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THE HAZARDS OF PREGNANCY IN WOMEN WITH HEART DISEASE*

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It is a terrible disappointment to a young woman to be told that, because she has a bad heart, it would be unwise for her ever to have children. Fortunately, in the great majority of cases, heart disease is no contraindication to pregnancy. The risk has in the past been grossly exaggerated, because writers on the subject have based their opinions on general impressions, which are notoriously fallacious.

In my clinic at the Manchester Royal Infirmary, during the last twenty-five years, my colleagues and I have followed through pregnancy, labour, and the puerperium more than 1,600 patients with organic heart disease. Many of these patients have been followed through more than one pregnancy, and others have been kept under observation for a year or more after delivery. Two samples from this group have been carefully analysed. In 1938 Edith Longson and I reported our findings in the first 350 cases (Bramwell and Longson, 1938), and an analysis of 500 of the more recent cases, studied by my colleagues Morgan Jones (1952) and Samuel Oleesky, has now been completed. It is interesting to compare these two series of cases and to see how our views regarding the management of this condition have changed during this period.

Assessment of the Risk

In attempting to assess the probable risk of pregnancy in patients with heart disease, it is convenient to classify cases in three groups:

I. In the first group are those patients in whom the heart disease is so trivial that it does not add appreciably to the risk of childbirth. Provided they are kept under medical supervision, these patients rarely cause any anxiety.

II. The second is the largest group. It consists of patients in whom the heart disease is such that it does add appreciably to the risk, but the risk is not regarded as prohibitive. The more severe cases in this group call for much discrimination and judgment on the part of the physician. Many factors other than the severity of the heart disease, such as the age of the patient, the facilities for antenatal and post-natal care, and the number of children in the family, must be taken into account in arriving at an assessment.

III. The third and smallest group consists of those patients in whom the risk is obviously so great that it

would be unwise to sanction pregnancy, or if pregnancy is already established termination should be advised. Unfortunately some patients in this group are not seen until pregnancy is far advanced, and the risk of termination may then be greater than the risk of allowing pregnancy to continue. When termination of pregnancy is refused on religious grounds the decision is clearly no longer in the hands of the physician.

In assigning patients to their respective groups we have relied, in the first instance, on an estimate of the functional efficiency of the heart, based on the patient's exercise tolerance prior to pregnancy. I emphasize the words "prior to pregnancy," for as pregnancy proceeds the tolerance for exercise diminishes, and if a patient is not seen till late in pregnancy a false impression may be formed of her cardiac disability.

Roughly speaking, Group I consists of patients who have been able to undertake their household duties and other normal activities without breathlessness or other symptoms, while Group III consists of those who had experienced one or more episodes of congestive heart failure prior to pregnancy and also those in whom the rheumatic process appeared to be still active, or the cardiac condition showed evidence of rapidly progressive deterioration. Patients whose mobility had been limited to a greater or lesser extent, but who had not actually been in failure and whose heart disease appeared to be quiescent, are placed in Group II.

We must, however, consider not only the risk to the mother but also the prospect of a successful pregnancy which makes that risk worth taking. In our later series, four out of five pregnancies yielded living children, but of 53 patients with severe heart disease, who either refused termination or were first seen too late to terminate pregnancy, only one in four had a living child.

The Hazards of Pregnancy

(1) Congestive Heart Failure

Clearly the most important consideration in these patients is the risk of death from heart failure. There were 15 deaths from this cause in our earlier series, and these cases may be divided into two groups.

Four were women aged 39 or over (Table I), three of whom were in their seventh or later pregnancy, and three had established auricular fibrillation. In these four cases the patients' expectation of life was already very limited owing to the advanced state of the disease. Any additional strain, whether physical or due to intercurrent infection,

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TABLE I.—Deaths from Heart Failure

Age	Parity	Time after Confinement	Remarks
40	7	5 months	
43	7	3 "	A.F. A.C.
39	14	2 "	A.F. A.C.
39	5	3 weeks	A.F. A.C.

A.F.—Auricular fibrillation. A.C.—Attended antenatal clinic.

might have proved fatal. In their case the strain happened to be pregnancy. They were, in fact, all cases in which we should regard pregnancy as contraindicated, and would have advised termination had they been seen earlier in pregnancy.

