FIG. 1.—Case 1.—Carcinoma arising in the apical segment of the lower lobe, extending on to the left main bronchus, and surrounding the vagus nerve.

FIG. 2.—Case 1. Photomicrograph showing the vagus nerve surrounded but not invaded by growth.

fever, neuropathy, myopathy, and migrating thrombophlebitis. We cannot rule out the possibility that a humoral mechanism was responsible for gastro-intestinal symptoms in some of our cases. On the other hand, in nine instances the vagus nerve was surrounded by the growth though the nerve was never actually invaded (see Figs. 1 and 2). In these cases (and perhaps in others) the vagus may have been chronically irritated by compression. After prolonged irritation the nerve might become tolerant to compression or even be paralysed. This could be one reason for the cessation of abdominal symptoms before operation.

Gastric hypersecretion, hypermotility, and acute erosions can be produced in animals by stimulation of one vagus nerve (Talma, 1890). Focal haemorrhagic erosions and ischaemic lesions have been observed repeatedly after chronic vagal stimulation, though chronic peptic ulcer has not been produced experimentally in this way (Ivy, Grossman, and Bachrach, 1950). In men, peptic ulcer may be associated with various

intracranial lesions (Cushing, 1932), and the neurogenic theory of duodenal ulcer was based largely on the concept of continuous vagal overactivity. Whatever reservations one may have about the validity of this theory, it must be admitted that chronic vagal irritation would be expected to produce gastro-intestinal symptoms and possibly peptic ulceration.

Whatever the mechanism involved, the coexistence of bronchial carcinoma and dyspepsia poses a diagnostic problem. Error is particularly likely when the only symptoms are gastro-intestinal, a peptic ulcer is demonstrated, and routine chest x-ray examination shows minimal changes of doubtful significance.

Summary

Seventeen cases of bronchial carcinoma presenting with gastro-intestinal symptoms are reported.

It is suggested that irritation of one of the vagus nerves by the growth in the thorax may be responsible for the production of symptoms.

We thank Mr. Vernon Thompson and Mr. Geoffrey Flavell for permission to report these cases and for their advice, and Professor Clifford Wilson for helpful criticism.

REFERENCES

- Cushing, H. (1932). *Surg. Gynec. Obstet.*, 55, 1.
 Doll, R., and Jones, F. A. (1951). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 276.
 Hutchinson, J. (1855). *Med. Tms Gaz.*, 31, 383.
 Ivy, A. C., Grossman, M. I., and Bachrach, W. H. (1950). *Peptic Ulcer*. Blakiston, Philadelphia.
 Jones, F. A. (1957). *Brit. med. J.*, 1, 719.
 Philip, A. P. W. (1824). *Treatise on Indigestion*, 4th ed. London.
 Talma, S. (1890). *Z. klin. Med.*, 17, 10.

EXCRETION OF PREGNANETRIOL DURING THE NORMAL MENSTRUAL CYCLE

BY

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The excretion of oestrogens, pregnanediol, and gonadotrophins during the normal menstrual cycle has been investigated and reviewed (Brown, Klopfer, and Loraine, 1958). With the development of methods for estimating 5β -pregnane- $3\alpha,17\alpha,20\alpha$ -triol in urine, it was of interest to determine whether the excretion of this steroid varied during the menstrual cycle and whether any variations were related to the excretion of other steroids.

Materials and Methods.—The subjects were six normal females. Each subject collected urine daily from the last day of one menstruation until the first day of the next. Pregnanetriol was estimated as described by Fotherby and Love (1960) and pregnanediol by the method of Klopfer, Michie, and Brown (1955).

