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ACTIVE LIPIDS IN MENSTRUAL FLUID

V. R. PICKLES

Department of Physiology, University of Sheffield

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Abstract—A group of lipid smooth-muscle stimulants is liberated from the human endometrium during menstruation, and may in part be recovered from the menstrual fluid. These stimulants probably cause the strong rhythmical uterine contractions that expel the decidua menstrualis.

HUMAN menstrual fluid contains a group of uterus-contracting lipids. These are formed in the secretory endometrium, are liberated during menstruation, are in part carried to the myometrium, and there cause the rhythmical contractions of normal menstruation. An excess of such an effect is probably an important factor in causing the intense uterine cramps of primary dysmenorrhoea.

Origin

Active lipids of approximately the same properties can be extracted from: (1) menstrual fluid,[1] (2) endometrial curettings, particularly during the secretory and pre-menstrual phases,[2, 3] and (3) circulating blood during menstruation.[4] The amount of the stimulant substances in the circulating blood is far too small for this to be the source of the stimulants in the menstrual fluid; the stimulants there almost certainly originate in the endometrium, and are carried in the blood-stream to the myometrium. For the active substance or substances carried in this way, the name "menstrual hormone" has been proposed.[4]

Method of extraction and chemical nature

Acetone extracts of menstrual fluid or endometrial curettings have been fractionated by liquid–liquid partition and by silica-gel chromatography. Two principal fractions containing active lipids are separated in this way from much inactive material, and since they are carboxylic acids the active substances can be further concentrated by extraction from organic into aqueous $NaHCO_3$ solution.[5] The main active fractions are provisionally called "component *A*" and "component *B*", until their individual constituents can be precisely identified.

Effects on smooth muscle

The main effect is on the uterus.[6] *In vitro*, the effect varies with the dose from a simple co-ordination of the activity of the different parts of the preparation, giving smooth strong cycles of contraction and relaxation, to complete spasm (Fig. 1). These effects are seen both with human and guinea-pig uteri, and in the human preparations they reproduce respectively the rhythmical contractions of normal menstruation, and the intense spasm of primary dysmenorrhoea.

In an earlier paper[6] the guinea-pig uterus was stated to be less sensitive than the duodenum. We now know that whereas uteri from multiparous guinea-pigs such as were used in those experiments are relatively insensitive, uteri from virgin guinea-pigs of 350–500 g body weight are much more sensitive. They respond to less than 1 μg/ml of component *A* preparations made by the method described,[5] and since these preparations contain much inactive material, the effective concentration of the pure stimulant may well be much less.

Although intestinal muscle of some laboratory animals is contracted by the menstrual stimulants, human intestinal muscle may be unaffected (Fig. 1). Feeble stimulation has, however, been seen in human gastric muscle (Fig. 2). Ricinoleic acid, the "classical" hydroxy-fatty-acid stimulant, is said to stimulate the upper part of the human gastrointestinal tract more than the lower part; and a similar effect of blood-borne menstrual stimulant (the menstrual hormone) might well account for the small increase in gastrointestinal motility that has been found during the menstrual phase.[7, 8]

Dysmenorrhoea

Some recent experiments[9] suggest that primary dysmenorrhoea may be of two kinds. In one, an excessive amount of menstrual stimulant is produced; in the other, there may be a physiological impediment to the outflow of menstrual fluid from the uterus, resulting in increased absorption of the menstrual stimulant.

Mode of action on smooth-muscle cells

Both component *A* and component *B* have remarkably slow and prolonged effects on smooth muscle. According to a hypothesis proposed recently[10] with respect to component *A*, this may result from their slow penetration to an intracellular site of action.

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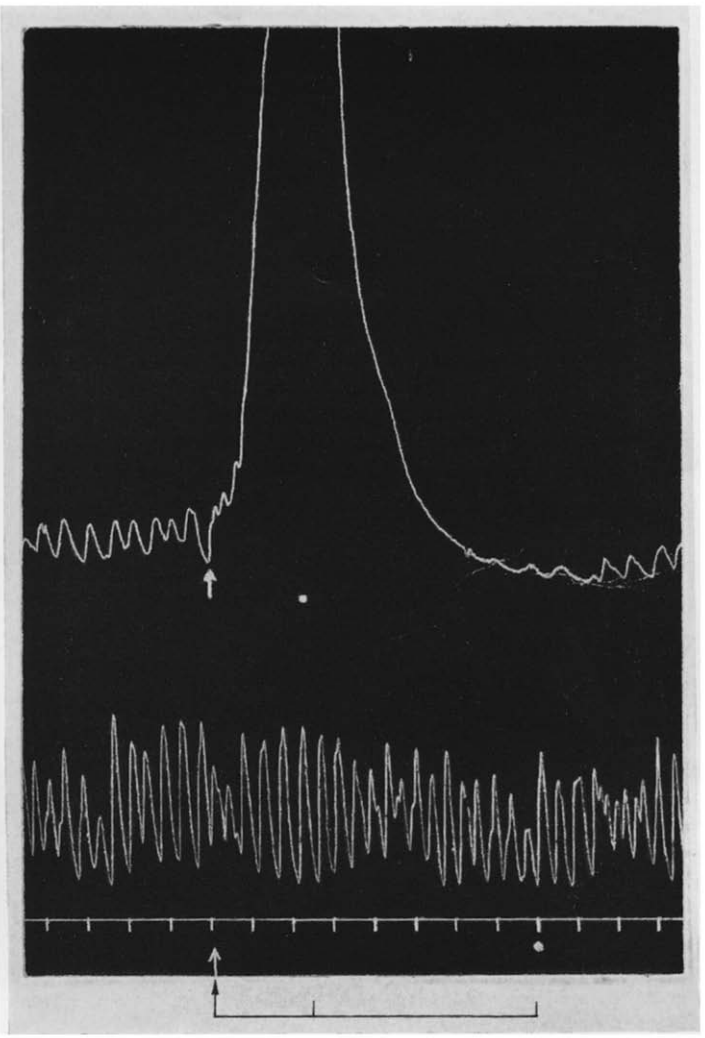

FIG. 1. Kymograph record from human myometrial preparation (above) and circular muscle strip from human terminal ileum (below). At the arrows, the same quantity of ether-soluble menstrual lipid was added to each preparation, and washed out after 2½ min (myometrium) or 8 min (ileum). Time-marker, minutes.

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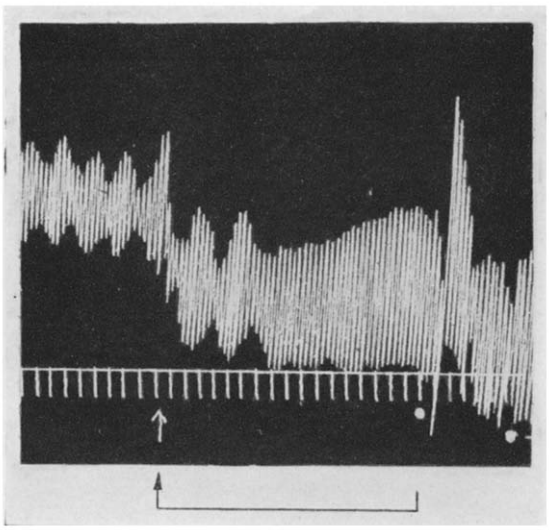

FIG. 2. Kymograph record from human stomach muscle preparation. One milligram of ether-soluble menstrual lipid was added to the 10-ml organ bath at the arrow, and washed out at the dot 18 min later. The muscle decreased in tone when the lipid was added but the co-ordination and overall amplitude of its contractions increased. Time-marker, minutes.