The other 11 cases (Table II) were of quite a different type. They were younger women, seven of them primigravidae, their heart disease was less advanced, and all but

TABLE II.—Deaths from Heart Failure

Age	Parity	Time After Confinement	Remarks
29	1	Undelivered	
25	1	Same day	
27	3	1 day	
32	2	3 days	A.F.
30	1	3 "	A.F. A.C.
24	1	3 "	
27	2	6 "	
33	1	4 weeks	
36	2	5 "	
25	1	6 "	
24	1	9 "	

two had normal rhythm. There was another common factor in this group—only one of these patients had attended the antenatal clinic, the other 10 had been admitted to hospital in the later months of pregnancy as "urgencies" on account of heart failure. This we regard as most significant, for it is our experience that, in women who are pregnant, congestive heart failure, if recognized early, responds well to treatment, and it is only when the condition is allowed to run on unchecked that it becomes irreversible. Adequate antenatal supervision is, we believe, the most important single measure in limiting the risk to which these patients are subject.

Intercurrent complications, especially bronchial infection and anaemia, are apt to precipitate heart failure in patients with rheumatic heart disease. Bronchitis, influenza, and even the common cold must be treated with great respect in these patients. In foggy weather they should be confined to the house, crowds and places of public entertainment should be avoided, and in the event of infection they should be put to bed and kept there until they are fully convalescent. In our experience anaemia is often overlooked. This is particularly unfortunate, since adequate treatment of the anaemia will usually relieve the heart failure.

The common sequence of events in the later stages of mitral stenosis is the development of auricular fibrillation followed by congestive heart failure. The onset of heart failure is usually insidious, with gradually increasing oedema of the dependent parts of the body, enlargement of the liver, and engorgement in the veins of the neck. These signs are easily recognized. A few weeks' treatment in hospital will generally suffice to restore the normal balance, and the cardiac function may be satisfactorily controlled throughout the remainder of pregnancy, provided the patient is kept under supervision. If this were the only danger we had to face, assessment of the risk would be easy, but occasionally things take quite a different course.

(2) Acute Pulmonary Oedema

When congestion affects the pulmonary instead of the systemic circuit, heart failure manifests itself by paroxysmal dyspnoea (cardiac asthma) and acute pulmonary oedema. The suddenness with which these symptoms may develop contrasts strikingly with the more insidious onset of congestive heart failure in the systemic circuit. They constitute a grave emergency, which may prove rapidly fatal. In our

later series, 7 of the 11 deaths from heart failure which occurred during pregnancy or within eight months thereafter were due to this cause, a very heavy mortality considering that only 16 patients in the whole series developed acute pulmonary oedema.

Acute pulmonary oedema used to be regarded as a rare complication of mitral stenosis, and its greater frequency in association with pregnancy was attributed to the increased blood volume and the increased retention of salt and water in the body. The successful surgical treatment of mitral stenosis, however, has led to a more intensive study of this valvular lesion and has shown that acute pulmonary oedema is not nearly such a rare complication as we used to believe. It is, in fact, one of the most urgent indications for mitral valvotomy.

In the earlier years of investigation we did not fully appreciate the importance of acute pulmonary oedema, and regarded it merely as a type of heart failure. In 1941, however, our attention was urgently directed to the matter by two cases under my care, both of which proved fatal. The post-mortem findings in these two patients (reported by Bramwell and Jones, 1944) were illuminating. During life both had normal rhythm with a very loud crescendo presystolic murmur, and at necropsy were found to have a buttonhole mitral stenosis with great hypertrophy of the wall of the left auricle. This combination suggested that the rheumatic process had hit the valve hard, but spared the muscle. In spite of the extreme degree of stenosis the hypertrophied auricle had for many years been able to maintain ventricular filling, when suddenly, under the strain of pregnancy, it failed, the lungs were flushed with blood, and pulmonary oedema developed, rapidly proving fatal.

