A STUDY OF THE CONTRACTIONS OF THE NON-PREGNANT HUMAN UTERUS.*

By EDWIN M. ROBERTSON, F.R.C.S.Ed., M.C.O.G.
(*From the Departments of Midwifery and Pharmacology, University of Edinburgh.*)

THE study of the activity of the uterine muscle has revealed much of importance in many problems in gynæcology and obstetrics, and has brought to light many aspects of the complicated interplay between the sex hormones and their action on the uterus. That there is yet much to understand, however, may be gathered from the difficulty, sometimes experienced, of dealing satisfactorily with the painful spasms of primary dysmenorrhœa and of initiating uterine contractions in premature labour. Thus it seems that information of practical value with reference to the treatment of painful menstruation in women might be gained from further investigation of the physiological and pharmacological responses of the human uterus. This paper is a preliminary report on certain features of uterine action which, although they have been already investigated to some extent, have not yet been clearly defined.

Theoretical Considerations.

Since 1927, when Knaus carried out his original research into the functional relationship between the corpus luteum and the uterine muscle, much work has been directed towards the problem of uterine control, and it is now apparent that spontaneous uterine activity, and also the type of response of the muscle to chemical, hormonic and physical stimuli depend upon many factors such as species of animal, phase of sex cycle, pregnancy and the stage of pregnancy.

In seeking the solution of problems in the physiology of the human uterus—as with other organs—it is not always practicable to rely solely on the results of animal experimentation, and although *in vitro* experiments with human uterine muscle strips have been performed (Podleschka, 1934 ; Robson, 1936) and have yielded valuable information, there remains the necessity for the investigation of the human uterus in the

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living subject. In order to understand the aim of such direct studies in women, it is necessary to trace some of the fundamental steps in animal experimentation which have led to the investigation now under consideration.

In the rabbit (an animal in which ovulation takes place only after mating and always at a fixed time *post coitum*) it has been shown (Knaus) that the spontaneous contractions of the uterus, as well as the reactions of the muscle to posterior pituitary extract, vary according to the phase of the sex cycle at which the observations are made. Much of the experimental evidence obtained by Knaus and others supports the conclusion that uterine motility is greatest about the time of full development of the follicles in the ovary, when the secretion of œstrin is high and the endometrium is in the proliferative phase, and least during the dominance of the corpus luteum when the endometrium shows progestational growth. It has also been found that, prior to mating, posterior pituitary extract raises the tone of the uterine muscle and causes an increase in the contractions of the organ, whereas after ovulation and the development of a corpus luteum the uterine muscle remains quiescent and gives no response to stimulation by posterior pituitary extract. Although uterine quiescence and corpus luteum activity are so nearly approximated in the sex cycle, it must be noted that, in rabbits, the reduction in uterine motility which appears after mating actually precedes ovulation (Reynolds, 1932) and also, therefore, the development of the corpus luteum. This observation alone reveals the freedom of, at least, the pre-ovulatory phase of uterine quiescence from the influence of the corpus luteum. It does not, however, prove that the fully developed corpus luteum has no influence over uterine motility, but along with certain other indications that the corpus luteum is not the prime regulator of the muscular activity of the uterus, it is of great significance. However, so closely are the changes in uterine activity associated with changes in the ovary that it is possible in suitable circumstances to determine what phase of ovarian development has been reached at any stage of the cycle from an examination of the activity and reactivity of the uterus. Simultaneous examination of the endometrium provides corroborative evidence of ovarian function.

In the rabbit, therefore, it will be seen that not only the endometrium but also the uterine muscle reflects, to some

extent, the structural and functional changes in the ovary—and possibly other endocrine glands—and that at least one aspect of this association can be demonstrated by recording the reaction of the muscle to posterior pituitary extract.

