FEMALE GENITAL TUBERCULOSIS

By J. A. STALLWORTHY, M.A., F.R.C.S., F.R.C.O.G., F.A.C.S.(Hon.)

Area Department of Obstetrics & Gynaecology, United Oxford Hospitals

The last 15 years have been remarkable in the history of medicine. Old enemies have been conquered and new ones discovered at such a rate that it is difficult to follow the continual progress. The story of genital tuberculosis deserves but a small paragraph in this great chapter of events, but the reference is both interesting and important.

Tuberculous pelvic disease has been recognized as a pathological entity since Morgagni's first description in 1744. Appreciation of the clinical problems it can present is of much more recent origin. Study of the many papers published in the last few years from clinics all over the world, reveal that the greatest interest has been shown in unsuspected endometrial and tubal infection. The attention focused on this has caused some to forget that it is only part of a much wider problem.

In 1938, Dr. Robb-Smith of the Department of Pathology, United Oxford Hospitals, reported tuberculous endometritis in curettings taken from three patients with disordered menstruation, but with no clinical indication of infection. The diagnosis seemed so unusual that a letter was sent to several senior British Gynaecologists asking advice on treatment. All replied that being unaware of the condition they had no experience from which to comment. One of them, the late Mr. Victor Bonney, with his characteristic encouragement of junior colleagues, wrote—'but find out all you can about this; it is interesting and might be useful.' The message stimulated research at Oxford.

One hundred and thirty-two patients with proven acid-fast pelvic infection have been investigated and treated in this Department since then, and clinical details of many others have been forwarded for comment by colleagues elsewhere. Previous publications (Stallworthy, 1952, 1954, 1955) have dealt with the diagnosis of genital tuberculosis, the natural history of the untreated symptomless case, and the role of sanatorium treatment and surgery in the pre-antibiotic era.

Treatment and prognosis have now been revolutionized by the advent of new drugs. A Research Committee, sponsored by the Royal College of Obstetricians and Gynaecologists and

the British Tuberculosis Association, has conducted an extensive trial into methods of treatment and research continues (Sutherland, 1954). Based on experience to date, the present position will be summarized in relation to pathology, clinical manifestations, diagnosis, treatment and prognosis.

Pathology

The fallopian tube and endometrium are the sites most often involved. The ovary, cervix, vagina and vulva are infected much less frequently and in the order given. Asplund and Ryden (1952) believe that cervical infection is more common than is generally recognized, and demonstrated endocervical tuberculosis in 11 of 19 patients with endometritis, but tuberculous ulceration of the cervix visible on speculum examination, is rare. It can be confused with carcinoma. As with tuberculosis elsewhere, there may be active infiltration with little or no macroscopic evidence, extensive fibrosis, and caseation. In silent or unsuspected endometrial tuberculosis there is usually nothing abnormal to see on naked eye inspection. Even with the rare hyperplastic form, in which the endometrium is grossly thickened, proliferative, and vascular, there is nothing macroscopically characteristic to suggest the presence of infection. If it is found in association with post-menopausal bleeding it is likely to be mistaken for endometrial carcinoma.

The histological picture is of typical giant cell systems with one or more central Langhan's cells surrounded by epithelioid cells and lymphocytes. Endometrial caseation is uncommon, but is occasionally found in the deep basal layer, and in patients with long-standing amenorrhoea the whole endometrium may be affected. The stroma in most cases shows diffuse lymphocytic infiltration, but a diagnosis should not be made on this alone. Giant cell systems may be so few in an early infection that biopsy material reveals no evidence of disease. In late cases however they are much more frequent and caseation and fibrosis may become prominent features. Acid-fast bacilli can be found occasionally after prolonged search, but are revealed more easily by culture or animal

inoculation. The responsible mycobacterium is usually of the human strain, although bovine types are occasionally isolated.

The histological picture characteristic of tuberculosis must be differentiated from the chronic granulomatous reaction to such foreign bodies as lipiodol used in salpingography, or silk and other non-absorbable uterine sutures following section or myomectomy.

