

INFERTILITY IN FERTILE COUPLES

ARTHUR P. CAMILLERI

M.D., M.R.C.O.G., M.M.S.A., D.C.H.

Professor of Obstetrics and Gynaecology

Royal University of Malta.

Senior Accoucheur, St. Luke's Hospital

A paper read at the Annual Conference of the Society for the Study of Fertility, at Newcastle-upon-Tyne, 11th July, 1968.

In selecting this title for my brief contribution I felt that a little time of this Conference could deservedly be devoted to the plight of those married couples whom we *know* to be fertile who yet remain childless. It is in this sense that I speak of infertility in those cases where the husband's semen is normal, the wife ovulates regularly, and indeed fertilization occurs repeatedly, but where yet the pitiful couple continue to yearn for a viable child.

Clinicians will support my view that in too many cases childless couples actually owe their plight to recurrent or habitual abortion. In many of us this condition may fail to arouse the same excitement and interest as would the study of azoospermia or anovulation or difficulty in fertilization. Yet it is no less tragic for the two individuals concerned, and to the clinician it is particularly distressing and frustrating.

One of the principal factors militating against the correct management of recurrent abortion is that the possible causes are indeed numerous, and very often the aetiological factor is arbitrarily assumed to be endocrine deficiency. Many a woman today, who has already aborted once or twice, expects her doctor to prescribe the weekly hormone injection early in her next pregnancy in the usually unjustified belief that this will prevent another miscarriage. This lay expectation must reflect current gynaecological practice.

At a time when for the treatment of recurrent abortion one is so easily tempted to resort to depôt progesterone, it is important to bear in mind three aetiological conditions whose correction is clinically sound and seldom unrewarding. All three are morphological abnormalities of the uterus. I refer to congenital uterine malformations, to cervical incompetence, and to intra-uterine synechiae, three well-defined clinical entities which will continue to be missed so long as they are not habitually recalled to mind in every case of recurrent abortion. One cannot but agree with

Rozin's (1967) maxim that "uterography is indicated routinely whenever two spontaneous abortions have occurred". Here I wish to emphasize that this investigation is useful not only for the diagnosis of congenital malformations (as Rozin indicates) but also for the detection of intra-uterine adhesions and possibly also of cervical incompetence.

Double Uterus

Double uterus is one example of uterine malformations where, even after the correct diagnosis has been reached, this cause of recurrent abortion might wittingly continue to be neglected and proper treatment to be delayed unnecessarily.

Elsewhere (Camilleri, 1968) I have drawn attention to the fact that there is considerable clinical value in recognizing two distinct types of double uterus, Bicornuate and Septate. They constitute two separate clinical entities. Their effect on pregnancy is apt to be different. Their management should be different.

The bicornuate double uterus has its two halves entirely or almost separate: there is no tissue joining the medial borders of the two uterine cavities. These two horns in an individual case are often unequally developed. Either of them may carry a pregnancy, but the initial attempts usually end in abortion or very premature labour. A practically full-term pregnancy, however, is quite feasible in the bicornuate double uterus, either because both horns are well developed from the very beginning, or because one horn is well developed (while any pregnancy in the other horn will continue to result in an abortion), or because one or both of the originally under-developed horns will grow capable of carrying an advanced pregnancy after a series of abortions. It is, therefore, the bicornuate uterus which might justify Strassmann's (1952) assertion that between 25 and 40 per cent of women with double uterus have no disturbances and do not need surgery.

In the septate type of double uterus the clinical course is apt to be very different. Here the two halves have fused so

that the external appearance resembles a single uterus, with or without a median sulcus in the fundus. The risk of recurrent abortion in these cases is much greater and more likely to remain permanent. It is especially so if the septum between the two cavities is rather thick, as may be demonstrated by the hystero-gram. Holmes (1956) and Jones *et al.* (1956) have pointed out the considerable difference in the abortion rates associated with these two types of double uterus. I submit, indeed, that once the available evidence shows the abortion rate to be so high in the septate double uterus, and the chances of a viable pregnancy are so small, then in these cases surgery should be seriously contemplated from the moment of undoubted diagnosis. I am proposing that for the septate type of double uterus we should operate early and no longer follow the maxim which has long been blindly applied to all forms of congenital uterine malformations, viz., that a plastic operation is not warranted except after four or more abortions.