This relationship between the corpus luteum and the reactivity of the uterine muscle suggested to Knaus a ready means of determining the time of ovulation in women. After elaborating a suitable apparatus with which the contractions of the human uterus could be recorded graphically, he carried out a series of experiments from which he deduced the time of ovulation, and by which he showed that in women the spontaneous and induced activity of the uterus alters from time to time throughout the menstrual cycle, as in the sex cycle of certain animals. The views of Knaus and his supporters may be expressed in terms of the menstrual cycle thus: during the proliferative, *i.e.* the follicular or œstral phase, the uterine muscle is spontaneously active and highly sensitive to posterior pituitary extract, whereas during the secretory, *i.e.* the luteal phase, when the corpus luteum is active and up to about twenty-four hours before the next menstrual period, the muscle is quiescent and refractory to posterior pituitary extract.

The recording apparatus used by Knaus, and later by others, to observe the movements of the human uterus, consists of a small rubber balloon which can be easily inserted into the cavity of the uterus and connected by means of pressure tubing to a mercury manometer. The whole system is filled with water and may be adjusted so that fluctuations due to contractions of the uterus can be recorded on the smoked paper of a recording drum.

Schultze (1931) carrying out similar investigations and using the method of filling the uterine cavity with a non-irritating fluid, and Moir (1934) and also Tachezy (1934), working with the small recording balloon, have obtained results which differ in important respects from those of Knaus. These investigators have found that the premenstrual phase of the menstrual cycle is not characterised by quiescence of the uterine muscle, and that during the luteal phase marked reactivity to posterior pituitary extract exists.

Thus, there are two views current at the present time regarding the contractility of the human uterine muscle in the second half of the menstrual cycle. Because of this

difference of opinion it has been necessary, in the course of further investigations into the physiology and pharmacology of the uterus and the cause of dysmenorrhœa, to repeat the experiments outlined above. Moir and Knaus have already made known the details of the apparatus which they have employed, and the apparatus used in this investigation differs in no essential details from that already described.

Observations.

(a) *Methods*.—The balloon is made of condom rubber and its capacity when full, but not distended, is 3 c.c. The balloon is bound to the end of a thin canula, similar in dimensions to a " Simpson's " sound, and the end of the canula enclosed by the balloon is finely perforated. About two feet of pressure tubing connect the canula to one limb of a mercury manometer, and the other arm of the manometer carries the floating writing point. Regarding this series of experiments at the beginning of each recording, the average fluid content of the balloon in the uterus has been 2 c.c. and the average pressure in the system has been 45 mm. Hg. The balloon, thread, canula, tubing and one limb of the manometer have always been sterilised before use, and all aseptic and antiseptic precautions have been taken in introducing the balloon into the uterine cavity. In certain cases in this series a small curette has been used immediately after the withdrawal of the balloon from the uterus to obtain a specimen of the endometrium with which to verify, as far as it is possible by this means, the menstrual dates and to provide evidence of luteal activity. No difficulties have been encountered in introducing the balloon into the uterus of the unanæsthetised woman, whether parous or non-parous, and neither at the moment of insertion of the balloon nor during the curettage has there been any complaint of undue discomfort. This last point is of great importance in the determination of variations in uterine motility because the non-pregnant uterus, like the pregnant organ, is easily affected by emotional disturbances.

(b) *Results*.—For this investigation twelve women were selected and a total of 20 records of uterine contractions have been made. Several examples of the curves obtained are shown in Fig. 1. The main interest, however, lies in an examination of the records obtained in the second half of

