Long-acting Contraceptives

It appears from lay press reports[1] that scientists working for the Population Council at the Rockefeller Institute in New York have prepared subcutaneous steroid implants which have a contraceptive action lasting for many years. There is no evidence that the new departure is due to any startling innovation in the pharmacology of the synthetic progestational compounds. It seems to be largely a hopeful prediction based on a possible marriage of two ideas which have been current for some years; firstly, that small continuous doses of progestins can promote infertility without interfering with the menstrual cycle, and, secondly, that by an ingenious use of plastics the parenteral absorption of some compounds can be greatly prolonged.

The new feature of this use of steroidal contraceptives is the claim that the menstrual cycle is not suppressed. Present-day oral contraceptives cause what is in effect a form of medical castration, and many of the untoward effects from their use are due to the inability of the synthetic hormones completely to mimic the metabolic effects of the natural substances. The nortestosterone derivatives which are found in nine out of every ten oral contraceptives on the British market almost certainly act by suppressing gonadotrophin secretion, either by preventing the production of releasing factors by the hypothalamus, or by inhibiting the release of pituitary gonadotrophin. Direct action on the ovary[2] has now been amply disproved, though much of the contraceptive effect of these compounds may derive from their secondary effects on tubal motility, on the state of the endometrium, and on the composition of cervical secretion.

The great success of oral contraceptives is due in large measure to their effectiveness, which in turn is due to their multiple sites of action. For the Western woman at least this has been the consideration which has made her often tolerate a degree of discomfort which would not be acceptable in any other drug. Effectiveness is likely to be the prime criterion applied to the new technique. The usual progestins act mainly by inhibition of ovulation,[3] probably largely through their oestrogenic component,[4] although suppression of ovulation is not a prerequisite for their antifertility action.[5] The new approach is likely to involve the use of progestins which do not give rise to oestrogenic metabolites such as the 17-hydroxyprogesterone derivatives. G. Pincus[6] is known to be working on norandrostane derivatives which prevent implantation if administered to animals after mating, but these again are highly oestrogenic in action and very likely to upset the normal menstrual rhythm.

If the new contraceptive lives up to the promise of the press release its role is likely to be concerned with the prevention of implantation. It is difficult to see how alterations of tubal motility can be consistently effective in this respect, and a change in the receptivity of the endometrium to the fertilized ovum is the most likely mechanism. When it is considered that the ovum can implant and grow in all manner of recherché places such as the surface of the kidney, it seems surprising that its normal habitat, the endometrium, could be made consistently to refuse it lodgement. There is some evidence, however, that the endometrium, of all tissues, is best able to resist the intrusion of a fertilized ovum at the wrong moment. It may be that the endocrine process which at specific times suspends this immunity to invasion is an integrated series of events capable of being harmlessly and temporarily interrupted by mild progestational stimulation in the proliferative phase of the cycle.

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Mycoplasma Infections

Though reports have appeared on the epidemiology of *Mycoplasma pneumoniae* infections in both military and civilian populations[1,2] relatively little information has been published on the pattern of transmission of this respiratory pathogen. A recent report from Seattle[3] on the spread of *M. pneumoniae* within family groups goes some way toward filling this gap in our knowledge. It stems from a study of the incidence of pneumonia due to *M. pneumoniae* among members of a large Group Health Co-operative.[4]

In 36 out of 114 families which were followed up, the "index" patient was infected with *M. pneumoniae*. Transmission to other members occurred in 23 families. It is of interest that there were more young children in these families than in the 13 where there was no spread of infection. Moreover, the incidence of secondary infection in the 23 families suggested that children under 15 are particularly susceptible, for 64% of the children became infected, compared with 17% of the adults. While the infection rate was highest in children under 15, the highest incidence of asymptomatic and mild infections was also found in this age group. The greater frequency of the asymptomatic carrier state among children points to their potential role in transmitting the disease, and the child of school age may be an important factor in introducing it into a family group.

Transmission outside the family seemed to be less frequent. *M. pneumoniae* was found in only one contact—the playmate of a child from a family with the disease. Throat swabs from 23 contacts of other patients were negative, as were 8 from the office colleagues of a positive case and 26 from the classmates of a child with persistent positive throat cultures of *M. pneumoniae*.

The prerequisites for the spread of *M. pneumoniae* thus seem to be prolonged, close contact and the presence of susceptible individuals. The greater susceptibility of children than adults suggests that immunity may develop. Investigations into *M. pneumoniae* vaccines[5-7] indicate that the level of growth-inhibiting antibody is a useful index of protection, but this method of assessment has not yet been used in epidemiological surveys.

In the Seattle survey the average incubation period was estimated to be 23 days. Intervals of about three weeks were

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