The need for accurate diagnosis becomes more obvious. The hystero-gram alone cannot normally distinguish whether the particular case of double uterus is of the bicornuate type or the septate (*Fig. 1*). This patient was 31 years old, and she had had five miscarriages at between 8 and 13 weeks. Examination under anaesthesia had repeatedly revealed one single uterine contour; and at operation (*Fig. 2*) the rather broad uterus showed also three myomata of variable size. A longitudinal median uterine incision was employed to shell out the myomata and to divide the thick septum separating the two endometrial cavities (*Fig. 3*). The upper part of the septum was considered to be too thick and muscular for effective excision to be attempted. Hystero-gram was performed three months later, this time employing only one cannula (*Fig. 4*).

It might be concluded that the management of the two types of double uterus varies not only in the timing of operative intervention, but also in the surgical procedure actually carried out. In the bicornuate cases the operation of choice may be the Strassmann metroplasty, basically

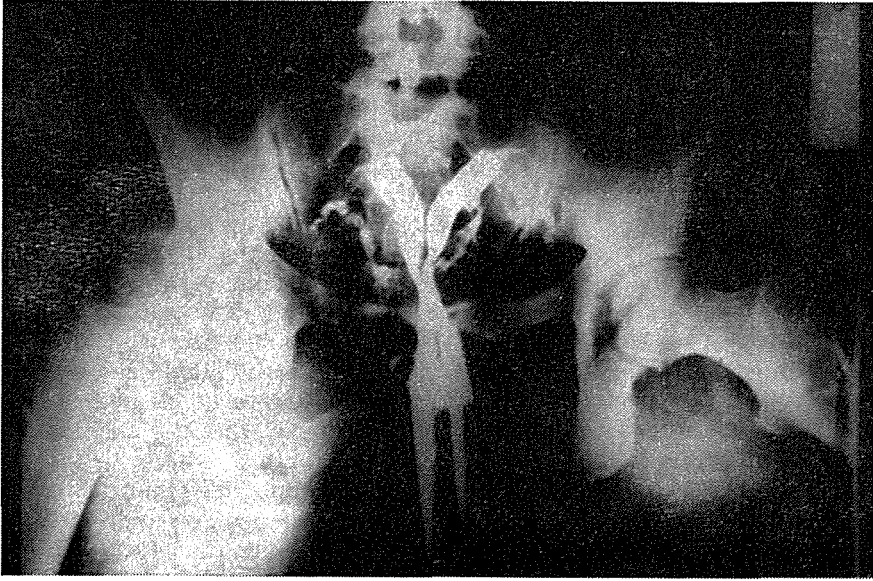


Fig. 1

employing a transverse incision along the medial edges of the two horns which is then sutured in an antero-posterior direction. On the other hand, in the septate cases of double uterus it may be advisable to excise the septum through an anterior longitudinal incision.

