

TUBERCULOUS INFECTION OF THE FEMALE GENITAL TRACT

A REVIEW OF 50 CASES

J. DOMMISSE, M.B., CH.B., M.R.C.O.G., *Consultant, Department of Obstetrics and Gynaecology, University of Cape Town and Groote Schuur Hospital*

During the 5-year period 1960 - 1964 50 patients suffering from primary pelvic tuberculosis have been seen and treated in this unit. This series excludes cases of abdominal tuberculosis where involvement of the genital tract was only part of a more widespread disease process.

The purpose of this review is to stress the presenting symptoms and diagnostic methods and to compare these with other recently published series.

Awareness of the existence and presenting features of this often slowly progressive and silent disease and the advent of effective chemotherapy have resulted in a greater 'pick up' in recent years. Early diagnosis and adequate treatment considerably improves the prognosis.

PRESENTING SYMPTOMS

The incidence of the presenting symptoms is reflected in Table I. Most gynaecologists are actively aware that approximately 5% of cases of infertility are due to pelvic tuberculosis.¹ Similarly, patients presenting with unexplained oligomenorrhoea, hypomenorrhoea or amenorrhoea are usually investigated for pelvic tuberculosis. Unfortunately, many other patients with less well-known symptoms such as irregular or excessive menstruation, chronic or unexplained pelvic pain and 'pelvic infection'

are not as fully investigated. For this reason the symptoms as tabulated may not be a true reflection of their incidence. It will be noted that 50 patients presented with a total of 72 main symptoms. Also included in the table are the number of patients in whom menstrual function was apparently normal.

TABLE I. PRESENTING SYMPTOMS IN 50 PATIENTS

Symptom	
Infertility	25 { Primary 21 Secondary 4
Reduced menstruation	26 { Primary amenorrhoea 4 Secondary amenorrhoea 13 Oligo/hypomenorrhoea 9
Abnormal uterine bleeding	5 { Meno/metrorrhagia 2 Postmenopausal bleeding 3
Pain (diagnosed pelvic infection)	12
Incidental	4 { Ectopic 1 Postabortal 1 Fibromyomata 2
Regular menstruation	19

Table II compares these symptom incidences with those of some other series and reveals several marked differences.²⁻⁵

TABLE II. COMPARATIVE LIST OF PRESENTING SYMPTOMS (SOMETIMES MULTIPLE)

Symptom	Present series (50)	Sutherland (250)	Ylinen (348)	Stallworthy (186)	Francis (135)
Infertility	50%	41.6%	43.1%	60.2%	46.5%
Oligo-amenorrhoea	52%	10%	32.2%	7.0%	22.5%
Meno-metrorrhagia	10%	16.4%	11.7%	17.7%	11.5%
Pain	24%	21.6%	50.6%	16.1%	18.5%
Vaginal discharge	—	4.8%	4.0%	3.7%	—
Normal menses	38%	—	56.4%	—	—

Infertility

Approximately 4-6% of all patients complaining of infertility suffer from pelvic tuberculosis.^{4,6} This may be due to one or more of several causes.

There may be tubal obstruction owing to gross involvement particularly of the fimbrial ends of the fallopian tubes. However, Sutherland⁶ demonstrated tubal patency in 36% of his cases. Secondly, although patency may still be demonstrable, the tubal mucosa is so destroyed by the infection that there is loss of function, i.e. of motility, secretion and ciliary action. This explains the high incidence of ectopic pregnancy in both treated and untreated cases. Thirdly, there may be destruction of the endometrium preventing adequate implantation, so that abortion is common in treated and probably also untreated cases. Finally, there would appear to be some depression of ovarian function by the tuberculous toxin with possible failure of ovulation. This occurs not only in genital tuberculosis, but also in pulmonary tuberculosis where amenorrhoea is a common feature. Occasionally ovarian function is so depressed that there is a rise in the follicle-stimulating hormone level. Jeffcoate⁷ states that this may occasionally give rise to a false biological pregnancy test result.