Results

The results are shown in the Table. For comparison of the menstrual cycles, which varied in length between the subjects, the day on which the peak excretion of oestrone and oestradiol occurred during the follicular phases was referred to as Day 0. The mean values and

Excretion of Pregnanetriol and Pregnanediol (mg./24 hours) in Six Subjects

Day of Menstrual Cycle	Case A (24 Yrs)		Case B (25 Yrs)		Case C (40 Yrs)		Case D (27 Yrs)		Case E (28 Yrs)		Case F (19 Yrs)		Pregnanetriol Mean $\pm$ S.D.	Pregnanediol Mean $\pm$ S.D.
	Pregnanetriol	Pregnanediol	Pregnanetriol	Pregnanediol	Pregnanetriol	Pregnanediol	Pregnanetriol	Pregnanediol	Pregnanetriol	Pregnanediol	Pregnanetriol	Pregnanediol		
-8			0.5	0.5					0.75	1.0				
-7			0.5	0.5			1.7	3.8	0.75	1.4	1.6	2.4		
-6			0.4	0.6	0.5	0.9	1.5	2.7	0.8	0.9	1.3	1.4	0.90 $\pm$ 0.43	1.30 $\pm$ 0.74
-5			0.5	0.7	0.5	1.0	1.3	2.8	0.8	1.3	2.0	1.3	1.02 $\pm$ 0.57	1.42 $\pm$ 0.72
-4			0.5	0.9	0.6	0.9	1.6	2.6	0.85	1.4	1.7	1.9	1.05 $\pm$ 0.53	1.54 $\pm$ 0.65
-3			0.6	0.7	0.5	1.1	2.1	2.6	0.8	1.4	1.4	1.4	1.08 $\pm$ 0.55	1.33 $\pm$ 0.63
-2	1.1	0.8	0.6	0.6	0.7	1.1	2.5	3.0	0.65	1.8	1.2	2.0	1.12 $\pm$ 0.65	1.55 $\pm$ 0.82
-1	0.7	0.6	0.6	0.9	0.6	1.2	2.0	2.6	0.85	1.2	1.3	1.3	1.01 $\pm$ 0.50	1.30 $\pm$ 0.63
0	1.5	1.1	1.0	0.9	0.9	1.2	2.2	2.4	0.85	1.2			1.29 $\pm$ 0.51	1.36 $\pm$ 0.53
1	1.6	1.4	1.0	1.1	1.6	1.2	2.2	2.7	1.0	1.8	2.0	1.8	1.57 $\pm$ 0.44	1.67 $\pm$ 0.53
2	1.5	1.2	1.1	1.4	0.8	1.5	3.4	4.6	0.9	2.1	1.7	1.5	1.57 $\pm$ 0.87	2.05 $\pm$ 1.17
3	1.3	1.5	1.1	2.4	1.5	2.0	3.1	3.6	1.0	2.5	2.2	2.6	1.70 $\pm$ 0.73	2.43 $\pm$ 0.64
4	1.7	2.1	1.2	3.9	1.3	3.0	3.1	5.3	1.0	3.0	1.6	2.5	1.65 $\pm$ 0.69	3.30 $\pm$ 1.05
5	1.9	3.5	1.3	5.5	1.4	3.8	3.4	6.2	1.1	4.0	1.9	2.7	1.83 $\pm$ 0.76	4.28 $\pm$ 1.20
6	—	—	1.0	5.9	1.3	4.0	2.8	5.5	1.2	4.7	2.0	2.1	1.66 $\pm$ 0.66	4.44 $\pm$ 1.34
7	2.2	3.5	1.0	5.9	1.4	4.4	3.0	6.8	1.0	5.5	1.8	4.0	1.73 $\pm$ 0.71	5.02 $\pm$ 1.14
8	2.1	2.3	1.5	7.5	1.3	3.7	1.6	6.4	1.3	5.6	1.6	4.1	1.57 $\pm$ 0.27	4.93 $\pm$ 1.75
9	2.3	3.3	1.1	5.9	0.8	4.2	1.8	7.4	1.0	6.0	1.8	3.6	1.47 $\pm$ 0.53	5.07 $\pm$ 1.47
10	1.6	2.6	1.2	4.9	1.4	3.5	1.4	6.5	1.2	4.7	2.2	4.1	1.50 $\pm$ 0.34	4.38 $\pm$ 1.22
11	1.3	2.6	0.8	4.7	1.8	3.8	2.0	5.8	0.7	3.5	1.7	3.6	1.38 $\pm$ 0.50	4.0 $\pm$ 1.01
12	1.4	2.8	0.7	3.1	0.7	2.8	3.1	7.0	1.2	3.8	1.5	1.9	1.43 $\pm$ 0.81	3.57 $\pm$ 1.63
13	1.2	2.2	0.7	2.2	0.7	2.6	2.2	5.8	0.7	3.0	1.5	2.1	1.17 $\pm$ 0.55	2.98 $\pm$ 1.30
14	1.6	2.5	0.6	1.2	0.7	2.2	1.9	4.6	0.75	2.4			1.11 $\pm$ 0.53	2.58 $\pm$ 1.11
15	1.2	1.7	0.5	1.2	0.7	1.1	2.0	3.4	0.8	1.9			1.04 $\pm$ 0.53	1.86 $\pm$ 0.82
16							2.0	3.0						
17							2.1	3.0						

