

Genital Tuberculosis

by

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Genital tuberculosis is by far a symptomless disease and unless one is aware of the non-symptomatic gynaecological problems and vague gynaecological symptoms that the patients with the disease may present with, and investigate for the possibility of Koch's infection of the genital tract, the diagnosis may often be missed. Most of these patients lead a normal life for many years before their general health or menstrual functions are grossly affected for them to seek medical advice. However, in countries where medical facilities are more advanced and more readily available, the diagnosis of genital tuberculosis is being made more often. This is so in spite of the overall reduction in the incidence and mortality of pulmonary and other forms of generalised tuberculosis. This is largely due to the increasing awareness among the medical practitioners of the silent nature of the disease and to the more thorough methods of investigations that are carried out. A striking illustration of this point is the difference in discovery of tuberculous endometritis by Sutherland and Gary (1951) during the ten years, 1930-1939 and from 1940-1949. The first decade yielded 37 cases (0.12 percent of total admissions) but during the second decade there were 141 cases representing 0.30 percent of total admissions.

Although, the incidence of pulmonary tuberculosis, which by far forms the largest percentage of tuberculosis in any part of the world, is still very high in Singapore and Malaysia, as opposed to many western countries, the diagnosis of genital

tuberculosis is made very infrequently and often by chance. This is largely due to failure in recognising the variable modes of presentations of the disease and due to inadequate investigation even when the possibility of the disease is realised.

The purpose of this talk is not to discuss the subject in a textbook manner nor is it the results of a prospective study of the problem as encountered in this country. It is hoped that at the end of the talk, the speakers would have conveyed to the audience the message that "genital tuberculosis is a silent disease and may present itself in variable forms and for adequate diagnosis and treatment, routine investigations including histology, culture and guinea pig inoculation of endometrial curetting and/or menstrual flow must be carried out in all patients presenting with the disease". It is therefore logical that the emphasis of today's talk is going to be on the various symptom that the patient with genital tuberculosis may present with and the investigations that should be performed on these patients. However, it will be incomplete not to discuss on the treatment because the outlook has been completely revolutionalised during the past two decades.

Common Symptoms:

The symptoms that commonly bring these patients to hospital are listed in Table I. Infertility being the commonest while menstrual disturbances, pelvic pain, postmenopausal bleeding and congestive type of dysmenorrhoea being the others.

Table I

Symptoms of Genital Tuberculosis				
Complaint	Fedberg's 225 cases (1950)	Sutherland's 205 cases (1958)	Ylinen's 348 cases (1961)	Winifred J. A. Frances 135 cases (1964)
Infertility	35.5%	55%	43.1%	69 %
Abdominal or pelvic pain	51.1%	13%	50.6%	17 %
Heavy or irregular bleeding	21.0%	19%	20.4%	33.3%
Amenorrhoea and Oligomenorrhoea	0.5%	6%		
Other symptoms	12.9%	7%		

1. Infertility

In 1940 Schockaert and Ferin reported finding tuberculous endometritis in 5 percent of women complaining of primary infertility. Sharman (1943) found tuberculous endometritis in 5 percent of women complaining of primary infertility and in 1961 gave an incidence of 5.7 percent in patients with primary infertility being due to genital tuberculosis. The study included 4,817 cases. Similar findings were made by Haines (1952), Halbrecht (1947). Other workers namely Jedberg (1950) and O'Brien and Lawlor (1947) reported much lower incidence of 2.1 and 1.9 percent respectively. It is generally reckoned that 4 to 6 percent of infertile marriages in the United Kingdom are explained by genital tuberculosis. The incidence will vary with the prevalence of the generalised form of the disease in any community and as such the incidence should be higher in Singapore. However, in 43 successive patients attending the infertility clinic at the University Unit of this hospital routine endometrial biopsies has so far failed to reveal a single case of tuberculous endometritis. The number is grossly inadequate for conclusions to be formed nor is it significant for comparative purposes. Furthermore in none of these cases was guinea pig inoculation carried out due to want of animals.

