ADDENDUM.—Since this paper was written three further cases of hypopituitarism have been given A.C.T.H. Two had post-partum Simmonds's disease, and the other had had a chromophobe adenoma which had been treated surgically and with pituitary irradiation. A.C.T.H. was given in doses of 12.5 mg. every six hours by intramuscular injection. All the patients showed both subjective and objective improvement, and the only undesirable effect was slight oedema in one case.

REFERENCES

- Callow, N. H., Callow, R. K., Emmens, C. W., and Stroud, S. W. (1939). *J. Endocr.*, 1, 76.
 Daughady, W. H., Jaffe, H., and Williams, R. H. (1948). *J. clin. Endocr.*, 8, 166.
 Marrian, G. F. (1951). *J. Endocr.*, 7, lxix.
 Robertson, J. D., and Kirkpatrick, H. F. W. (1951). *Lancet*, 2, 54.
 Robson, H. N., and Duthie, J. J. R. (1950). *British Medical Journal*, 2, 971.
 Roche, M., Thorn, G. W., and Hills, A. G. (1950). *New Engl. J. Med.*, 242, 307.
 Summers, V. K., and Sheehan, H. L. (1951). *British Medical Journal*, 2, 564.

TUBO-UTERINE IMPLANTATION*

BY

V. B. GREEN-ARMYTAGE, M.D., F.R.C.P., F.R.C.S.
F.R.C.O.G.

Consultant, Department of Obstetrics and Gynaecology,
Postgraduate Medical School of London,
Hammersmith Hospital

Practitioners and consultants alike are often confronted by a patient who gives a history of miscarriage, one pregnancy, one curettage, or one caesarean section, and yet of never again being able to conceive. Close investigation will almost invariably elicit the fact that the abortion was induced or that the pregnancy was followed by a few days of fever which quickly yielded to antibiotics or chemotherapy. When seen months or maybe years later rarely is it possible to palpate anything abnormal in the pelvis, though further study with Rubin's kymograph will show that no gas passes even at high pressures, and that the area of distension pain is low and entirely central, indicating that the blockage is at the internal ostia (Fig. 1), a conclusion even more definitely confirmed by lipiodologram.

FIG. 1

* Address delivered at the All-India Surgeons' Conference in Calcutta, December, 1951.

In some parts of France and the United States of America further proof, as well as valuable information regarding the morbid anatomy of the tubes and ovaries, is thought to be obtained by culdoscopy or coelioscopy (Decker and Cherry, 1944). In this country, however, when the history is that of an induced abortion or infected pregnancy, and gas and oil investigations have been systematically carried out, it is almost invariably the rule to find at laparotomy in 82% that the isthmal and interstitial portions of the tube are alone impermeably sclerosed, whereas the distal parts of the ampullae and fimbriae are perfectly healthy (Fig. 1)—a condition almost pathognomonic of infected secundines. Very occasionally the same morbid anatomy may be present with a history of gonorrhoea, but in these cases there will always be found peritubal as well as periovarian adhesions, conditions often stultifying a good prognosis.

Implantation in the Past

Hitherto, salpingostomy or tubo-uterine implantation has raised scant enthusiasm among gynaecologists. Indeed, as Te Linde (1946) remarks, such operations are practised sometimes by some, rarely by others, and never by many. In the past, the reasons for such an attitude of mind have been (1) that the necessary apparatus for investigation of the patient before and after operation was wanting; (2) the previous history was thought too unreliable for an exploratory laparotomy; (3) the time and labour consumed were not justified by results; (4) the technical skill for a finicky plastic operation was lacking; and (5) the essential instruments were not forthcoming.

But perhaps the real death warrant lies at the door of Greenhill (1937), who, despite Solomons's (1936) questionnaire, sent a similar document to 107 leading American gynaecologists. Of these, 56% utterly condemned all plastic operations on the tube. The remaining 44% had, however, among them performed 818 operations, which altogether had resulted in only 54 pregnancies (6.6%), and from these only 36 live babies were born (4.4% success), for 18.5% aborted and 14.8% were ectopic pregnancies.

Such dismal results, recorded of course long before the era of antibiotics and chemotherapy, should neither depress us nor nowadays be accepted, for, as a result of much trial and careful attention to detail, the pathway is now floodlit for all to follow. Indeed, Raoul Palmer (1951), in a recent follow-up of 26 personal cases in which he had done a tubal implantation alone for the reasons specified, records eight full-term pregnancies and one ectopic, a 37.5% birth success; whereas in 18 other cases in which salpingolysis or salpingostomy was done the pregnancy success rate was only 11%. This figure corresponds with our own experience; for a fimbrial or ampullary block, with or without a hydrosalpinx, implies a pathological endosalpinx unfavourable to the passage of an ovum, whereas a clear-cut tubal implantation denotes, as a rule, a healthy mucous membrane beyond the block at the isthmus. In the 10 full-term pregnancies which Palmer records following 44 operations, caesarean section was necessary in only three. Moreover, in his latest 20 cases he has had six full-term pregnancies (30%) and no ectopics.

Such small numbers and short-term statistics are rightly looked at askance, but when they are backed by personal experience and that of many others in this country they surely challenge emulation.

