tion and so lessening the damage caused by alcohol. It remains to be seen whether the Government has the courage to act.

[1] *The Times*, 25 July 1977.
[2] *Alcohol and Alcoholism*. Report of a Special Committee of the Royal College of Psychiatrists, London, Tavistock. 1979.

Fertilisation in vitro

In vitro fertilisation? Extracorporeal fertilisation? Embryo transfer? Test-tube baby? All are terms for a procedure designed to enable a woman with blocked or absent fallopian tubes to become pregnant and bear a normal child. Last month at a meeting at the Royal College of Obstetricians and Gynaecologists Mr Patrick Steptoe and Dr R G Edwards described in detail the methods that have succeeded in four pregnancies and the birth of two healthy babies.

The first step is to recover one or more oocytes (eggs) from the patient's ovaries at the preovulatory stage, that is, just before they would have been shed spontaneously. In order to render the ovaries accessible a laparotomy may be needed to clear away adhesions resulting from pelvic infection or earlier unsuccessful tubal surgery. Treatment with gonadotrophic hormones (HMG+HCG) will stimulate several ovarian follicles to develop simultaneously, so that several preovulatory oocytes can be recovered by laparoscopy at an appropriate interval (usually 32 hours) after the injection of HCG; but such hormone treatment has the unfortunate side effect of increasing the level of follicular oestrogen and hence decreasing the length of the luteal phase of the cycle. Steptoe and Edwards found that even if an embryo was able to implant in the uterus the pregnancy was not maintained under these conditions, and they therefore abandoned the idea of stimulating ovulation by hormone treatment.

Using the woman's natural cycle, the onset of the rise in luteinising hormone (LH) that precedes ovulation can be picked up by monitoring urinary LH. At an appropriate interval after the rise begins, her single preovulatory oocyte is sucked from its follicle through a fine cannula. As soon as the oocyte is located it is transferred to a drop of some suitable medium (usually Tyrode's). Freshly collected and washed spermatozoa from the husband are then added. If fertilisation occurs the two pronuclei will be visible after 18 hours, and at this time the egg is transferred to another culture medium for cleavage. Steptoe and Edwards use Ham's F10, supplemented with pyruvate and some of the patient's own serum. If the culture conditions are good Edwards reckons that half the embryos will have reached the 2-cell stage by 36 hours, the 8-cell stage by three days, and the early blastocyst stage by about four and a half days.

We do not yet know which is the best stage of development for transfer. The four recent pregnancies were all from embryos transferred at the 8-16 cell stage. The embryos were placed gently in the uterus through a fine cannula inserted via the cervix, without anaesthesia. Every effort was made to avoid stress to the patient, and late at night seemed the most successful time for the operation. The pregnancies were closely monitored, using hormone assay, radiography, ultrasound, and amniocentesis.

The advantages of the procedure are obvious, since for many women with badly damaged tubes no other hope of pregnancy exists. What are the hazards? In animals, work along these lines has been going on for nearly 100 years. Tens of thousands of animals, including mice, rabbits, and sheep, have been born from embryo transfer; a few hundred of these have resulted from in vitro fertilisation. No young have been born with abnormalities that could be attributed to the treatment. With in vitro fertilisation, eggs may occasionally be fertilised by two spermatozoa rather than one, giving rise to triploid embryos with three chromosome sets, but these invariably die early in pregnancy. Since about $1\frac{1}{2}\%$ of recognised natural conceptions result in triploidy, it is hard to say whether or not any particular case of triploidy should be attributed to the in vitro fertilisation.

Although abnormal births would not be expected the success rate may be low. Probably fewer than half even of natural conceptions go to term, and since most patients requesting in vitro fertilisation are already in their 30s their chance of a normal pregnancy is below average. Judging by animal experience a further loss rate, perhaps in the region of 50%, must be expected from technical causes, so it is unlikely that any embryo transfer will have more than a one in four chance of success. Fortunately, Steptoe finds that laparoscopic oocyte recovery is a very untraumatic procedure, so the same patient can be treated on several successive occasions.