Table II

Incidence of Genital Tuberculosis		
In Infertile patients	No. of Patients	Per cent with genital tuberculosis
Jedberg (1950)	1,168	2.1
O'Brien & Lawlor (1947)	898	1.9
Halbrecht (1946)	820	5.5
Sharman (1961)	4,817	5.7
Haines (1952)	200	4.0

Until Rabou in 1952 reported a pregnancy (which ended in abortion) following treatment, tuberculous endometritis was stated as a cause of absolute infertility. However, since Rabou's report, a number of successful pregnancies have been reported. Snaith and Barnes (1962) reviewed the whole question of fertility in genital tuberculosis. There were few reported cases of pregnancy in untreated tuberculosis and most of them were ectopic pregnancies. Sial chemotherapy has been available there have been at least 77 cases of successful pregnancies ending in a living child. The crude conception rate for

all cases treated with chemotherapy was 6 percent, if those not exposed to the risk of pregnancy are excluded the figure becomes 12 percent. Unfortunately only one-third of conceptions end in viable pregnancy; one-third are ectopics and one-third end in abortion. The Oxford group, Stallworthy et al reported a conception rate of 18 percent, and an ectopic rate of 33 percent.

The low conception rate even in patients treated with Chemotherapy is not easily explained. Sharman (1952) reported tubal occlusion in 91 (66.9 percent) of 136 patients with endometrial tuberculosis while Frances (1964) reported patency in 55%. Investigations for ovulation such as premenstrual biopsies and basal temperature records will confirm that ovulation occurs in many of these patients. In spite of patent tubes and evidence of ovulation, conception often fails to occur.

2. Menstrual Disturbances:

Menstruation may be normal, it may be suppressed or there may be menorrhagia, irregular bleeding or post-menopausal bleeding. It is generally agreed that menstrual upsets occur in approximately one-half of the women who suffer from genital tuberculosis (Stallworthy 1963a; Frances 1964). Most writers (Jedberg 1950, Sutherland 1956, Stallworthy 1952 and 1963a) stress that amenorrhoea and oligomenorrhoea are relatively uncommon and often associated with advanced endometrial disease where as Frances 1964 reported a higher incidence from the Department of Obstetrics and Gynaecology in Liverpool. They had 45 patients in a series of 135 who presented with either amenorrhoea or scanty menstrual flow. The overall analysis give a far incidence of menorrhagia and irregular bleeding as opposed to amenorrhoea or oligomenorrhoea. Post-menopausal bleeding is a relatively uncommon symptom. In 78 cases reported by Stallworthy in 1952, there was only one case with post-menopausal bleeding.

3. Pain:

Pain is usually not a leading symptom but is present in about 50 percent of cases. The patient may present with constant lower abdominal pain or recurrent attacks of pain or discomfort. Although dysmenorrhoea is often said not to be a feature of pelvic tuberculosis, it is not uncommon for these patients to have congestive dysmenorrhoea (Stallworthy 1963). The pain is often situated in the iliac fossa and may be referred to the sacrum. It is made worse by exercise and intercourse and is usually maximum in the premenstrual phase of the cycle. Super-

imposed pyogenic infection is not uncommon and give rise to acute or sub-acute exacerbation of symptoms. Especially if the pain and tenderness is unilateral, in a young girl with no history suggestive of pyogenic or gonococcal infection, the possibility of tuberculous infection must be seriously considered. The correct diagnosis becomes even more important in the presence of a tubo-ovarian mass or when surgery is being contemplated for, failure to recognise a tuberculous lesion may result in chronic fistulae. Pain localized to the right iliac fossa has led to the wrong diagnosis of appendicitis (Snaith 1958; Aburel et al 1961, Stallworthy 1963; Frances 1964).

The other less common forms of presentations include symptoms of peritonitis and various forms of fistulae. Pelvic peritonitis when associated with encysted ascitis may be mistaken for an ovarian cyst. Careful palpation for the adnexa will reveal some degree of thickening and fixicity. Fistulae of all forms have been reported especially in the pre-chemotherapeutic days. These often follow inadequate surgery but may occur spontaneously.

Diagnosis of Genital Tuberculosis:

The diagnosis of pelvic tuberculosis will be made with increasing frequency if the practitioners become conscious of the common forms of its presentation and fully investigate all patients suspected of suffering from the disease. The logical steps in the diagnosis would therefore be to identify the cases that need investigation and subsequently to investigate them adequately.