standard deviations for the excretion of pregnanetriol and pregnanediol are shown in the Figure.

From the beginning of the cycle until Day 0 the daily excretion of both pregnanetriol and pregnanediol was fairly constant. From Day 0 onwards the excretion of pregnanetriol began to increase; by Day 3 it had reached a value almost twice the follicular phase level, and remained at this elevated level until Day 7, when it began to decrease. The pattern of pregnanetriol excretion was different from that of pregnanediol excretion, which started to rise on Day 1 and reached

a maximum value between Days 7 and 9. Thus the excretion of pregnanetriol reached a maximum value two to four days before that of pregnanediol and began to decrease two days before that of pregnanediol.

Estimations of 17-ketosteroids, 17-hydroxycorticosteroids, and dehydroepiandrosterone in urine from subjects C, D, and F showed that the excretion of these steroids did not vary during the menstrual cycle.

Discussion

It has been suggested by Solomon, Vande Wiele, and Lieberman (1956) that 17α -hydroxyprogesterone, the main precursor of urinary pregnanetriol, is an intermediate in the conversion of cholesterol to oestrogens, and Zander (1958) has identified 17α -hydroxyprogesterone in extracts of human ovaries. The pattern of pregnanetriol excretion during the menstrual cycle would probably suggest that 17α -hydroxyprogesterone has a function other than that of being an intermediate in oestrogen biosynthesis. It is of interest that esters of 17α -hydroxyprogesterone are active progestationally (Junkmann, 1957).

Pickett, Kyriakides, Stern, and Sommerville (1959), who studied only one normal subject and one adrenalectomized subject, have reported that pregnanetriol excretion varied during the menstrual cycle, but, contrary to the present results, found that in their normal subject the pregnanetriol excretion closely followed that of pregnanediol.

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REFERENCES

- Brown, J. B., Klopper, A., and Loraine, J. A. (1958). *J. Endocr.*, **17**, 401.
 Fotherby, K., and Love, D. N. (1960). *Ibid.*, **20**, 157.
 Junkmann, K. (1957). *Recent Progr. Hormone Res.*, **13**, 389.
 Klopper, A., Michie, E. A., and Brown, J. B. (1955). *J. Endocr.*, **12**, 209.
 Pickett, M. T., Kyriakides, E. C., Stern, M. I., and Sommerville, I. F. (1959). *Lancet*, **2**, 829.
 Solomon, S., Vande Wiele, R., and Lieberman, S. (1956). *J. Amer. chem. Soc.*, **78**, 5453.
 Zander, J. (1958). *J. biol. Chem.*, **232**, 117.

Excretion of pregnanetriol and pregnanediol (mean $\pm$ standard deviation).