Four patients in this series presented with *secondary infertility*, a less well-recognized symptom.

All patients who complain of infertility should have histological and bacteriological examinations of the endometrium. This should preferably be done before insufflation or hystero-salpingography since there is evidence that either of these procedures may flare up a tubal tuberculous lesion.⁴

The results of treatment with regard to fertility have been very disappointing in this series. As far as could be ascertained, no pregnancies have occurred. In many cases this was due to delay in diagnosis and, in others, to inadequate treatment—the patients having failed to complete therapy or attend for follow-up examinations.

In a review of this aspect of pelvic tuberculosis, Schaeffer, in 1964,⁸ was able to confirm only 31 successful pregnancies in the world literature. Many other reported successes failed to provide either conclusive histological or bacteriological proof of the diagnosis. To date only 2 pregnancies^{9,10} have been reported in patients with palpable adnexal masses, and it would therefore seem that the best prognosis is in those patients where treatment is early and adequate. The use of corticosteroids^{11,12} may also improve this prognosis, and Halbrecht¹² is of the opinion that it should be possible to attain a 20% success rate using corticosteroid therapy. It is important to bear in mind that the ensuing pregnancy may be ectopic (20-30%),

prone to abortion (20-30%) and only in about one-third of cases proceed successfully to term^{4,10,11} where placental insufficiency may be another factor.¹¹

It has also been suggested that pregnancy may rekindle a dormant infection.¹¹

Menstrual Disturbances

The most important feature is that in all published reviews 40-60% of patients continue to have normal regular menstrual cycles. In this series 40% of patients had no menstrual disturbance, the diagnosis being made while investigating infertility or some other complaint.

Stallworthy¹³ states that in 50% of cases menstruation is normal; in 40% it is excessive or irregular, and in only 10% is there oligomenorrhoea or amenorrhoea. In this series the comparative figures are 38% normal menstruation, 10% excessive or irregular menstruation and, in contrast, 52% of patients had a reduced menstrual flow. Francis⁴ showed a similar distribution, 33% of his patients having oligomenorrhoea or amenorrhoea and only 17% showing excessive or irregular bleeding. He suggests that this may be due to failure to culture the endometrium in cases of menorrhagia, whereas all patients with infertility or oligo-amenorrhoea have bacteriological investigations performed. This may be a factor in the present series and, if this is so, it is a serious omission. Sutherland² found that in patients under 20 years of age with excessive uterine bleeding, 4.1% had proven pelvic tuberculosis. It is also possible that depression of menstrual function is a later symptom, and certainly in some of our patients oligo- and amenorrhoea were preceded by a period of excessive menstruation.

Primary amenorrhoea is a less well-recognized symptom. Four patients presented with this symptom. Their ages were 18, 20, 22 and 42. Unfortunately, 3 of these patients received inadequate therapy and defaulted, so that it is not known whether menstrual function has been restored. The patient aged 42 was treated by hysterectomy and found to have extensive tuberculosis of the fallopian tubes, myometrium and cervix.

Postmenopausal bleeding is also a rare symptom. Francis⁴ described 4 cases and in all of these the menopause was at an early age so that these may well have been cases of secondary oligo- or amenorrhoea. The ages in this series were 52 and 51 and were, therefore, certainly true postmenopausal bleeds. These two patients were treated by hysterectomy following 3-6 months of medical treatment. No residual evidence of tuberculosis was found.

Abdominal Pain

Abdominal pain diagnosed in most cases as chronic or recurrent pelvic infection was the presenting feature in 12 patients, and in 10 of these there was a palpable tubal mass which was unilateral in all except one patient.

The presence of a unilateral tubal or tubo-ovarian inflammatory mass should arouse suspicion of pelvic tuberculosis, and histological and bacteriological analysis of the endometrium should be performed before laparotomy.

Similarly, the diagnosis of pelvic infection in a virgo intacta is suspect until tuberculosis has been excluded. Francis⁴ found that 20% of patients in whom pain was a presenting symptom had had previous appendectomies

and that in all these the appendix was found to be histologically normal.