Method of Tubal Implantation

Many techniques have been tried, with varying success. I advocated (Green-Armytage, 1937) the coronal uterine incision which had been advised by Bonney (see Bonney, 1947): in this the implanted tube is threaded with silk-worm gut, which is brought down into the vagina. Later, ureteric catheters and stainless silver wire were employed

as tubal guides, being removed on the fifth to the eighth day through the vagina. Out of 14 such operations three pregnancies resulted—two going to term, both delivered by caesarean section, the other aborting at the fifth month.

Solomons (1927) recorded an 8.2% success rate after bisection of the uterus and leading the catgut-threaded tube through a window at the cornu into the uterine cavity. Moore-White (1951) reported two pregnancies after cornual resection using gossamer silk, and employing the usual technique when implanting ureters into the colon. Others prefer first to excise a triangular wedge from the cornu and then gently repose the patent tubal end into the somewhat large ragged hole laid bare. In one of my own cases, using this last method, the contents of the pregnant uterus herniated and ruptured at the seventh month, necessitating hysterectomy in another hospital. During the past two years I have been employing a simpler method with some success.

Before Operation

The husband and wife having been fully investigated, the date for section is fixed for a time immediately following a menstrual period; this lessens the likelihood of oozing and enhances the chances of conception at the time of ovulation five to six weeks later.

The patient is given 300 mg. of vitamin C daily for a week beforehand and a million units of penicillin daily for two days before and two days after operation.

In the theatre, under anaesthesia, a Rubin CO₂ cannula (attached to its cylinder and kymograph) is anchored to the cervix uteri. This is done for greater scientific accuracy, in that, when the abdomen is opened and the gas turned on, verification of the block at the cornu and/or the isthmus can be seen by distension and blanching. Should, however, the block be at the ampulla or fimbria, the operation of salpingolysis or salpingostomy is made easier and more satisfactory, for the bubbles can be seen rippling along the tube to explode at the external ostium—a very satisfying feature. The gas, of course, must be turned off directly the abdomen is closed, though at the end of the operation verification of patency can be repeated.

Technique

A Bonney myomectomy clamp being *in situ*, a fine probe is gently passed from the fimbrial end to the site of blockage. This is easier and quicker than distension by air, using a ball and syringe. A fine Stille forceps is applied at the block and the patent portion of the tube is cut distal to it (Fig. 2). The patent tubal end, held by delicate toothless forceps, is cut for 0.5 cm. above and below, and each flange

FIG. 2

is secured by a single knot, using silkworm-gut 5X on an eyeless needle (Fig. 2). Then, using the forceps on the isthmal blocked portion as a tractor, the myosalpinx is cut and a cylindrical tunnel the size of a pencil is cored out with a 9-mm. Silcock punch operating in the line of the interstitial portion of the tube until it reaches the uterine cavity (Fig. 3).

FIG. 3.—Using a Silcock punch, a tunnel the diameter of a pencil is cut at the cornu ready for implant.

At this stage a branch of the uterine artery lying between the folds of the broad ligament should be ligated lest troublesome bleeding or a haematoma occur later. Having taken great care to see that the mesentery of the tube to be implanted is conserved and its vessels are intact, the silkworm-gut needles on the two flanges are passed through the tunnel and made to emerge through the uterine wall, the one above and the other below; then, using them as reins, the tube is gently drawn through the cylindrical tunnel into the endometrial cavity. The two long loose ends depicted (Fig. 4) are then brought through the wall of the

FIG. 4

uterus, using a straight or ordinary Reverdin needle, and the two sutures secured. The external orifice of the tunnel is lightly sutured to the wall of the tube above and below (Fig. 4), great care being taken not to strangle the implanted tube in its new bed.

The procedure is then repeated on the opposite side and the myomectomy clamp removed.

Before closing the abdomen see that the haemostasis is complete, and if necessary, using the French method of plication of the round ligaments, ventrosuspend the uterus.

The patient is put back to bed with the foot of the bed raised in order to lessen pelvic congestion. A follow-up CO₂ test is done in six to eight weeks' time. A lipiodologram is not recommended.

After using the above technique 6 patients out of 17 have conceived and gone to term. Four were confined naturally and two by caesarean section. There was one ectopic pregnancy. It is perhaps worth recording that in one of these patients, a nurse, the distal block on both sides extended almost to the ampulla and was less than 5 cm. from the fimbrial end. With an 11-mm. Silcock punch I was able to implant the wider portion of the tube with ease, the end appearance of the uterus being somewhat like that of a penguin. She conceived, however, within a few months and went to term.

Discussion

One-conception infertility is very often seen to-day. Close and scientific investigation of such cases shows that in a great majority (82%) the tubes are only blocked at the internal ostia or isthmus. The increased skill that results from experience has greatly added to our success rate in recent years—indeed, rising from 8% to more than 30%—and there can be no question that when larger numbers of gynaecologists throughout the world undertake these operations the end-results will be greatly improved and, we hope, reach that of 50% from the point of view of full-term pregnancies; for close observation and study of a number of previous failures revealed the fact, now so obvious, that it was the coning out of a jagged wedge from the cornu of the uterus with a knife that so often spelt strangulation of the tube, or later resulted in constriction by muscle scar tissue. The smooth clean-cut tunnel made by the 9 mm. modification of the Silcock punch (Fig. 3) obviates this.