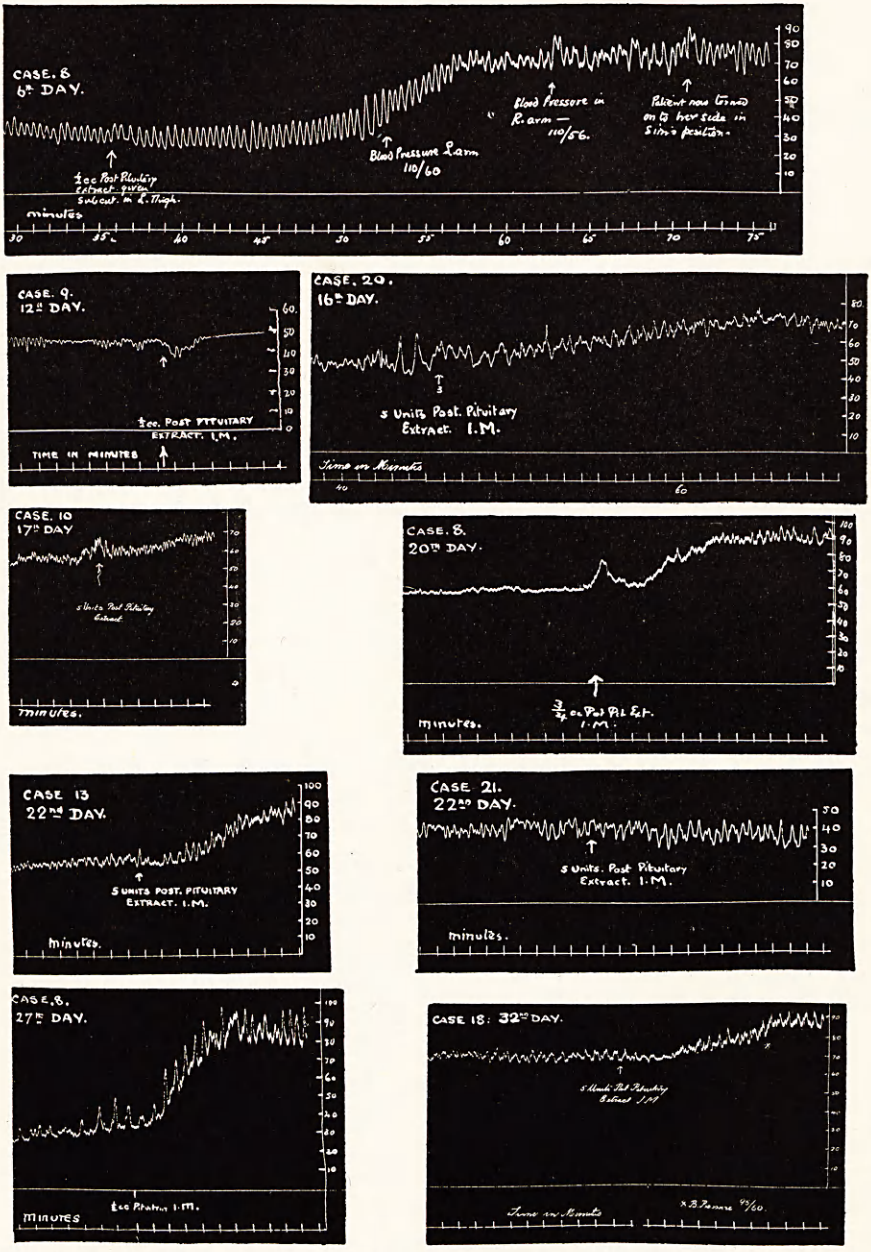

FIG. 1.—Tracings of the movements of the human non-pregnant uterus at various stages of the menstrual cycle.

the cycle, and from the Table it will be seen that 16 records were made at this time. Of these, 14 show not only spontaneous

TABULATION OF RESULTS.

Muscular Responses of the Human Non-Pregnant Uterus to Posterior Pituitary Extract.

CASE	AGE	PARA	AVERAGE DAYS IN CYCLE	DAY OF CYCLE & RESPONSE TO PITUITRIN					ENDOMETRIUM.
				1-7	8-14	15-21	22-28	29-35	
8	24	2	28-30	6 +	13 +	20 +	27 +		——
9	20	0	28-35		12 +	20 +			——
10	22	2	16-26	2 −		17 +			17. PROLIFERATIVE
13	23	2	28-30				22 +		——
14	26	2	26-30			17 +	23 +		17 SECRETORY
17	18	0	28-30			17 +		29 +	——
18	40	11	28-35					32 +	32 SECRETORY
20	30	4	28-30			16 +			16 SECRETORY
21	20	2	23-35				*22 − 22 −		*22 SECRETORY
22	21	0	28-30					34 +	34 SECRETORY
23	37	7	28-30			21 +			21 SECRETORY
24	24	3	28-30				22 +		22 SECRETORY

uterine activity but also good responses to posterior pituitary extract. In 8 of these 14 cases endometrial specimens (Fig. 2) were obtained immediately after the termination of the recording, and 7 of these specimens show secretory changes in the glandular and stromal cells. This proves that in 7 cases, at least, uterine activity was recorded in the presence of an active corpus luteum and not in the absence of luteal influence as would have been the case in an anovulatory cycle.