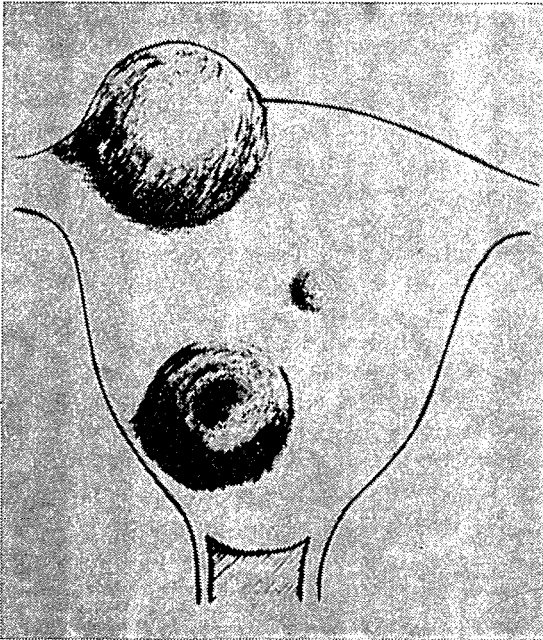


Fig. 2

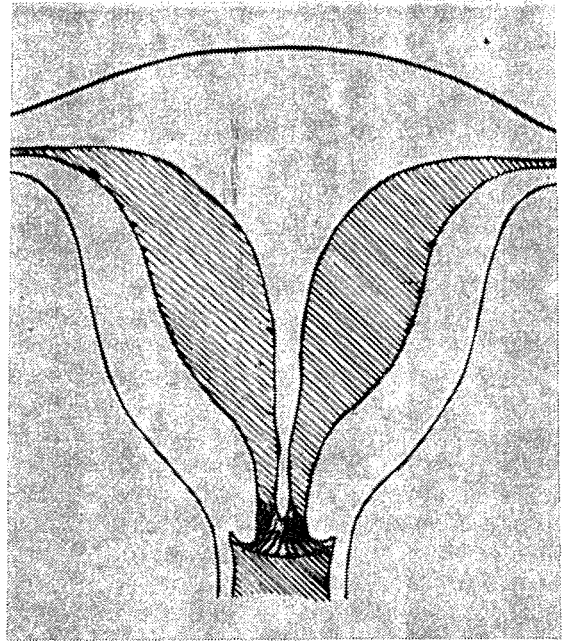


Fig. 3

Cervical incompetence

The incompetent cervix as a cause of habitual abortion, usually in the middle trimester, has lost its novelty today, although twenty years ago this problem had not yet been discussed. Nevertheless the condition remains a cause of needless re-

Intra-Uterine Synechiae

This third condition, like the previous one, is often iatrogenic in origin. When adequately sought out, it is undoubtedly found to be much commoner than most clinicians are apt to believe. Unnerus *et al.* (1965) carried out a hystero-graphic study on 55 women who had one or more curet-tages following abortion, and they found evidence of intra-uterine synechiae in 27 per cent. Since Professor Comninos of Athens drew my attention cogently to this condition some months ago, I have been impressed by its unexpected incidence. In a recent series of 425 women with secondary infertility who had had an abortion, Comninos (1967) found that in no less than 36 per cent, endometrial adhesions were the cause.

It should be emphasized that less than half of these women will observe any abnormality in their menstrual flow, and only in about 20 per cent is there a diminished flow, varying from oligomenorrhoea to secondary amenorrhoea.

The carefully produced hystero-gram reveals the extent of these synechiae. They may be mostly confined to the endo-cervical region and the lower part of the isthmus (*Fig. 5*). They may be rather extensive, limiting the endometrial cavity (*Fig. 6*). At times they assume the form of smaller adhesions distributed irregularly (*Fig. 7*). All these illustrations are reproduced from photographs kindly supplied to me by Professor Comninos.

Various procedures have been recom-mended for the treatment of this condi-tion, and new methods are proposed from time to time (Comninos and Zourlas, 1967; Louras *et al.*, 1967). One very effective method employs a Foley catheter after the adhesions have been separated by means of the curette. The catheter is pre-viously prepared by having its pointed end cut off just above the drain hole. The balloon is filled with 5 to 10 c.c., and then further amounts of 5 c.c. are injected at intervals of 3 to 5 days for the progressive distension of the intra-cavitary balloon up to a total amount of 20 to 30 c.c. The catheter remains in situ for three weeks, the patient not being confined to bed.

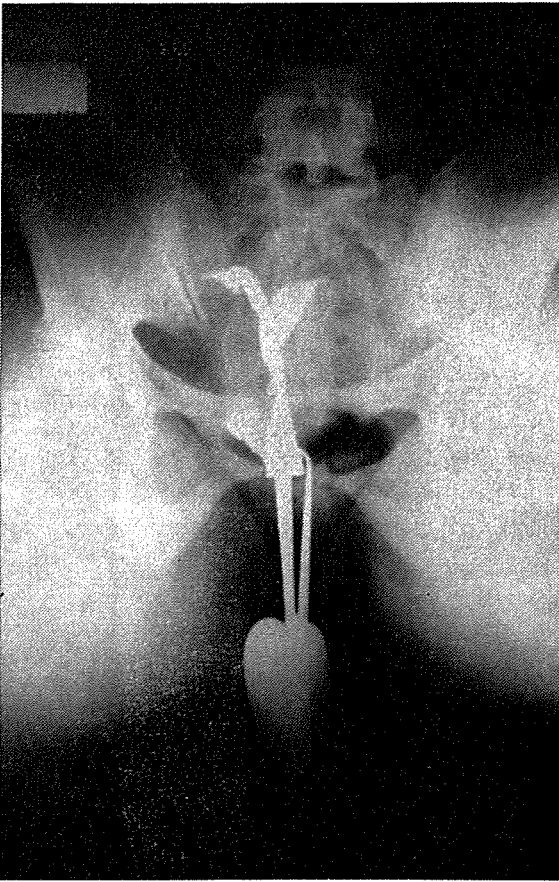


Fig. 4

current abortion and this in spite of the fact that the history is so very often true to type.