Salpingostomy

As already indicated, it is a common finding that a cuff or spoon operation on the tubes, or for that matter simple salpingolysis, does not give the results one would expect, even though, in some, CO₂ tests repeated month after month are positive, with excellent oscillations.

The lessened incidence of pregnancy and the increased occurrence of ectopics in these cases would seem to point to a failure of the endosalpinx and its cilia to transmit the ovum. In others, however, although at the time of operation there is perfect bubbling rippling CO₂ patency, it has been found, on tests being made one, two, or three weeks afterwards, that no gas passes. Moreover, the area of gas-distension pain is referred right out to both iliac fossae, indicating recurrent closure at the spoon aperture or fimbrial end. To counter this it is suggested that in a suitable case the operation should be performed on the sixth to the eighth day of the cycle, and that on the first day of verified ovulation we should give a saline-and-dextrose douche and then do as Hunter did with success in 1799—namely, hornspoon into the vagina a fresh specimen of the husband's semen.

REFERENCES

- Bonney, V. (1947). *Textbook of Gynaecological Surgery*, 5th ed., p. 643. London.
 Decker, A., and Cherry, T. H. (1944). *Amer. J. Surg.*, 64, 40.
 Green-Armistage, V. B. (1937). *British Medical Journal*, 2, 6.
 Greenhill, J. P. (1937). *Amer. J. Obstet. Gynec.*, 33, 39.
 Moore-White, M. (1951). *J. Obstet. Gynaec. Brit. Emp.*, 58, 381.
 Palmer, R. (1951). *Mém. Acad. Chir., Paris*, 77, 216.
 Solomons, B. (1927). *J. Obstet. Gynaec. Brit. Emp.*, 34, 222.
 — (1936). *Ibid.*, 43, 619.
 Te Linde, R. W. (1946). *Operative Gynecology*, p. 523. Philadelphia.

According to the census commissioner in Delhi the population of India was 356,829,485 on March 1, 1951 (*The Times*, June 2). The ratio of females to males was 947 to 1,000. Since 1941 the population has increased by 12.5%. Over two-thirds of the population depend on agriculture for a livelihood, and nearly 83% of the people live in rural areas. Seventy-three cities have more than 100,000 inhabitants.

SULPHONE AND STREPTOMYCIN IN PULMONARY TUBERCULOSIS

BY

PETER W. EDWARDS, M.B., Ch.B.

A. CLARK PENMAN, M.D.

AND

LESLIE J. CUTBILL, B.Sc., A.R.I.C.

(From the Cheshire Joint Sanatorium)

Diaminodiphenylsulphone (D.D.S.) was the first sulphone to be synthesized by Fromm and Wittman (1908), but it was not until the work of Buttle *et al.* (1937) that its remarkable pharmacological and therapeutic properties in streptococcal infections in mice became known. Rist *et al.* (1940) demonstrated the action of sulphone in experimental tuberculosis in animals, and soluble derivatives—"promin" ("promanide" in Great Britain) and "diasone"—were used extensively in America and elsewhere in the treatment of animal and human tuberculosis.

Feldman *et al.* (1944) thought that D.D.S. itself was too toxic for use in man. From 1940 onwards the use of sulphones was largely confined to the soluble derivatives, promanide, diasone, and "sulphetrone," which could be tolerated in much larger doses. It was some time before it was generally realized that the efficacy of a compound was not wholly decided by the magnitude of the dose tolerated. Hinshaw and Feldman (1941) found that considerably larger doses of promanide could be given parenterally than orally without producing cyanosis. Francis and Spinks (1950) reviewed earlier work, and presented their own results, indicating that the activity of the soluble sulphones depended on the amount of free sulphone (D.D.S.) which was liberated in the body, the breakdown occurring mainly in the stomach and in the intestinal tract. The therapeutic ratio of D.D.S. proved just as good as any of its soluble derivatives.

Lowe (1950) concluded that, contrary to general belief, D.D.S. is not too toxic for use in man, and in the treatment of leprosy he established a regime of oral administration of small doses, rising from 100 to 500 mg. a day, over a period of five weeks. These small doses could be maintained for long periods, and proved at least as effective as the much larger doses of the complex soluble sulphones. Lowe (1951) now recommends a regime of 400 mg. of D.D.S. twice a week.

The small observed effects of D.D.S. on tuberculosis have been overshadowed by the discovery of streptomycin, which has a much greater demonstrable influence on the disease. The great drawback to streptomycin is the rapidity with which the tubercle bacillus acquires resistance to the drug. The possible preventive effect of sulphone administered with the streptomycin on the emergence of resistant strains was investigated by Bernard *et al.* (1950), and they showed that sulphone retarded the emergence of resistant strains, though the clinical success was not great. Francis (1952) showed that small doses of sulphone, when administered with streptomycin to guinea-pigs infected with tuberculosis, gave better results than streptomycin given alone.