In one instance (Case 21) the curves were atypical. In this case two recordings were taken on the twenty-second day

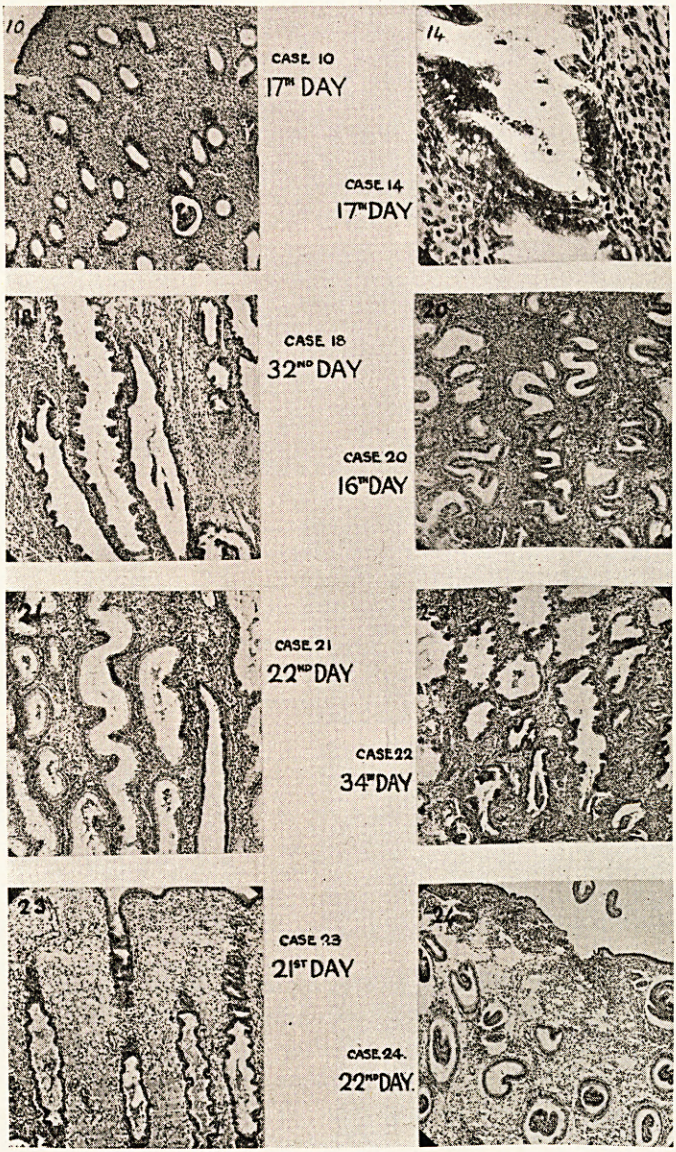

FIG. 2.—Endometrium removed by curettage following the recording of uterine movements.

of two successive cycles and on both occasions, although there was marked spontaneous activity, no rise of muscle tone or increase in the contractions resulted from the injection of posterior pituitary extract. No clue to the cause of this refractoriness was revealed either by palpation of the pelvic organs or by microscopic examination of the endometrium. It is also interesting to note that in Case 10, although the menstrual dates placed the day of the observation of the uterine behaviour as the seventeenth of the cycle, and it was known that the inter-menstrual periods usually lasted less than 28 days, the endometrium was proliferative in type and not, as was expected, secretory. This case demonstrates well the importance of endometrial examination as a means of obtaining collateral evidence of ovarian function, especially as regards the recognition of an anovulatory cycle.

(c) *Summary.*—The results obtained with the intra-uterine balloon method of recording contractions of the non-pregnant human uterus in the living subject show that it was possible to detect spontaneous activity of the uterus at various times from the beginning to the end of the menstrual cycle. The results also show that in eleven out of twelve women, tested in the second half of the menstrual cycle, posterior pituitary extract caused increased muscular activity of the uterus.

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