How about cost? The procedure is essentially simple, and does not require a great deal of expensive equipment. If it is to succeed, however, it does require a high degree of skill, experience, and teamwork, and is therefore inevitably going to be expensive in terms of human resources.

Kielland's forceps

Kielland's forceps are widely used and make an important and distinctive contribution to obstetric practice. When they are applied in mid-cavity with the fetal head in the transverse or occipitoposterior position an accurate biparietal grip is possible, and the head can be brought down to the roomiest part of the pelvis, turned to the occipitoanterior position, and delivered. Manipulative skill must be matched by good judgment: if either is lacking, serious injuries can be inflicted on mother or baby or both. Parry-Jones[1] has admirably described the place of the instrument in today's practice, and has emphasised the almost complete absence of injury to the baby if the forceps is correctly and gently used.

In two recent reports[2,3] from St Mary's Hospital, Manchester, Chiswick and James described the results obtained by a group of consultants and resident staff, all experienced in the use of Kielland's forceps. The technique was used 86 times between January and December 1976. Three of the babies died from tentorial tears; and when the infants were compared with a matched group of babies born spontaneously there was a higher incidence of delayed onset of respiration, birth trauma, and abnormal neurological behaviour in those delivered by forceps. Nevertheless, all the babies with neurological symptoms were normal within seven days and seemed well when allowed home. Chiswick and James suggest that obstetricians, prewarned of the events that may lead to rotational forceps delivery, should be specially vigilant and try to identify those cases where caesarean section should be selected—for example, where there is slow progression to full cervical dilatation and evidence of fetal asphyxia.

Certainly attention should be drawn to this difficult obstetric problem, but it is hardly surprising that the results of rotational

forceps delivery should compare so unfavourably with spontaneous vaginal delivery. In no sense was the Manchester study a controlled trial, but the report cannot be discounted or the results attributed to inexperienced operators. The pulling and turning associated with rotational forceps delivery must be a cause for concern. Chiswick and James attribute the transient neurological symptoms to cerebral oedema, but there are more sinister possibilities. Yates[4-6] has described the injuries that may occur to the cervical portions of the vertebral arteries—two of the principal arteries supplying the brain—when the baby's neck is pulled or twisted during delivery. His purpose was to draw attention to traumatic lesions in the necks of infants delivered by various methods and to underline the part they possibly played in the production of brain damage in those infants who survived. Short of killing the child, these injuries to the vertebral arteries could, in his view, leave ischaemic damage in the brain stem or cerebral hemispheres that might in later years be associated with spasticity, deafness, or epilepsy. In general, Yates found that the injuries to the vertebral arteries were most severe after breech delivery, but the pulling and twisting of the baby's neck that take place during rotational forceps delivery are comparable.

The concept of a "continuum of reproductive casualty" proposed by Lilienfeld and Pasamanick[7] raises the worrying possibility that survivors of any form of difficult delivery are more liable to suffer some form of brain damage. In extreme examples, cause and effect seem to be clearly established; but this is a difficult, complex problem and the obvious conclusions may not be the correct ones. The subtle interplay of social and medical factors that contribute to the long-term outcome for survivors of breech delivery has been studied in Newcastle upon Tyne,[8 9 10] where the conclusion reached was that the overall picture of handicap in that community would not be altered significantly by increasing the rate of caesarean section in breech presentation. Other studies of the aetiology of handicap in Aberdeen[11 12] broadly support the view that though obstetric trauma may kill children at birth it seems less important than social factors in causing handicap among survivors.

In the face of a difficult delivery, the obstetrician's immediate concern must be to reduce the risk of fetal death. This may well justify an increased caesarean section rate, as envisaged by Chiswick and James. But caesarean section with the fetal head jammed firmly in mid-cavity carries risks. It can be quite difficult to disengage the head from above, and the skull or brain may be damaged; moreover, there are immediate and long-term risks for the mother which must be placed in the balance when a decision is being made between vaginal and abdominal delivery. There is nothing simple or straightforward about the decision that has to be made and very little hard evidence to help the obstetrician in his choice. At present he is guided largely by experience and by confidence in his manipulative skill. A controlled trial, especially one including long-term assessment of survivors, would be difficult to organise. Nevertheless, until this sort of information is available the obstetrician must continue to rely heavily on his clinical judgment.