Incidental Presenting Features

Tubal tuberculosis both active and healed is a definite predisposing factor to an ectopic pregnancy. Unless the tube is histologically studied by multiple sections, this diagnosis is liable to be missed. Only one such diagnosis was however made in this group in spite of a very high incidence of ectopic pregnancy. In 1963, for example, 114 ectopic pregnancies were treated surgically.

In one patient the diagnosis was made following an abortion at 12 weeks. Histological examination of these curettings showed evidence of recent pregnancy, caseation, and acid-fast bacilli. This method of presentation is quite well recognized and it is best to avoid the use of streptomycin as a routine antibiotic cover following abortions, since this may produce a resistant organism.

In 2 patients evidence of pelvic tuberculosis was found after hysterectomy for fibromyomata. There would not appear to be any association between these two conditions.

Age Incidence

The average age was 30 years. The oldest patient was 51 years of age and the youngest 18. This age distribution is similar to that in other published figures.

DIAGNOSTIC METHODS

There is no doubt that the most important factor in the diagnosis is a 'high index of suspicion'.

A family history or a past history of a pulmonary or other tuberculous lesion must be sought in all suspected cases. Ylinen³ found coexistent active lesions in 3.4% of patients and earlier tuberculous manifestations in no less than 64%. There would seem to be a time interval of from 5 to 10 years between the primary focus and the development of symptoms due to genital tuberculosis.

Chest X-ray should always be performed. Tuberculin testing and estimation of the erythrocyte sedimentation rate are not of much diagnostic help. The latter test is normal in the majority of cases, and a raised ESR should thus raise a suspicion of secondary infection or an active pulmonary lesion.

Pelvic examination is often normal, but the finding of unilateral or bilateral adnexal masses is significant. Tuberculous cervicitis is uncommon, occurring in less than 4% of cases. Sutherland² took biopsy specimens from the cervix in 250 patients with proven genital tuberculosis. Only 4 cases were positive.

X-ray of the abdomen occasionally shows calcified glands or foci.

Culture of vaginal discharges is seldom of use in establishing the diagnosis. Halbrecht²² has reported considerable success with cultures of menstrual blood. This has not been our experience, and several other workers have also found this to be an unreliable test.

In suspected cases it is essential to perform a careful curettage in the pre-menstrual phase. This procedure is much more reliable in excluding the diagnosis than is simple endometrial biopsy. The tissue obtained must be carefully examined for tuberculous endometritis and acid-fast bacilli; and in all cases the major portion of the curettings must be sent, in approximately 3-5 ml. of nor-

mal saline, for guinea-pig inoculation and culture. Culture should be on 2 media such as Lowenstein-Jensen and modified Kirschner culture, and sensitivity tests should be performed if possible. Histological proof *per se* is not always acceptable, although Novak and also Haines and Taylor²³ maintain that in a typical case histology is sufficient proof. Certainly, the presence of acid-fast bacilli or caseation would seem to be diagnostic, but lesser degrees of endometritis may be mimicked by various other granulomatous lesions.

Treatment should not be withheld while awaiting bacteriological confirmation of a histological diagnosis.

A positive culture can also occasionally be misleading since this may be due to bacilli other than *Mycobacterium tuberculosis*, e.g. atypical mycobacteria, *Mycobacterium fortuitum* and *Nocardia asteroides*.²⁶ Screening tests to distinguish between these have been described by Huppert *et al.*²⁶ To confirm the diagnosis finally a positive culture should be subjected to guinea-pig inoculation and sensitivity tests.

Jamieson²⁷ and Vollum,²⁸ reviewing their results in the bacteriological diagnosis of tuberculous endometritis, concluded that all 4 methods should be used in all cases, i.e. histology, guinea-pig inoculation and culture on 2 separate media.