Clinical Manifestations

Silent Tuberculosis

There are more women with silent unsuspected genital tuberculosis than with symptoms leading to its detection. When the diagnosis is made it is usually by endometrial examination in the investigation of infertility or disordered menstruation. Increasing use of the biopsy curette in recent years has been responsible for the detection of the many unsuspected cases now reported in the literature (Sutherland, 1943, 1950; Rabau, 1943; Schockaert and Ferin, 1939; O'Brien and Lawlor, 1947; Sharman, 1947). Even in this group however there are often indications which it is now recognized might arouse suspicion. The pelvis usually appears perfectly healthy on examination, but if there is either a family or personal history of tuberculosis, the possibility of the endometrium and tubes being involved should be considered seriously when complaint is made of infertility or menstrual disturbance. In approximately 50 per cent. there is a history of pleurisy, or of abdominal symptoms earlier in life suggestive of glandular disease. It is wise in these circumstances to obtain both a bacteriological and pathological report on the endometrium before proceeding further with investigations for tubal patency. Insufflation of tuberculous tubes can cause peritonitis and prolonged illness. Seventy-three per cent. of 107 women with proven genital tuberculosis had evidence of other forms of tuberculosis (Barnes, 1955). Dr. Barnes believes that the genital infection occurs usually within three years of a primary focus in the lungs, glands or elsewhere. It is in the main a risk of adolescence.

There is evidence to suggest that dilatation of the cervix may disseminate infection when there is uterine activity, and for this reason many surgeons prefer to make a preliminary endometrial study in doubtful cases with a biopsy curette. A full curettage is performed later if this is negative. There are experienced workers however who feel that the risk of missing infected areas if only biopsy material is used is sufficiently great to justify a full curettage. At Oxford the routine is to use the biopsy curette first, and to examine the endometrium both pathologically and bacteriologically before employing full curettage.

Menstrual Disorders

There is no alteration of menstrual rhythm characteristic of pelvic tuberculosis. For practical purposes it can be considered that in 50 per cent. of cases the menstrual behaviour is normal. In the other 50 per cent. approximately half will complain of increased losses, while the remainder will record oligomenorrhoea, irregular bleeding, and occasionally amenorrhoea. When amenorrhoea is due to endometrial infection the lesion is advanced and caseation is extensive. It is obvious from the above that while there is no menstrual disturbance typical of genital tuberculosis, the possibility of infection should be remembered when a woman complains of disordered menstruation—whether this be in the nature of menorrhagia, oligomenorrhoea or amenorrhoea. Tenderness in the fornix, suggesting chronic salpingitis, or the presence of an adnexal mass, or adnexal masses, would make the diagnosis more likely, particularly if there were no history of pyogenic infection. The importance of a personal history of tuberculosis has already been stressed. Intermittent menstrual bleeding, contact bleeding, and post-menopausal bleeding can all be caused by tuberculous ulceration of the endometrium, cervix or vagina, but as previously stated, lesions of the lower genital tract are rare.

Pain

This is not a prominent symptom of genital tuberculosis. With pyosalpinx formation congestive dysmenorrhoea, with pre-menstrual pain in one or other iliac fossa, is likely to occur, and if there is associated peritonitis with exudation and adhesions, a low midline sacral backache is occasionally present. Difficult cases from a diagnostic point of view are those in which a pyogenic infection is added to pre-existing tuberculous disease. This is particularly liable to follow insufflation or salpingography. When acute symptoms develop within a day or two of the use of an oily medium in salpingography they are probably due to reaction at the site of a pre-existing infection, but occasionally as with symptoms following gas insufflation, the evidence suggests a secondary pyogenic infection.