[1] Parry-Jones, E, *Kielland's Forceps*. London, Butterworth, 1952.
[2] Chiswick, M L, and James, D K, *British Medical Journal*, 1979, **1**, 7.
[3] James, D K, and Chiswick, M L, *British Medical Journal*, 1979, **1**, 10.
[4] Yates, P O, *Archives of Disease in Childhood*, 1959, **34**, 436.
[5] Yates, P O, *Spastics Quarterly*, 1962, **11**, No 3, 15.
[6] Yates, P O, in *Physical Trauma as an Etiological Agent in Mental Retardation*, ed C Angle and E Bering, p 167. Bethesda, National Institutes of Health, 1970.
[7] Lilienfeld, A M, and Pasamanick, B, *American Journal of Obstetrics and Gynecology*, 1955, **70**, 93.
[8] Russell, J K, *et al*, *Lancet*, 1963, **1**, 711.
[9] Russell, J K, *et al*, in *Physical Trauma as an Etiological Agent in Mental Retardation*, ed C Angle and E Bering, p 101. Bethesda, National Institutes of Health, 1970.
[10] Neligan, G, *et al*, *The Formative Years*, p 125. London, Oxford University Press, 1974.
[11] Fairweather, D V I, and Illsley, R, *British Journal of Preventive and Social Medicine*, 1960, **14**, 149.
[12] Birch, H G, *et al*, *Mental Subnormality in the Community. A Clinical and Epidemiologic Study*, p 200. Baltimore, Williams and Wilkins, 1970.

Synovial biopsy in arthritis

Percutaneous synovial biopsy of the knee is little known and much underused. Yet it is safe and easily repeated and is as simple as liver or pleural biopsy, though it shares the problem of sampling errors, since only small pieces of tissue are obtained. Synovial biopsy may be performed on outpatients with little more discomfort than a routine joint aspiration. Sufficient tissue may be obtained for routine histological and immunofluorescent and electron microscopical examination, and the quality is such that open biopsy can be reserved for less accessible joints.[1]

Synovial biopsy is indicated in inflammatory joint disease when the cause remains in doubt—usually when only one joint is affected. If examination and culture of the synovial fluid produce unhelpful results a biopsy should distinguish conditions such as tuberculosis, other subacute infection, and villonodular synovitis, in which specific treatment is indicated, from the more common chronic inflammatory joint diseases or osteoarthrosis. The early characteristic changes of rheumatoid arthritis are usually evident even in the first weeks after the clinical onset, with synovial hyperplasia and infiltration with plasma cells and lymphocytes. Biopsy may also be diagnostic in inflammatory polyarthritis when the conventional tests are unhelpful; it is particularly helpful in separating diseases such as sarcoidosis, amyloidosis, Whipple's disease, haemochromatosis, or malignancies presenting as polyarthritis from the usual rheumatic diseases.[2] Occasionally gross infiltration of the synovium with crystals of uric acid or calcium pyrophosphate will be found in this group, particularly if the specimen is alcohol-fixed.

Some overlap occurs in the histological appearances of biopsy specimens from the chronic forms of inflammatory arthritis, particularly in rheumatoid arthritis and psoriatic arthritis, and occasionally in Reiter's syndrome.[2] There is gross hyperplasia of the synovial membrane, deposition of fibrin on its surface, and infiltration with plasma cells. All these changes are more frequent and more appreciable in rheumatoid arthritis, and the presence of lymphoid follicles is usually confined to this disease. Such follicles are usually a feature of chronicity, but they may occasionally be found within three months of the clinical onset of the disease. Again, while hyperplasia of the synovial lining cells may occur in several diseases, considerable synovial hyperplasia from the usual one or two cells to a layer up to six cells thick is virtually confined to rheumatoid arthritis.[3] A predominantly polymorph leucocytosis in the synovium may be found early in a few patients with rheumatoid arthritis but is more often due to bacterial infection; a heavy polymorph infiltrate is highly characteristic of infection. Such an infiltrate may, however, also be found in Behçet's disease, in which it may progress to