

Conclusions

We have noted no other similarities in our cases, but the manufacturers have been searching for some cause. The possibility of some reagent used in the sterilization of the syringes causing instability of the iron dextran complex has been suggested, but seems unlikely. However, until the problem can be solved, this method of iron therapy has been suspended. It certainly has many advantages, but we have noted that oral iron, with sufficient coercion of the patient, will give satisfactory haemoglobin levels in the great majority; the remainder appear to be those who have a folic-acid deficiency in addition to their iron deficiency.

Summary

One hundred and fifty maternity patients were treated with intravenous Imferon by the total-dose-infusion technique. Thirteen reactions occurred, of which seven were severe and demanded emergency treatment. All those who suffered reactions were later safely delivered of healthy infants. All the babies were girls. No reactions occurred in any of 22 post-natal patients treated. In view of the reactions, treatment by this method was suspended. We were unable to discover the cause for the reactions.

This account is published in order to point out that, despite the reported safety of this method, such was not our experience.

We wish to thank Mr. George Winchester and Miss J. M. B. Muirhead, consultant obstetricians, Hull Maternity Hospital, for their encouragement in the writing of this paper, and permission to quote cases under their care. We also thank Messrs. Bengers Ltd. for their advice, unceasing help, and co-operation.

NOTE.—Since this article was written the manufacturers have sent an undated letter to members of the profession reporting the death of a diabetic patient attributed to this technique. Further, in view of the occasional occurrence of thrombophlebitis, it is now recommended that Imferon be dissolved in normal saline.

REFERENCES

- Basu, S. K. (1963). *Lancet*, **1**, 1430.
 Davidson, W. M. (1957). *Practitioner*, **178**, 161.
 Giles, C., and Burton, H. (1960). *Brit. med. J.*, **2**, 636.
 Golberg, L. (1959). In *Iron in Clinical Medicine*, edited by R. O. Wallerstein and S. R. Mettier. Cambridge, London.
 Lane, R. S. (1963). *Lancet*, **2**, 1015.
 Laurence, D. R., and Moulton, R. (1960). *Clinical Pharmacology*, Ch. 24, 388. Churchill, London.
 Richmond, H. G. (1959). *Brit. med. J.*, **1**, 947.

Preliminary Communications

Effect of Intrauterine Silk Thread Suture on Fertility of Female Rats

Brit. med. J., 1965, **1**, 31–32

A plastic intrauterine loop is being investigated as an anti-fertility agent, and studies are being carried out in humans. This method of fertility control, which appears to be cheap and efficient, can finally be accepted only after its mechanism of action and possible toxic effects have been thoroughly investigated in experimental animals. The presence of a loop in the uterine horn of the female rat also interferes with pregnancy, and this is a situation similar to that observed in humans (Doyle and Margolis, 1963). We have investigated the effect of an intrauterine silk thread suture in the lumen of one and both horns of the uterus on (a) pregnancy, (b) the gonadotrophin content of the pituitary, (c) the oestrous cycle, (d) lactation, (e) teratogenicity of the litter born when there is a suture in one horn, and (f) sperm migration in the uterine horn with the suture. The effect of removal of the suture on later pregnancy has also been studied.

EXPERIMENTAL

Sixty female rats were operated upon under ether anaesthesia, and a silk thread was inserted in 30 rats in one horn of the uterus. The suture was introduced through the muscular layers into the lumen of the horn, down which it ran for about 4 mm. The thread was then brought to the surface of the horn again and anchored by knots at each end. Twenty of these rats were sacrificed on the 14th day and 10 were allowed to go to term. In 30 rats the silk thread suture was placed bilaterally into the lumen of both horns of the uterus. Twenty of these rats were also sacrificed on the 14th day and 10 were allowed to go to term. In 20 animals a sham operation was

performed in that the rats were operated on under ether anaesthesia and the silk thread suture was inserted bilaterally in both horns and immediately removed. The sutures in all experiments were placed longitudinally and did not block the patency of the tube. After a week the oestrous cycle of the rats was studied and they were mated with males of proved fertility. Pregnancy was detected by the presence of spermatozoa, and only those animals with thick masses of spermatozoa in the vaginal smear were used. Our experience in earlier antifertility studies in over a thousand rat matings leads us to believe that 98% of the rats that show masses of spermatozoa in the oestrous smear after being mated with proved males go on to successful pregnancy.

The rats were allowed to proceed to term or were killed on the 14th day and the uteri were examined to show whether implantation had occurred or not. The loop was removed under anaesthesia in 10 experiments, and after a further period of rest of 15 days the rats were mated again. A bilateral intra-uterine suture was placed in 10 rats with normal cycles and a unilateral suture in another 10 to study the effect of the suture on the oestrous cycle. Sperm migration was studied in 20 female rats with unilateral sutures when the presence of sperm was detected microscopically in both horns to see if there was any difference in the rate of upward migration of the sperm.

RESULTS

Effect on Pregnancy.—When there was a suture within one uterine horn implantation did not occur on that side in any of the 20 animals, but there were normal living implants in the contralateral horn. When 10 animals with a similar suture were allowed to go to term they produced a normal litter but with fewer young, the average number being four. On examining the uterus it was observed that all the foetuses were from the side in which there was no suture. When both horns had uterine sutures there were no implants on either side in the 20 rats that were sacrificed on the 14th day, and when 10 such

animals were allowed to go to term there was no evidence of pregnancy up to 30 days after successful mating. When a sham operation was performed there was normal implantation in all 20 rats.