Clinical Features suggesting the Diagnosis of Genital Tuberculosis:

1. The disease should be suspected in **infertile patients** especially when they present with symptoms of pelvic inflammatory disease. It is uncommon to find the disease in women who have had children although a number of cases appear to begin soon after a delivery (Sutherland 1952a, Ylinen 1961; Knaus 1962). The endometrium should be routinely investigated in all cases in whom no definite cause can be attributed for the infertility. The endometrium should be collected in the pre-menstrual phase of the cycle. Half the specimen must be fixed in formalin and sent for histology and the other half sent for culture and guinea pig inoculation.
2. Routine investigation of endometrial in all patients **with amenorrhoea** and in women **with irregular vaginal bleeding** with no cause will help in the detection of a number of

cases. Although irregular vaginal bleeding is a common gynaecological disorder, unless a search is made for genital tuberculosis the diagnosis may never be made.

3. Pelvic Pain:

Pelvic pain, especially in a young nulliparous girl or in an unmarried girl with no history suggestive of an ascending infection should warrant investigation for genital tuberculosis. Evidence of tubal disease in the above group of patients is again very suggestive of genital tuberculosis. This is especially so if the lesion is unilateral and if the E.S.R. is normal. Stallworthy (1958) emphasises that a raised E.S.R. is very suggestive of pyogenic or gonococcal infection where as normal E.S.R. is in favour of tuberculosis infection.

Investigations in Suspected Cases:-

Chest X'ray:

Genital tuberculosis is almost always secondary to a primary lesion elsewhere in the body and the commonest mode of infection being by the blood stream. Since the lung is the commonest site for the primary lesion, the patient should be examined radiologically for evidence of a pulmonary tuberculosis.

E.S.R.:

The erythrocyte sedimentation rate is a useful aid in the diagnosis of genital tuberculosis. If in the presence of signs of pelvic inflammatory disease, the E.S.R. is raised the infection is more likely to be of pyogenic or gonococcal in origin whereas if the E.S.R. is normal the diagnosis is more in favour of genital tuberculosis.

Endometrial curetting:

Table III

Special Investigation	
Blood —	(1) Hb.% TWC and DC (2) E.S.R.
Tuberculin Test	
Chest X-ray	
Endometrial Curetting —	
	(i) Histology
	(ii) Culture: (a) Lœwenstein Jensen Medium (b) Kirschner's Medium
	(iii) Guinea-pig inoculation

Endometrial biopsies:

Endometrial biopsies should be taken in all married women suspected of genital tuberculosis. Because fresh tubercles are formed during the growth of the endometrium at each cycle, the curettings should be removed in the week preceding the onset of the next menstruation. The lesions are often scattered and few and careful search has often to be made to find the lesions. Because of this Haines (1952) recommends curetting rather than biopsy so as to obtain sufficient material for the pathologist. Often repeated curettings are needed and this is not without its own danger. As a preliminary procedure endometrial biopsy may be more suitable and curetting be reserved for cases where the diagnosis is not made on the biopsy. (Bourne and Williams, 1962).

Perfunctory histology of the endometrium alone is insufficient. It is well accepted fact that the diagnosis of tuberculosis from endometrial curetting is not reliable. The exact percentage of endometrial tuberculosis associated with tuberculous salpingitis is not definitely known but is believed to be about 50 percent. Even when the endometrium is involved, Vollum 1954 showed histology found 51 percent positive, culture 50 percent positive and guinea pig 58 percent positive. 95 cases of Vollum's 164 specimens were negative when investigated by all three methods. Repeated examinations of the endometrium may be needed, before a positive diagnosis is made.

In unmarried girls and as a follow-up measure, the 1st and 2nd day menstrual flow may be cultured for tubercles. Halbrecht found a positive culture in about one-third established genital tuberculosis.

Thus in the investigation of endometrial curetting for genital tuberculosis all three methods, histology, culture and guinea pig inoculation should be employed in all cases. It is advisable to employ two culture media in each case, the Loewenstein-Jensen medium and the Krischner medium.

4. Hysterosalpingography:

In 1945 Magnusson described the radiological appearance of genital tuberculosis as seen in a hysterosalpingogram. Since then various contradictory reports have appeared on the reliability of the findings. The overall opinion is that the results are unreliable and often misleading and in fact the procedure is dangerous.

5. Culdoscopy and Laparoscopy:

These aids to diagnosis have been used extensively in France and certain American clinics but have not found favour in the Commonwealth countries. Schaefer (1956) found that the diagnosis was often inaccurate and that the procedure was not free from danger.