Secondary infection does from time to time arise spontaneously, due presumably to contamination by intestinal coliform organisms. These cases are dangerous in that untimely surgical intervention, with or without drainage, can result in the formation of tuberculous fistulae. The surgical problems both in respect of prevention and cure have been discussed in an earlier publication (Stallworthy, 1952). It should be realized that there is seldom justification for exploratory laparotomy as an urgent or semi-urgent measure in these cases. Careful preliminary investigation would reveal the

presence of the underlying tuberculous lesion.

Peritonitis

The only reason for including this in a discussion on genital tuberculosis is that on occasions a correct appraisal of the abdominal condition will direct attention to the underlying pelvic disease. A typical example of mistaken diagnosis is seen in the young woman with an apparent ovarian cyst arising from the pelvis. She may or may not have menstrual disturbance. Generally speaking she is anaemic, complains of low sacral backache, and has some degree of leucorrhoea. An interesting clinical point is that she may volunteer the information that 'the cyst' varies in size from time to time. This should arouse suspicion for it is characteristic of an encysted ascites. Furthermore the association of low central sacral backache and anaemia, in the absence of menorrhagia to account for it, are both characteristic of pelvic tuberculosis with infiltration of the utero-sacral folds. Pelvic examination would reveal that 'the cyst' was fixed, the uterus restricted in mobility, and the utero-sacral ligaments tender when stretched. There may be fixed adnexal masses. Endometrial biopsy should confirm the diagnosis.

On rare occasions a tuberculous pyosalpinx can become so large that it presents itself as an abdominal tumour. It may be mobile and under such circumstances is generally mistaken for an ovarian cyst. The history, and the feel of the other appendages may give the clue to the correct diagnosis.

Symptoms and signs suggesting the development of a low grade peritonitis following abortion or delivery can be caused by tuberculosis. Endometrial biopsy is simpler and preferable to laparotomy in the investigation of such a case.

Fistulae

These are usually external and involving bowel or bladder, with the resultant discharge of faeces or urine. Uterine fistulae also occur with the periodic discharge of menstrual fluid. Spontaneous internal fistulae can develop as the result of rupture of a pyosalpinx into adjacent viscera, with communications between small and large gut, or between bowel and bladder, or bowel and uterus. Badly planned and inadequate surgical procedures are usually responsible for tuberculous fistulae of the external type. They most times follow damage caused by attempts to open an abdomen involved by tuberculous adhesions, from drainage of a tuberculous pelvic abscess, and from attempts to perform conservative surgery without realizing that the mycobacterium is responsible for the pelvic condition. It cannot be stressed too strongly that the *correct diagnosis and adequate*

treatment would prevent most tuberculous fistulae from occurring. When they have occurred the prognosis is good with antibiotic treatment. Reconstructive surgery is necessary from time to time once the infection has been overcome.

Pelvic Bone Infection

This is not common but is included because errors of diagnosis can easily be made. The two usual sites are the sacro iliac joints and the symphysis pubis. The low backache of which many women complain is typically lumbo-sacral

FIG. A.—Tuberculous sinus on abdominal wall.

FIG. B.—Tuberculous osteomyelitis of symphysis

and associated with a lumbar lordosis and faulty posture. A true sacro-iliac backache, with pain over the joint, merits careful radiological examination of the pelvis. Tuberculous disease of the symphysis is rare. It is liable to be confused both clinically and radiologically with the more common osteoporosis associated with pregnancy. When sinuses form the disease is advanced and the diagnosis easy (Figs. A and B). Culture of the sinus exudate or biopsy of its wall provides the necessary proof.

Diagnosis

Give a dog a bad name ! It has long been accepted that the diagnosis of pelvic tuberculosis is difficult, so difficult that some suggest laparotomy as the only way of making certain. This counsel of despair is as inaccurate as it is dangerous. The mortality, and morbidity due to fistulae, associated for so long with the treatment of this disease are almost entirely the result of unnecessary or inadequate surgery. As discussed later surgical treatment is now seldom required and it is the more necessary therefore to make the correct diagnosis before advising operation. There are safer ways of doing this than by unnecessary laparotomy.