It is in cases such as these, with normal rhythm and a loud presystolic murmur, that pulmonary oedema is most likely to develop. Whereas in children the murmur of mitral stenosis is generally heard in mid-diastole, in older patients the most striking feature is the crescendo murmur in presystole. This difference can be accounted for by the fact that in young subjects the blood flow from auricle to ventricle is most rapid when the mitral valve first opens, whereas in older people the auricle, having had time to hypertrophy, expels its contents much more forcibly, and consequently the rate of blood flow through the mitral orifice attains its maximum during auricular systole. In patients with a loud crescendo presystolic murmur during life, an extreme degree of narrowing of the mitral orifice is often found at necropsy. The high degree of mitral obstruction having called forth a compensatory work-hypertrophy in the auricle, which manifests itself clinically by a loud crescendo presystolic murmur. Such hypertrophy occurs only when the heart muscle is healthy; a damaged auricle, when subjected to strain, fibrillates.

The grave nature of acute pulmonary oedema makes it vitally important to be on the look-out for any signs which give warning that it may develop, for if these are manifest during the early months of pregnancy therapeutic abortion is indicated. Unfortunately, acute pulmonary oedema usually first makes its appearance in mid-pregnancy, by which time emptying the uterus has become a much more serious matter on account of the dangers of embolism, shock, and haemorrhage. An isolated attack of acute pulmonary oedema should always be regarded as a warning that further trouble of a similar nature must be expected in the future. Although systemic and pulmonary congestion often occur together, pulmonary congestion may lead to fatal acute pulmonary oedema before any systemic oedema or other signs of right heart failure are evident, and it is then that it is most likely to take us by surprise.

The importance of the early recognition of pulmonary congestion cannot be over-emphasized. Its clinical manifestations are paroxysmal dyspnoea and repeated haemoptysis; later, persistent moist rales appear at the lung bases. A rapid increase in weight during mid-pregnancy should lead one to suspect excessive water retention in the body. There is a progressive diminution in vital capacity, but the most

convincing evidence is derived from radioscopic examination of the chest, which yields direct visual proof of the congested state of the lungs. In any clinic devoted to heart disease in pregnancy, facilities for x-ray screening are an absolute essential. The electrocardiogram, on the other hand, gives us little help in these cases.

Before the introduction of mitral valvotomy we used to advise termination of pregnancy in all such cases, but within the last few months Baker, Brock, Campbell, and Wood (1952), in London, and Logan and Turner (1952), in Edinburgh, have reported cases in which valvotomy has been successfully performed during pregnancy, and the pregnancy allowed to proceed to a normal termination. In patients with pulmonary congestion, valvotomy should be undertaken before they become pregnant.

Brock also suggests, on theoretical grounds, that patients with coarctation of the aorta who are pregnant should be submitted to operation. With this suggestion I cannot agree. This is a very serious operation which carries a high mortality, and the only risk these patients run is rupture of the aorta at the time of delivery, a risk which can be avoided by caesarean section.

(3) Auricular Fibrillation

This is a common precursor of heart failure. It is a milestone well down the road of rheumatic heart disease and a warning that heart failure is not far ahead. As such, it merits especially careful consideration in assessing the risk of pregnancy.

In the early days of this investigation we were unduly afraid of this complication, having been impressed by the high mortality reported by some earlier workers (Table III).

TABLE III.—*Auricular Fibrillation*

	Cases	Deaths
Carr and Hamilton (1933) ..	14	6
Robinson (1927)	18	13
Hunt (1926)	22	8

Further experience, however, has led us to believe that under favourable circumstances it is not incompatible with successful pregnancy.

In our earlier series of cases, 24 patients developed auricular fibrillation either before or within six months of delivery. Of these, seven died. This is a heavy mortality, but careful scrutiny (Table IV) of our fatal cases suggests that the picture is not quite so gloomy as it appears at first sight.

TABLE IV.—*Fibrillators who Died*

Fibrillation Developed	Parity	Age	Remarks
Before pregnancy	14	39	Cerebral embolism. C.S.
	1	35	
	1	30	
	2	32	
During pregnancy	1	26	"Urgency" Induced 36 weeks. "Urgency"
	7	43	
After delivery ..	5	39	

C.S.—Caesarean section.

In three cases pregnancy was clearly contraindicated, and termination would have been advised had they come under observation earlier in pregnancy. Two were women who developed fibrillation after delivery in their fifth and seventh pregnancies respectively. They were aged 39 and 43. In both of these patients the strain of labour undoubtedly precipitated a final breakdown in a heart which was nearing the end of its tether in the normal course of the disease. The third was a woman of 39 in her fourteenth pregnancy who had fibrillation when first seen. Of the remaining four fatal cases in this group, two died of intercurrent post-operative complications and one other had not received adequate antenatal care. Thus it is conceivable that under the most favourable circumstances we might have lost only one of these seven patients.