In patients where the diagnosis has been confirmed, other tuberculous foci should be excluded by chest X-ray, intravenous pyelography and cultures of fresh and 24-hour urine specimens. About 3-4% of patients have active associated lesions.³

Hystero-salpingography and tubal insufflation are best avoided until genital tuberculosis has been excluded. Either of these procedures may cause an acute flare-up of a tuberculous infection and even result in a miliary spread.⁴ Jedberg²⁹ has described in detail the X-ray appearances which suggest genital tuberculosis, but these are not diagnostic *per se*.

The method of diagnosis in the present series is shown in Table III. It is noted that in only 17 cases was there bacteriological proof, although in another 7 acid-fast

TABLE III. DIAGNOSTIC CRITERIA IN 50 CASES

Method	Number
Endometrial histology	20
Endometrial histology revealing acid-fast bacilli	7
Endometrial histology and bacteriology	11
Endometrial bacteriology only	6
Histology of fallopian tube	6

bacilli were seen on histological examination. The reason for this discrepancy was that in many cases tissue was not submitted for bacteriological examination. In others treatment was commenced before bacteriological tests were done and in many cases there was considerable delay in the transfer of specimens for bacteriological examination. The culture should preferably be set up within a few hours of obtaining the specimen.

Attempts to obtain positive cultures by means of endometrial suction or lavage have been made.³ We attempted endometrial suction and lavage but found it unsatisfactory since only small amounts of material were obtained and there seemed to be a very definite risk of spreading the infection into the peritoneal cavity.

Laparotomy or peritoneoscopy with tubal biopsy may be necessary in some cases.

TREATMENT

The treatment of genital tuberculosis is similar to the treatment of tuberculosis elsewhere. General measures include adequate rest and diet. For some patients sanatorium regime may be necessary.

There is no doubt that this is a progressive disease and, although spontaneous resolution may occur, progression is the usual course. For this reason active chemotherapeutic management is essential.

Wherever possible sensitivity tests should be performed. In a series compiled by Sutherland²⁰ sensitivity was tested in 107 cultures of which 15 were found to be streptomycin-resistant and 12 resistant to INH. Sensitivity to PAS was not tested.

Our present regime is to treat all cases for a total period of 2 years. For the first 6 months patients receive streptomycin sulphate, 1 G daily; PAS, 12 G daily, and INH 300 mg. daily. After this the streptomycin is discontinued and PAS and INH continued for a further 18 months. Bacterial resistance to streptomycin develops rapidly, and there is therefore little to be gained from repeating this drug.

We have had very few drug reactions or side-effects. Where these occur, treatment must be modified. It is also advisable to administer vitamin B complex supplements throughout treatment.

There seems to be no value in assessing response before the therapeutic course is completed. This has no practical importance since there is no possible alteration to a more effective regime. There is also a definite risk of exacerbation following curettage. However, patients are examined regularly; the ESR is performed, and the presence or progress of pelvic masses noted.

At the completion of the 2-year course a full diagnostic curettage and repeat bacteriological culture are performed. Cure should then be complete. If the disease is still active, surgical treatment will be necessary.

THE PLACE OF SURGICAL TREATMENT

Knauss,²¹ writing in 1962, still advocated conservative surgery in all cases. He removes the diseased fallopian tubes and then continues chemotherapy. In his opinion, tuberculous endometritis almost invariably subsides after the extirpation of the diseased tubes. He states: 'the physician should not be guided by isolated successes in the treatment of sterility, but should rather follow the course shown to be most effective in combating this highly dangerous disease'.

We have, however, been impressed by the occasional successes and hesitate to remove the tubes in a young woman, destroying her slenderest hope of fertility. The results of conservative surgery, particularly salpingostomy or partial salpingectomy, have been singularly disappointing. Therefore, if surgery is undertaken this should be more extensive, removing the uterus, fallopian tubes and, in some cases, one or both ovaries.

The indications for surgical treatment have been well outlined by Stallworthy²² as follows:

1. In menopausal or peri-menopausal women without active tuberculosis elsewhere.

2. If adnexal masses appear or enlarge during drug therapy.
3. For fistulae which fail to heal.
4. When health-impairing menorrhagia is associated with tuberculous endometritis.