The importance of a personal or family history of tuberculosis has been stressed. Attention should be given to obtaining information on this whenever there is complaint of infertility, disordered menstruation, or pelvic pain. The detection of adnexal inflammatory masses when there is no history of pelvic infection makes the diagnosis of tuberculosis probable. When there is neither history nor physical sign to suggest the lesion it is

revealed occasionally radiologically during tests for tubal patency. The characteristic findings of thickened pipe-stemmed tubes with strictures, opaque areas and dilatations, and sometimes fistulous penetrations into the surrounding tissue have been extensively described in the literature which was well reviewed by Sun (1948). Other contributions have been from Magnusson (1945), Jedberg (1950), Ekengren (1955), and Williams (1955). If oily opaque media such as Lipiodol are used there is a danger of acute exacerbation of infection and peritonitis, with the formation of large adnexal masses which may reach as high as the umbilicus and cause months of serious illness. With water soluble media this risk is almost entirely eliminated but recently some doubt has been thrown on the wisdom of using media containing polyvinyl alcohols. As yet unconfirmed American work has suggested that in certain animals these alcohols can be carcinogenic and in some clinics the use of contrast media containing them has been suspended.

Final proof of tuberculous infection is provided bacteriologically and histologically. Greenhill (1941-1942) cultured the mycobacterium, and injected guinea-pigs from the material obtained by puncturing pelvic masses. He also examined uterine and cervical secretions for the organism. Halbrecht (1947) cultured menstrual blood collected on the first and second day of a period. This is a neat method but is subject to considerable error and while a positive result is conclusive a negative one does not exclude the presence of active infection. The Oxford method is to take two endometrial strips in the pre-menstrual phase

with a biopsy curette. One is sent to the Pathologist for Histological examination and one to the Bacteriologist for Culture and Animal Inoculation.

Treatment

It is essential to remember that the patient requires a careful general examination to exclude infection elsewhere. Pulmonary activity, renal tuberculosis, and glandular disease may all be associated with a genital infection. Anaemia is common and requires treatment. The advent of powerful antibiotic drugs has not removed the necessity for careful attention to diet, adequate rest, and fresh air, although it has made it possible for the necessary treatment to be supervised as an outpatient procedure if the home conditions are satisfactory. Once the diagnosis has been confirmed, preferably bacteriologically, treatment is commenced with Streptomycin 1 g. daily intramuscularly in a single dose together with PAS 4 g. three times daily. This should be continued for three months, at the end of which time further biopsies are taken and treatment continued if the lesion is still active.

Although there is a theoretical risk of auditory nerve lesions when Streptomycin is used, regular tests on patients treated at Oxford revealed no evidence of trouble. It would seem reasonable in view of this to dispense with routine testing unless facilities are readily available. Other toxic manifestations occur occasionally. These include dermatitis, oedema, headache and alopecia.

It can be anticipated that three months' treatment as outlined will cause adnexal masses to resolve, some fistulae to heal, and negative biopsies to be obtained from the endometrium. When activity persists the sensitivity of the organism to Streptomycin, PAS and Isoniazid should be re-investigated, the treatment prolonged and amended as necessary. The therapeutic value of Isoniazid is being investigated by the Research Committee previously referred to. The results of treatment with PAS and Streptomycin have already been published by Sutherland (1954).

When there is no further evidence of infection, the patient should be kept under observation until three negative biopsies taken consecutively have been obtained. These should be taken in the premenstrual phase of the cycle and should be examined both pathologically and bacteriologically. After two successive negative tests it is wise to perform a full curettage for the final examination.