These considerations led us to modify our previous opinion and to believe that, although auricular fibrillation does undoubtedly add to the risk of pregnancy, it does not constitute a bar to pregnancy, provided the patient can be kept under observation and receive adequate treatment. In our later series 19 patients had auricular fibrillation, and only two died.

(4) Other Considerations

In patients in Group II, who have never actually been in failure but whose tolerance for exercise is limited to a greater or lesser extent, the strain on the heart adds in varying degree to the risk of pregnancy. Those in whom there is considerable limitation of activity are the most difficult to assess, and various factors other than the severity of the heart disease must be taken into account in framing the prognosis.

Clearly a previous trouble-free pregnancy affords the surest ground for optimism, provided the patient's cardiac condition has not deteriorated since her last confinement. The first pregnancy eliminates most of those likely to succumb. Women under 35 are better risks than those over that age. Consequently the risk is smallest in young women who have already had one or more children.

Some workers have attached more weight than others to the size of the heart in assessing the risk of pregnancy. Our own experience leads us to believe that it is much less important than the functional efficiency of the heart as estimated by the exercise tolerance, and in this connexion it is especially significant that many patients who develop acute pulmonary oedema have but little cardiac enlargement.

When we embarked on this investigation we expected to find that patients whose only valvular lesion was mitral stenosis would do better than those who had both a mitral and an aortic lesion. This forecast has not proved to be correct. Whereas, in our earlier series, amongst 260 patients with uncomplicated mitral stenosis there were 20 deaths (8%), there was only one death (3%) amongst the 31 patients with both mitral stenosis and a lesion of the aortic valve. Our experience is similar to that of most other workers in this country.

Aetiology

Let me refer very briefly to the question of aetiology. About 90% of cases of heart disease in pregnant women are rheumatic, and most of the remaining 10% congenital.

In rheumatic heart disease the orthodox teaching was that the more attacks of rheumatic fever or chorea from which a patient had suffered, the more severe was the heart lesion likely to be. This seemed a reasonable assumption, since each attack was likely to add to the previous damage. It therefore came as somewhat of a surprise to us to find that the mortality was highest in those cases in which there was no history of rheumatic infection, and in which heart disease, previously unsuspected, had been discovered either at a routine medical examination or when the doctor had been called in to attend the patient for some minor ailment.

Out of 293 cases of mitral stenosis, admittedly a rheumatic lesion (Table V), 173 gave a history of rheumatic fever or chorea, and, of these, nine died before or within six months

TABLE V.—*Mortality in Patients with Mitral Stenosis*

History	No. of Cases	No. of Deaths
Rheumatic fever or chorea ..	173	9 (5%)
No previous illness ..	32	9 (28%)

of confinement. Of the remaining 120, 88 dated their symptoms from an attack of muscular rheumatism, tonsillitis, or some other acute infection, while in 32 there was no history of any antecedent disease, their first manifestation of ill-health having been cardiac. Of these 32, 9 died before or within six months of confinement. Thus the mortality in patients with a rheumatic history was 5%,

whereas the percentage of those with no previous history of illness was 28%. I think the explanation of this is that children with acute articular rheumatism or chorea are put to bed and kept there to prevent cardiac damage, whereas in those whose joint and nervous manifestations are minimal the true nature of the illness is apt to be overlooked, and consequently no such precautions are taken.

There were 19 cases of congenital heart disease in our earlier series, and in 13 of these the lesion was of a relatively trivial nature. The only patient who died was a 3-para of 27 with cyanotic heart disease and great cardiac enlargement, first seen at the eighth month of pregnancy.

Subacute bacterial endocarditis is an important complication of pregnancy. In 1946-7 my department participated in the investigation, planned by the Medical Research Council, on the treatment of this condition with penicillin (Bramwell, 1948). Of the first 33 cases in our series 22 were women, 7 of whom were pregnant. Of these seven, two were moribund when first seen, the true nature of the condition having escaped recognition, and the infection having been present for many weeks before treatment was started. Both these patients died, but their babies survived. The other five patients came under our care much earlier in the course of the disease and all survived, the infection having been satisfactorily controlled. In these seven cases we lost only one child—a macerated foetus.