To these indications may be added patients with positive culture following full chemotherapeutic treatment.

In 205 cases Sutherland²⁰ resorted to surgical treatment in only 2, whereas Knauss²¹ operated on 120 of 121 patients.

There is very little chance of infection of the male partner, although such cases have been reported.²³ During the first few months of treatment, and particularly in cases with cervical tuberculosis, a condom should be used.

There is increasing evidence that the administration of corticosteroids, together with chemotherapy in early cases, if there are no adnexal masses, will increase the chances of tubal patency and hence fertility.^{3,10-12}

Prognosis

Symptomatic relief is usual if treatment is maintained. Unfortunately, too few of the patients in the present series have completed treatment or returned for complete re-assessment. This is partly because in at least half of the patients the main complaint was infertility and many lose hope before treatment is completed. As far as can be ascertained there have been no pregnancies in the above series. The results obtained by other workers have already been outlined.

SUMMARY

1. The symptomatology and diagnostic methods in 50 cases of pelvic tuberculosis are presented.
2. The recent literature is reviewed and some aspects of the diagnosis and treatment discussed.
3. Stress is laid on a high index of suspicion, the value of bacteriological confirmation, and the need for prolonged treatment.
4. The possible use of corticosteroids in early cases is mentioned.

ADDENDUM

In an effort to improve our bacteriological results we are now placing the curettings directly into a specially prepared solution which consists of 5 ml. of Kirschner, 1 ml. of horse serum and 60 units of penicillin.

I wish to thank Dr. J. G. Burger, Medical Superintendent, Groote Schuur Hospital, for permission to publish this series and Professors A. Kipps and D. Davey for helpful criticism.

REFERENCES

1. Schaeffer, G. (1953): *Obstet. Gynec. Surv.*, **8**, 461.
2. Sutherland, A. M. (1958): *Obstet. and Gynec.*, **11**, 527.
3. Ylisen, O. (1961): *Acta obstet. gynec. scand.*, **40**, suppl. 2.
4. Francis, W. J. A. (1964): *J. Obstet. Gynaec. Brit. Cwlth.*, **3**, 418.
5. Stallworthy, J. (1965): Personal communication.
6. Sutherland, A. M. (1960): *Amer. J. Obstet. Gynec.*, **79**, 486.
7. Jeffcoate, T. N. A. (1962): *Principles of Gynaecology*. London: Butterworths.
8. Schaeffer, G. (1964): *Obstet. Gynec. Surv.*, **19**, 81.
9. Johnston, J. A. L. and Liggett, S. W. (1960): *Lancet*, **1**, 24.
10. Stallworthy, J. (1963): *Fertil. and Steril.*, **14**, 284.
11. Snaith, L. M. and Barns, T. (1962): *Lancet*, **1**, 712.
12. Halbrecht, I. (1962): *Fertil. and Steril.*, **13**, 371.
13. Lewis, T. L. T. (1964): *Progress in Obstetrics and Gynaecology*. London: Churchill.
14. Fisher, K. H. (1962): *Brit. Med. J.*, **2**, 711.
15. Haines, M. and Taylor, C. (1962): *Gynaecological Pathology*. London: Churchill.
16. Huppert, M., Wayne, L. G. and Jaurez, W. J. (1957): *Amer. Rev. Tuberc.*, **76**, 468.
17. Jamieson, D. G. (1963): *Tubercle (Edinb.)*, **44**, 491.
18. Vollum, R. L. (1954): *J. Clin. Path.*, **7**, 226.
19. Jedberg, H. (1950): *Acta obstet. gynec. scand.*, **31**, suppl. 1.
20. Sutherland, A. M. (1958): *J. Obstet. Gynaec. Brit. Cwlth.*, **65**, 450.
21. Knauss, H. H. (1962): *Amer. J. Obstet. Gynec.*, **83**, 73.
22. Stallworthy, J. (1952): *J. Obstet. Gynaec. Brit. Cwlth.*, **59**, 609.
23. *Idem* (1952): *Ibid.*, **59**, 721.