Treatment of Genital Tuberculosis

Since majority of patients with genital tuberculosis lead an apparently healthy life being quite unaware of their silent infection, were it not for the biopsy findings, one has to seriously consider whether treatment should be instituted in this group of patients. The experience with silent lesions in the lungs and the results of the clinical research conducted over the past twelve years by the Joint Sub-Committee of the R.C.O.G. and the Research Council of the B.T.A. have produced sufficient evidence to actively treat all cases. The following evidence gives adequate support for treating these patients actively.

1. The clinical and radiological evidence show that cases of early and symptomless disease respond well to conservative treatment with chemotherapy.
2. The increasing results of successful pregnancies in treated cases as opposed to the prechemotherapeutic days.
3. The condition may remain active but silent for many years with clinical evidence of extension. These cases have been followed up in the Oxford Department for more than ten years and in their series of 34 patients, 8 patients got worse and one of them succumbed to the disease.
4. At anytime and for no apparent reason, the disease may extend either locally or generally.

It appears from the above facts, that while a woman might lead a normal and apparently healthy life in spite of active infection, nonetheless while it remains active it constitutes a threat to her life or health.

Table IV

Treatment
Methods of treatment include:
1. Sanatorium treatment
2. Chemotherapy
3. Surgery — (a) conservative (b) radical

The advent of chemotherapy has completely revolutionised the treatment of Genital Tuberculosis. The main forms of treatment in the pre-chemotherapeutic days were adequate measures to assure both physical and mental rest through sanatorium treatment and surgery as a radical or curative measure in localised forms of the disease. Although sanatorium treatment may still have a place in the advanced and generalised forms of the disease, it is largely unnecessary in the majority of patients who are apparently healthy and symptomless chemotherapy may be effectively given in ambulant patients with equally good results. The place of surgery in genital tuberculosis has been largely modified with the advent of chemotherapy. While limited surgery was condemned because of the associated high morbidity and mortality in the pre-chemotherapeutic days, many surgeons will resort to local excision of diseased tubes following antibiotic treatment especially, if the endometrium showed no evidence of the disease.

Chemotherapy has also largely replaced surgery in the treatment of genital tuberculosis. Operative treatment is reserved for those patients who fail to respond to anti-tuberculous drug therapy. Following the combined research con-

ducted by R.C.O.G. and Research Council of the B.T.A., it has generally been agreed that the disease should be treated for long periods for at least two years. The recommended regime being three months of 1 gm.% daily streptomycin in combination with 300 mgs. of Isoniazid followed with a combination of isoniazid and P.A.S., 12 to 20 gm. daily in divided doses. Ideally the organism should be tested for drug sensitivity and the appropriate chemotherapeutic agent given.

The place of surgery in genital tuberculosis may be summarised as shown in Table V. Surgery should be radical unless the patient is young and the endometrium shows no evidence of disease.

Table V

Indications for Operation

1. When the local pelvic lesion fails to heal
2. When fistulae fail to heal
3. Fails to respond satisfactorily
4. Postmenopausal tuberculous endometritis
5. When adnexal masses persist after drug treatment

SUMMARY:

1. The silent nature of genital tuberculosis must be realized and patients presenting with symptoms suggestive of the disease should be fully investigated with repeated endometrial biopsies/curetting for histology, culture and guinea pig inoculations.
2. The common symptoms that should lead to the suspicion of genital tuberculosis are infertility, being the commonest, altered menstrual functions, irregular and heavy or excessive bleeding being more common than scanty bleeding and amenorrhoea. All patients with these symptoms should routinely be investigated for genital tuberculosis. Pelvic pain, especially in a young nullipara or an unmarried woman with no cause for ascending infection should also be investigated for genital tuberculosis.
3. All cases suspected of the disease should have a chest X'ray, E.S.R. and endometrial biopsy/curetting sent for histology, culture and guinea pig inoculation. Repeated curettings may be needed before a positive diagnosis is made.
4. Treatment of genital tuberculosis is primarily chemotherapeutic with surgery as a secondary measure in cases that fail to respond satisfactorily to treatment.
5. The incidence of the genital form of the disease appears to be very low in this country although the generalised and pulmonary forms of the disease are very common. Are we failing to diagnose the disease or are the local population immune to the localised form of the disease due to immunity from exposure since childhood? The chances are that diagnosis is being missed. However, it will be interesting to do a prospective analysis into all women with infertility and into women suffering from active pulmonary lesion to see the incidence of the genital form of the disease.

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