Unexplained fever in any patient with valvular or congenital heart disease who is pregnant calls for immediate blood culture, since the duration of infection is one of the most important considerations in prognosis in subacute bacterial endocarditis.

Remote Prognosis

Now what about the ultimate prognosis in these patients? Most earlier workers believed that pregnancy always produced a permanent aggravation of the cardiac disability. We now know that is not true. As patients grow older the disability resulting from rheumatic heart disease tends to increase, and if deterioration is observed it is often difficult to say whether this is attributable to pregnancy or merely to the normal course of the disease.

Gilchrist and Murray-Lyon (1933) made some interesting observations on this point. They studied the age at death in 109 cases of mitral stenosis that came to necropsy, in all of which death was directly attributable to heart disease. Forty of these cases were males and 69 were females—28 nulliparous and 41 parous. The average age at death was 39.3, 42.1, and 42.0 respectively. I think we can hardly blame pregnancy for the earlier death in the male group, though Mr. Punch, in one of his most famous cartoons, did suggest that childbirth was a great strain on the father! In the case of the females there is no appreciable difference between the parous and nulliparous women as regards the average age of death, but one must take into consideration the fact that only the fitter women marry, and, of those who do marry, the fitter are more likely to have children.

In these three groups there was little difference in the number of survivors at different ages, and had pregnancy exerted a detrimental influence one would have expected a higher mortality amongst the parous women during the child-bearing period.

Our own observations have convinced us that, in young patients at any rate, pregnancy is rarely detrimental. Morgan Jones followed up his cases after delivery until the cardiac condition had either shown deterioration or been stabilized at its previous level. Twenty-five patients died, and it was found that, of the 475 who survived, 427 (90%) showed no obvious deterioration as the result of pregnancy.

Treatment

If I were asked what I regarded as the most important consideration in the treatment of patients with heart disease who were pregnant, I should have no hesitation in saying that it is never, under any circumstances, to interfere with

pregnancy in a patient with heart failure until all has been done that can be done—and that is often a great deal—to relieve the heart failure. When a woman is admitted to hospital as an “urgency,” desperately ill with a failing heart, it is tempting to think that, to save life, the termination of pregnancy is indicated. It is not. In these circumstances surgical intervention is an unjustifiable risk. It is surprising how well many of these patients respond to treatment. A few days’ rest in bed, with skilled nursing, digitalis, and sedatives, will often convert what was a hopeless case into a reasonable surgical risk. When the heart condition has been stabilized, and not before, is the time to consider whether pregnancy should be terminated.

In such cases, when the heart failure had been relieved, we used to recommend caesarean section; but further experience has convinced us that normal delivery carries less risk, and, with the single exception of coarctation of the aorta, in which condition there is danger of rupture of the aorta at the time of labour, we always advise that, in the absence of obstetric indications, pregnancy should be allowed to pursue its normal course. Workers in other centres have come to the same conclusion (Haigh and Gilchrist, 1949).

The more we have studied this problem the more reluctant have we become to interfere with pregnancy. This change in policy is, we believe, partly responsible for the improvement in our results, seven deaths in our earlier series having been due to post-operative complications following termination of pregnancy.

When we first embarked on this investigation it was generally thought that the strain on the heart increased progressively as pregnancy advanced, and on this account the induction of premature labour (or caesarean section) before full term was often advised in women with heart disease to avoid the strain of the final month of pregnancy. We now know that the blood volume and cardiac output do not increase, but actually diminish, during the last few weeks of pregnancy. These facts have led us to modify our views regarding the management of such cases. There is little danger of heart failure developing during the last month of pregnancy if it had not been present previously, and there is therefore no purely cardiac indication for terminating pregnancy at this stage, since the strain on the heart will not be increasing but diminishing. Admittedly the presence of a cardiac lesion would justify operative intervention in those borderline cases in which there is some obstetric complication that by itself alone might not have done so.

Finally, let me remind you once again of the importance of adequate antenatal supervision. When Edith Longson and I came to analyse the first 350 cases in our series we found that 325 had attended the antenatal clinic and only 25 had been admitted as “urgencies.” Fourteen of the urgencies and 11 of the quiet cases proved fatal, so that the death rate among urgencies was 56%, as compared with 3% among quiet cases.