Surgery

The successful role this can play was discussed at the 13th British Congress of Obstetrics and Gynaecology, 1952 (Stallworthy). The danger of inadequate treatment was emphasized with its

sequelae of fistulae and death. Radical measures were proven safe even before anti-biotic drugs were available, and of 27 patients treated in this way there were no deaths and no recurrent disease. The need for surgery has decreased since then, but is indicated when fistulae fail to heal, when adnexal masses fail to resolve or increase in spite of prolonged treatment according to the routine described above. There are also patients with both active pulmonary and pelvic disease in whom the response to treatment is unsatisfactory because of severe menorrhagia with resultant anaemia. The response to total hysterectomy and bilateral salpingo-oophorectomy can be dramatic, and menopausal symptoms can be prevented by implanting 100 mg. of oestradiol beneath the rectus sheath when closing the abdomen. If intra-cavity radiation is used to control bleeding it is necessary to make sure beforehand that a submucous fibroid is not present. When there is doubt, hysterectomy should be performed if the menorrhagia persists after curettage.

Prognosis

This has been revolutionized by the new drugs. Untreated cases may remain quiescent for years and spontaneous cure undoubtedly occurs, but active infection is a source of constant danger. Ten of 52 untreated controls in the research series (Sutherland, 1954) deteriorated within the year they were observed and were given treatment. In the Oxford series before anti-biotic drugs were available, 9 of 28 patients under observation over a period of years became worse and one of them died. There was only one spontaneous cure. When treated with Streptomycin and PAS the results are very different. One year after treatment was commenced 24 of 27 patients in the research trial series were apparently cured as assessed by repeated negative biopsies. The relief of symptoms was equally dramatic. Pain was cured or eased in all cases. Normal menstruation returned in all patients complaining of menorrhagia and amenorrhoea. There was no instance of pregnancy following treatment in the Research Council's series, but since Rabau (1952) reported a successful pregnancy following treatment of proven tuberculosis there have been further examples of this. Three patients in the Oxford series have conceived, including one who recovered from a pelvic infection associated with miliary tuberculosis and tuberculous meningitis. It is probable that the chances of conception will improve with earlier effective treatment before tubes are disorganized. It is also probable that the encouraging results obtained will be further improved with increasing experience of the new drugs now available. The

Continued on page 525.

posteriorly. In extending the excision of the parametrium backwards along the utero-sacral ligaments, care must be taken not to damage the terminal branches of the superior haemorrhoidal artery since such an accident jeopardizes the blood supply to the bowel whereby a fistula may result. If anterior exenteration is to be performed, it is sufficient to transplant the ureters into the sigmoid at the most convenient spot. The amount of hyperchloraemic acidosis resulting from this procedure can be easily controlled by simple alkalis taken by the patient when she feels off-colour, nauseated, thirsty, or has an unpleasant taste in the mouth. An intelligent patient will soon know the warning symptoms. Control of the anal sphincter and moderation of fluid intake should give the patient an uninterrupted six to eight hours sleep and enable her to perform most social activities.

Total exenteration presents certain problems which must be solved if this operation is to survive as a reasonable surgical procedure :

a. It is universally acknowledged that a wet colostomy is unpleasant and often unmanageable.

b. The implantation of the ureters in the large bowel, as already pointed out, is fraught with grave risk to the kidney from infection and obstruction.

c. The electrolyte disturbance from the selective absorption of chloride from the bowel urine is upsetting and unpleasant to the patient and may prove a danger. It is, therefore, suggested that a separate artificial bladder made from an isolated loop of terminal ileum, one end of which is closed and the other brought out in the right lower quadrant as a permanent ileostomy, should be employed. Clean urine can thus be collected, uncontaminated with faeces, in a separate bag while an ordinary

colostomy in the left side of the abdomen can be trained to operate regularly once every morning, thus causing the patient little or no disability. The presence of the ureter in an isolated loop of ileum uncontaminated by bowel contents should diminish the risks of infection to the kidney.

There is one further danger of total exenteration to the patient, namely, the raw area left by the extirpation of the pelvic viscera. Infection in this raw area is unavoidable and the adhesion of coils of small bowel to it provide a real danger of intestinal obstruction. It is suggested, therefore, by the author that a two-stage operation should be performed for total pelvic exenteration. In the first stage, the permanent colostomy is formed and the artificial bladder is established with implantation of both ureters into it. Some form of peritoneal shelf should be constructed between these two artificial stomata so that the small bowel is unable to prolapse into the pelvis. After a reasonable interval, the total exenteration can be completed as a more or less extra-peritoneal procedure, if necessary by a transverse sub-umbilical incision. By this method, it is hoped to eliminate the risks of intestinal obstruction. This complication has too often proved a real and, in some cases, lethal danger to those cases in which total exenteration has been performed.

