

significantly different than in patients with healed duodenal ulcer.

3. Twelve-hour nocturnal gastric secretion in patients with healed duodenal ulcer and

who are without symptoms is significantly greater than that of normal healthy individuals.

16650

Can Gonadotrophic Hormones Cross Two Parabiotic Unions in Rats?

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It has been shown that when 3 rats are joined in parabiosis gonadotrophic hormones produced by the middle member of the triplet set affect both of the other rats at the same time.¹ The present experiment was designed to test the ability of gonadotrophic hormones to pass from one lateral member, through the middle animal, and into the opposite lateral triplet of 3 united rats. Preliminary results, reported in abstract form,² have been extended and confirmed.

Methods and Results. Results are given for 19 sets of triple parabionts. Eight sets were united on the 25th day of life and 11 on the 40th day. A total of 14 single females, littermates of the parabionts, were used as controls in the two groups. All animals were autopsied at the age of 50 days. The results for the 2 age groups substantiate each other.

In producing triple parabiosis the edges of the abdominal walls were sutured together without establishing a coelio-anastomosis. The scapulae were held together by 3 interrupted sutures. The skin was joined by metal wound clips from ear to base of tail after removing strips of skin from the adjacent sides of each animal.

Two females from the same litter were joined in parabiosis, and a castrated male was attached to the left sister to make the triplet set. In all but 2 cases the male was a littermate of the 2 females in the set. The passage of gonadotrophic hormones from the castrated

male to the center female was indicated by the enlarged ovaries and uterus and by the involuted thymus (Fig. 1 and Table I). The female to the right, not directly attached to the male, showed no ovarian stimulation, the ovaries weighing even less than those of the littermate controls. The uterus, however, appeared to be slightly stimulated and the thymus very slightly reduced in size. The stimulated ovaries of the middle female contained large follicles and large corpora lutea.

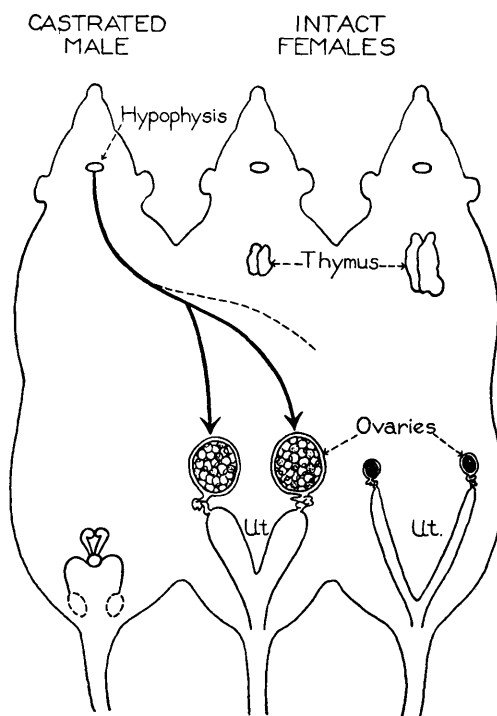


FIG. 1.

¹ Greep, R. O., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 214.

² Plagge, James C., *Anat. Rec.*, 1946, **94**, 489.