Many gynaecologists believe that the cervical suture is best inserted as soon as the condition is diagnosed, and preference is usually expressed for the procedure to be carried out in the absence of pregnancy. It is refreshing, therefore, to find that Shirodkar (1967), in a recent review of the long-term results of his series of 256 cases of his own operation for cervical incompetence, prefers to do it between the 12th and 16th week of pregnancy, though he has performed it even as late as the 28th week. In his view the only indication for performing the operation in the non-pregnant state is if the patient cannot attend when pregnant. This may well be a point demanding renewed consideration in some quarters.



Fig. 5

Expulsion of the catheter will not normally occur. A state of pseudo-pregnancy with gestagens is maintained for a period of 2 to 3 months.

Rapid tubal transport

We have reviewed some current concepts relating to three causes of childlessness in couples who are definitely known to be fertile. There are many other couples,

equally fertile, yet similarly childless, who have no detectable abnormality. Uncharted aetiological factors must be involved — and the rate of tubal transport may well be one such factor.

If tubal transport is excessively rapid in a woman, this may interfere with fertility in one of two ways. The early zygote may reach the endometrial cavity so prematurely that it will be physiologically incapable of achieving firm implantation.



Fig. 6

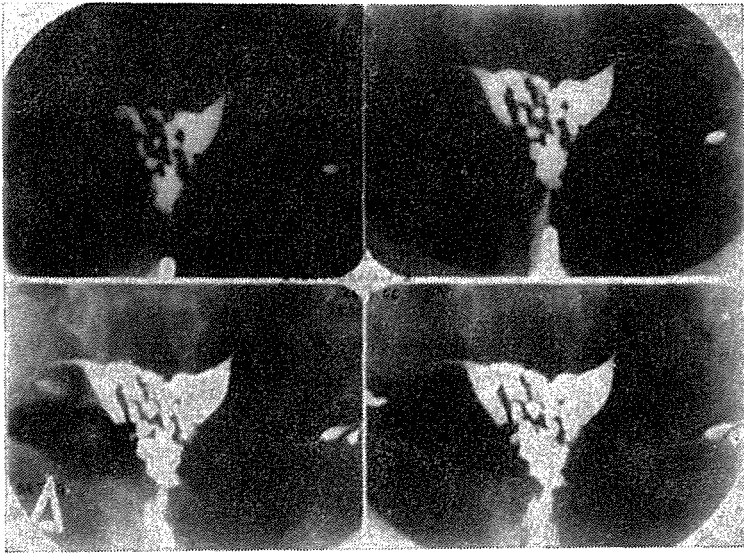


Fig. 7

It has been shown, for instance, that the implantation of a transplanted blastocyst will not occur unless its developmental age is within one day of the corresponding development in the host endometrium (Chang, 1950). Similarly, other studies (Dickmann and Noyes, 1960; Noyes and Dickmann, 1960) established that the uterus on a certain day of early pregnancy is a favourable milieu for embryos of a certain age, but it is a hostile milieu for embryos of a different age. For example: Day 5 eggs in the rat, i.e. blastocysts, survive and develop normally if transferred into a Day 5 uterus. By contrast, Day 4 eggs, i.e. morulae, die subsequent to their transfer into a Day 5 uterus. In other words, speedy tubal transport could have an early abortifacient effect.

Alternatively, if the freshly ovulated ovum is carried too rapidly along the Fallopian tube, the rather brief period when it is capable of being fertilised will be spent before the spermatozoa that meet it will have had the physiological opportunity to become properly capacitated. This possibility is supported by the well-known findings of Mastroianni and his co-workers in relation to the mechanism of action of intra-uterine contraceptive devices in the macaque monkeys. Kelly and Marston (1967) found no such increase in the speed of tubal transport, yet Wynn

(1968) reports that Mastroianni's current experiments continue to bear out his original observation.

