The effect of an intra-uterine device on uterine motility in women and rhesus monkeys

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PRESENT understanding of human female reproductive physiology has largely been derived from the results of animal experimentation, and particularly from studies on the rhesus monkey. This is also true of our present knowledge of the possible modes of action of an intra-uterine device (IUD).

Recent studies in the rhesus monkey have shown that an intra-uterine device is contraceptive in this species (Kelly & Marston, 1967; Kelly, Marston & Eckstein, 1969). The periodicity of the menstrual cycle is not affected by the presence of an IUD (Eckstein, Kelly & Marston, 1969), and the processes of ovulation, sperm transport, fertilization and early embryonic development within the Fallopian tube are not disturbed (Kelly *et al.*, 1969; Marston, Kelly & Eckstein, 1969a; Mastroianni *et al.*, 1967). The principal contraceptive effect of an IUD in the rhesus monkey is most probably exerted within the uterus by premature expulsion, destruction or failure to implant of the fertilized egg.

Clinical studies suggest that in women, too, the processes of sperm transport (Malkani & Suján, 1964; Morgenstern *et al.*, 1966) and tubal transport of the egg (World Health Organization, 1966; Noyes *et al.*, 1966) are not affected by the presence of an IUD. The contraceptive action of an IUD in women appears to be exerted within the uterus, and may be related to a disturbance in the normal pattern of uterine motility.

This possibility has been tested by Bengtsson & Moawad (1966, 1967) and Johnson, Ek & Brewer (1966) who employed the intra-uterine, open-ended catheter technique devised by Hendricks (1964). Behrman & Burchfield (1968) have used an IUD with a built-in, pressure-sensitive transducer to record the direct effect of myometrial activity on the IUD.

Johnson *et al.* (1966) studied post-partum women at the time of IUD insertion and again 2 weeks later. They found no differences between their two

groups of observations. The value of these results is, however, most doubtful because the authors did not state at what time their observations were made within the menstrual cycle, or whether their patients were cyclic. Bengtsson & Moawad (1967) found that a group of IUD patients showed no differences in myometrial activity until the fourth or fifth post-ovulatory day (i.e. about day 19), when there was a precocious appearance of the 'pre-labour like' activity, normally characteristic of the immediately pre-menstrual period. The onset of this activity was thought to be close to the time implantation could be expected to occur. They suggested that this abnormal pattern of myometrial activity might be one of the factors associated with the contraceptive action of an IUD. By contrast, Behrman & Burchfield (1968) could find no abnormal pattern of activity in patients fitted with an IUD containing a built-in transducer. There was some increase in myometrial activity immediately after insertion of this device, but it rapidly subsided and was absent 3 days after insertion. Their patients showed a period of quiescence from immediately after ovulation until the day before menstruation. The authors concluded that myometrial activity played a minimal role in the mechanism of IUD action. The difference between their results and those of Bengtsson & Moawad (1967) may have been due to differences in the sensitivity of the two techniques. The transducer-IUDs probably responded to local changes in muscle activity and not necessarily to changes in luminal pressure produced by activity of the entire myometrium. If groups of patients were first studied by using the open-ended catheter technique before being fitted with a transducer-IUD and then regularly examined with both techniques, this problem might be resolved.

The application of the open-ended catheter technique to rhesus monkeys has been investigated by Martin & Eckstein (1966) and Harry & Pickles (1968). In our experience (Eckstein *et al.*, 1969),

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satisfactory canalization of the endo-cervical canal cannot be achieved without gross traumatization of the cervix, unless the monkey is within 3 weeks post-partum. Therefore, if the open-ended catheter has to be placed in position for each observation (Martin & Eckstein, 1966) the monkey must be anaesthetized and there will inevitably be stimulation of the cervix. The recordings of uterine motility obtained after such manipulation may not be typical of the normal pattern of uterine activity. Harry & Pickles (1968) permanently implanted an open-ended catheter to by-pass the endo-cervical canal: by definition, their catheter must be regarded as an IUD. Moreover, their observations may not have been normal because they were made on deeply sedated animals.

We have attempted to compare uterine motility in fully conscious control and IUD rhesus monkeys by:

- (a) a direct technique, involving the use of a chronically implanted strain-gauge transducer (Bass & Callantine, 1964), attached to the external surface of the uterus, to record uterine motility in fully conscious monkeys held in a restraint chair; and
- (b) an indirect technique, based on the transfer of natural (rabbit eggs) and artificial (radio-active, resin spheres) substitutes for monkey eggs to the uterus on day 15 of the menstrual cycle. The monkeys were killed between 48 and 96 hr after the transfer of such eggs (Marston & Kelly, 1968; Marston, Kelly & Eckstein, 1969b).

In the direct method, the transducer unit was activated by deformation of the copper-beryllium clip on which a strain-gauge was mounted. As the transducer unit was itself mounted on the serosal surface of the uterus this deformation could be produced not only by uterine activity but also by peristalsis, excursions of the abdominal viscera, respiratory efforts or by gross bodily movements. In practice it was impossible to obtain satisfactory records and make a useful comparison of uterine motility. Moreover, it seemed neither justifiable nor practicable to attempt to compare the uterine motility of anaesthetized monkeys. However, if a sensing device small enough to be implanted in the myometrium and linked with an implanted radio telemetry system could be designed, it should be possible to compare the myometrial activity of wholly unrestrained, fully conscious monkeys.

Our indirect technique tested the ability of control and IUD uteri to expel eggs after they had been artificially transferred to the uterine lumen. The results showed that up to 48 hr after transfer there was little difference in the rate at which eggs were expelled. Later than 48 hr there may have been more rapid expulsion of eggs from the IUD uterus. This can, however, only be established by killing addi-

tional groups of monkeys at intervals of 6-8 hr between 48 and 72 hr after transfer, and at present, this seems unwarranted.

The egg-transfer experiments could not test whether the presence of an IUD induced subtle changes in myometrial activity. It seems reasonable to expect that implantation could be inhibited by slight alterations of myometrial activity, and degeneration of the fertilized egg might also be induced by such changes occurring during the pre-implantation period.

We conclude that premature expulsion of the egg from the uterus was not the principal contraceptive action of an IUD in the rhesus monkey. By inference, the evidence must favour the alternative explanation that, in the presence of an IUD, fertilized rhesus monkey eggs undergo premature degeneration within the uterine lumen.

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