Effect of Removal of Suture.—Ten female rats in which implantation did not occur when they had a suture in one or both horns had their sutures removed and were mated again. There was now evidence of implantation in all these rats.

Effect on Lactation and Litter.—Ten rats delivered a litter from only one horn because of the presence of a suture in the other. There was normal lactation as measured by the weight gain of the offspring before and after feeding. The litters of all 10 animals were normal and there was no evidence of teratogenicity.

Effect on Gonadotrophin Content of the Pituitary and the Oestrous Cycle of Female Rats.—Uterine sutures were placed in one horn of the uterus in 10 rats with normal cycles, while bilateral uterine sutures were placed in another 10. The sutures had no effect on the cycles, which continued to be regular. The gonadotrophin content of the pituitary gland was also not altered in any way in rats with bilateral or unilateral sutures.

Effect on Sperm Migration.—The intrauterine sutures had no deleterious effect on the upward migration of sperm after mating and sperm was detected in the upper third of both uterine horns in all 20 unilaterally sutured animals.

DISCUSSION

Our results indicate that an intrauterine suture in rats is an efficient antifertility agent which acts by preventing implantation on the side on which it is placed. It does not prevent implantation in the other horn. This fact, together with the findings that the gonadotrophin content of the pituitary gland is not altered and that the suture has no effect on the oestrous cycle or lactation or milk ejection, indicates clearly that the anti-implantation effect is not a central effect mediated by blocking the release of the pituitary hormones. This absence of any action of the intrauterine suture on the

pituitary in these studies is encouraging, as any antifertility drug or agent which has an effect on the pituitary would be regarded with justifiable caution before being recommended for general use. The suture does not appear to act either by blocking the release of the ovarian hormones or by preventing sperm migration. When the suture was removed the female rats became pregnant again, indicating that this is a reversible effect. There was no abnormal behaviour of the animals with sutures. Pharmacological studies are in progress to investigate the effect of various substances on the uterine horn itself and to see whether the horn with the suture behaves in any way differently from the contralateral horn without a suture.

SUMMARY

The effect has been studied of an intrauterine silk thread suture on the fertility of female rats.

An intrauterine suture in the lumen prevents implantation, after successful mating, in the horn in which it is placed. It has no effect on the release of the pituitary or ovarian hormones. There is no evidence of teratogenicity. There is no adverse effect on lactation or the growth of litter born from the other horn.

The animals with the intrauterine suture behave normally.

When the suture is removed the fertility is restored.

The suture must be in position to prevent implantation—a sham operation is not enough.

The intrauterine suture does not prevent the upward migration of sperm in the horn in which the suture is placed.

R. R. CHAUDHURY, M.B., B.S., D.PHIL,
T. K. TARAK, B.SC.,

Biology Division, Ciba Research Centre, Goregaon,
Bombay 62, and Department of Pharmacology, Insti-
tute of Postgraduate Medical Education and
Research, Chandigarh.

REFERENCE

Doyle, L. L., and Margolis, A. J. (1963). *Science*, **139**, 833.

Medical Memoranda

Infection due to *Mycobacterium xenopei*

Brit. med. J., 1965, **1**, 32-33

The name *Mycobacterium xenopei* was given by Schwabacher (1959) to an acid-fast bacillus isolated from a skin lesion in a South African toad, *Xenopus laevis*. This organism and another recently found in a second toad granuloma have now been examined by methods used to classify "opportunistic" mycobacteria—that is, mycobacteria sporadically pathogenic for man. They have proved to be indistinguishable from the bacteria placed in group 3 by Marks and Richards (1962), and the name *M. littorale* recently proposed for this group must therefore be discarded in favour of *M. xenopei*.

M. xenopei is not uncommon in human material, the Tuberculosis Reference Laboratory having collected in the last decade 50 strains in England and Wales, all from adults. Most have been submitted for identification in the last two years, but this almost certainly reflects greater use of the laboratory and not a recent increase in prevalence. In the following analysis we have assumed strains to be clinically significant when isolated

repeatedly from people who have disease unexplained by other causes. Lesions met with in these patients have usually been diagnosed as tuberculous clinically. Cases with an ambiguous history have been called "doubtful." In three patients infection was demonstrated in resected lung.

Significance of 50 Strains of *M. xenopei*

Clinically significant	...	20 pulmonary cases (16 M., 4 F.)
Doubtful significance	...	6 pulmonary cases (4 M., 2 F.)
		17 pulmonary cases (9 M., 7 F.,
		1 unknown)
Not significant (or information lacking)	6 urinary cases (2 M., 4 F.)
		1 post-operative sinus (M.)

Men appear to be more susceptible than women to *M. xenopei* just as with other opportunistic mycobacteria. All but three of the isolations were made in London and towns near the south and east coasts of England and Wales. None occurred in the Midlands or North England despite the frequency of other opportunistic mycobacteria in these areas. Sixteen non-significant isolations (including five from urine) were made in three particular laboratories which failed to provide a single significant or doubtful case, and it seems likely, therefore, that *M. xenopei* can occur as a contaminant during the collection or culture of specimens. In contrast, significant isolations were