It is, then, quite conceivable that undue rapidity in tubal transport may act as an aetiological factor in the infertility of otherwise fertile couples. Its measurement should become practicable. Lundborg and Ingelman-Sundberg (1967) recently reported a study of tubal transport rate on 22 women using an intra-uterine device. In each case 2 microcuries of colloidal Au 198 were injected into the peritoneal cavity; and the rate of tubal transport was consistently found to be significantly faster when the I.U.D. was in position. It might prove useful, therefore, to devise such a technique for measuring the rate of tubal transport in women in hitherto unexplained cases of infertility.

Summary

Too many childless couples actually owe their plight to recurrent abortion. This is particularly tragic because here the deficiency is not one of ovulation or fertilization.

At a time when abortion is so readily treated with depot progesterone, it is important to realize that three causes of habitual abortion are: Congenital malformation of the uterus, cervical incompe-

tence and intra-uterine adhesions. Hystero-graphy is indicated routinely after 2 spontaneous abortions.

Of the uterine malformations, double uterus is one example where the cause might wittingly be neglected and proper treatment delayed unnecessarily. There is considerable clinical value in recognising two distinct types of double uterus, Bicornuate and Septate. The management varies with the two types: in a high proportion of the bicornuate type surgery is not required, whereas for the septate type it is here proposed that surgery is indicated from the moment of undoubted diagnosis. In the bicornuate cases the operation of choice may be the Strassman metroplasty. In the septate cases it is usually advisable to excise the septum through an anterior longitudinal incision.

Cervical incompetence has lost its novelty but it remains a cause of needless recurrent abortion. The cervical suture may best be inserted during pregnancy.

A further iatrogenic condition lies in endometrial adhesions. It is commoner than most clinicians are apt to believe: in a recent series of 425 women with secondary infertility who had had an abortion, endometrial adhesions were identified as the cause in no less than 36 per cent. Only 20 per cent of these women complained of diminished menstruation. Good results seem to be attainable with resection followed by a progressively distended intracavitary balloon.

One is tempted to draw attention to Mastroianni's work on monkeys in eluci-

dating the mechanism of action of Intra-uterine Devices, and to suggest that it might prove useful to devise a technique for measuring the rate of tubal transport in women — possibly accounting for some of the hitherto unexplained cases of infertility.

References

- CAMILLERI, A.P., (1968). *Internat. Surg.* in the press.
 CHANG, M.C. (1950): *J. exp. Zool.*, 114, 197.
 COMNINOS, A. (1967): *Preventive Medicine and Family Planning*. International Planned Parenthood Federation, London. p. 112.
 COMNINOS, A.C., and ZOURLAS, P.A. (1967): in *Wood and Walters*, 1967, p. 868.
 DICKMANN, Z., and NOYES, R.W. (1960). *J. Reprod. Fert.*, 1, 197.
 HOLMES, J.A. (1956): *Brit. med. J.*, 1, 1144.
 JONES, H.W., DELFS, E., and JONES, G.E.S. (1956): *Amer. J. Obstet. Gynec.*, 72, 865.
 KELLY, W.A., and MARSTON, J.H. (1967): *Nature*, 214, 735.
 LOUROS, N.C., DANEZIS, J., and PONTIFIX, G. (1967): in *Wood and Waters*, 1967, p. 872.
 LUNDBORG, R., and INGELMAN-SUNDBERG, A. (1967): in *Wood and Walters*, 1967, p. 879.
 NOYES, R.W., and DICKMANN, Z. (1960): *J. Reprod. Fert.*, 1, 186.
 ROZIN, S. (1967): in *Wood and Walters*, 1967, p. 722.
 SHIROKDAR, V.N. (1967): *Triangle*, 8, 123.
 STRASSMANN, E.O. (1952): *Amer. J. Obstet. Gynec.*, 64, 25.
 UNNERUS, C.E., TURUNEN, A., and OSTMAN, C. (1965): *Ann. Chir. Gynaec. Fenn.*, 54, 63.
 WOOD, C., and WALTERS, W.A.W. (1967): *Editors. Fifth World Congress of Gynaecology and Obstetrics*. Butterworths, Australia.
 WYNN, R.M. (1968): *IPPF med. Bull.*, 2, 1.