REFERENCES

1. KOTTMEIER, H. L. (1955), *J. Obstet. and Gyn., Brit. Emp.*, **62**, 741.
2. DOBBIE, B. M. W. (1955), *J. Obstet. and Gyn., Brit. Emp.*, **62**, 765.
3. SCHLINK, H. H. (1950), *J. Obstet. and Gyn., Brit. Emp.*, **57**, 714.
4. CURRIE, D. W. (1952), *Proc. Roy. Soc. Med.*, **45**, 327.
5. GLUCKSMANN, A., and WAY, S. (1948), *J. Obst. and Gyn., Brit. Emp.*, **55**, 573.
6. HOWKINS, J. (1951), *Lancet*, April 21, p. 872.
7. CURRIE, D. W., Personal communication.

Continued from page 521—*J. A. Stallworthy, M.A., F.R.C.S., F.R.C.O.G., F.A.C.S.(Hon.)*

ultimate aim, however, should be to prevent pelvic infection from occurring by the better control of pulmonary tuberculosis and the immunization of infants exposed to infection.

BIBLIOGRAPHY

- ASPLUND, J., and RYDEN, A. B. V. (1952), *Acta. Obstet. Gynec. Scand.*, **31**, 186.
- BARNES, T. (1955), *J. Obstet. Gynaec. Brit. Emp.*, **62**, 162.
- EKENGREN, K. (1955), *Acta. Radiol. Stockh. Suppl.*, 123.
- GREENHILL, J. P. (1941), 'Year Book of Obstetrics and Gynecology,' The Year Book Publishers, Chicago.
- GREENHILL, J. P. (1942), *Ibid.*
- HALBRECHT, I. (1947), *Lancet* **ii**, 947.
- JEDBERG, H. (1950), *Acta. Obstet. Gynec. Scand.*, **31**, Suppl. 1.
- O'BRIEN, J. R., and LAWLOR, M. K. (1947), *J. Obstet. Gynaec. Brit. Emp.*, **54**, 639.
- MAGNUSSON, W. (1945), *Acta. Radiol. Stockh.*, **26**, 264.

- MORGAGNI, J. B. (1744). 'De Sedibus et Causis Morborum Epistola 38, No. 34. E. D. Radius.'
- RABAU, E. *et al.* (1943), *J. Amer. Med. Ass.*, **122**, 801.
- RABAU, E. (1952), *J. Obstet. Gynaec. Brit. Emp.*, **59**, 743.
- SCHOCKAERT, J. A., and FERIN, J. (1939), *Bull. Soc. Belg. Gynec. Obstet.*, **15**, 407.
- SHARMAN, A. (1947), *Brit. med. J.*, **ii**, 83.
- STALLWORTHY, J. A. (1952), *J. Obstet. Gynaec. Brit. Emp.*, **59**, 729.
- STALLWORTHY, J. A. (1954), *Med. World*, Vol. 80, **3**, 258.
- STALLWORTHY, J. A. (1955), in Bourne, A. (Ed.), *British Gynaec. Practice*, Heinemann, London, 530.
- SUN, K. (1948), *Amer. J. Obst. Gyn.*, **55**, 953.
- SUTHERLAND, A. M. (1943), *J. Obstet. Gynaec. Brit. Emp.*, **50**, 161.
- SUTHERLAND, A. M. (1950), *Lancet*, **ii**, 742.
- SUTHERLAND, A. M. (1954), *J. Obstet. Gynaec. Brit. Emp.*, **61**, 614.
- WILLIAMS, E. O. (1955), *Ibid.*, **62**, 823.