Similar results had been reported elsewhere (Table VI).

TABLE VI.—“Urgency” Death Rate

	No. of Cases	Total Deaths	“Urgency” Deaths
Bramwell and Longson (Manchester)	350	25	14 (56%)
Carr and Hamilton (Boston)	500	32	16 (50%)
B. P. Watson (1933) (New York)	240	17	8 (47%)

But we can go a step further, for in 10 of our 25 fatal cases death was due not to heart failure but to other causes. In the 15 patients who died of heart failure the figures are even more striking. Of these, 11 were urgencies and only 4 quiet cases. Thus the death rate from heart failure in our quiet cases was 1% as compared with 44% amongst urgencies. These figures convinced us of the importance of adequate antenatal supervision.

In our pregnancy cardiac clinic at the Manchester Royal Infirmary the almoner plays an important part. Her experience enables her to resolve many of the patients' difficulties and to arrange home help, to tide over the emergency, in case of need. From the psychological aspect, also, we believe this special clinic has proved useful. The newcomers get talking with the old hands, who have been through the mill before, and begin to realize that heart disease is not nearly such a terrible thing as they had been led to believe.

James Mackenzie

I cannot conclude my lecture without reference to the work of a very remarkable man—a man who was keenly interested in this problem and who wrote a book on heart disease in pregnancy (Mackenzie, 1921). He must have been a familiar figure to the older members of my audience, for he spent the Indian summer of his life in St. Andrews.

James Mackenzie was a Highlander. He was educated at Perth Academy and Edinburgh University. The next twenty-five years—the most productive years of his life—were devoted to general practice in Burnley. His work there is commemorated by a tablet on the wall of the house in which he practised. During the war this tablet was removed, for the powers that be considered that the word "Burnley," which appeared in the inscription, might prove helpful to the enemy in the event of invasion.

As an undergraduate Mackenzie won no special academic distinction. Later, however, he proved himself to be an investigator of outstanding merit and a man who made the fullest possible use of his opportunities. Mackenzie will probably go down to history as the man who solved the riddle of the cardiac irregularities. This he did by means of his clinical polygraph; all the earlier models of this instrument were made for him by Mr. Shaw, a local watchmaker.

But far more important was his work on prognosis, based on his own clinical observations. I have never ceased to marvel that such a popular and busy family doctor could find the time, and have the energy, to keep such wonderful records of his cases. The hours for research were literally snatched from the rush of general practice. It was these records of his cases in Burnley which enabled Mackenzie finally to overthrow the dictatorship of the stethoscope, which had dominated cardiology for nearly a hundred years.

Summary

The chief dangers to be faced in patients with heart disease who are pregnant are acute pulmonary oedema and congestive heart failure. The former calls for special vigilance on account of the suddenness with which it may develop, and in every case of mitral stenosis clinical or radiological evidence of pulmonary congestion must be regarded with grave apprehension. Congestive heart failure with oedema, if recognized early, usually responds well to treatment.

Auricular fibrillation, though a recognized precursor of heart failure, is not necessarily a bar to pregnancy, provided adequate antenatal and post-natal care can be assured. In assessing the risk, the previous obstetric history, age, economic conditions, and temperament of the patient must all be taken into account.

In patients with heart failure, surgical intervention should never be contemplated until the heart failure has been treated. Patients with heart disease tolerate pelvic delivery better than caesarean section.

In patients with advanced heart disease pregnancy is contraindicated. If, however, pregnancy is already established and the patient is seen within the first three months, it should be terminated, but, if she is not seen until later, it should be allowed to run its normal course. Alternatively, mitral valvotomy may be considered.

There is no purely cardiac indication for anticipating normal delivery.

All patients, however trivial their heart disease, should be kept under observation throughout pregnancy, and intercurrent infection and anaemia promptly treated.

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TREATMENT OF GENITO-URINARY TUBERCULOSIS FURTHER REPORT

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In 1951 we published a preliminary report on the treatment of 51 cases of genito-urinary tuberculosis (Ross *et al.*, 1951). The present communication includes a record of a further 47 patients similarly treated, and a follow-up of the earlier series. It is necessary to emphasize once more that a long-term view must be taken of this disease, as it is possible to encounter patients who have survived for many years after a bilateral renal lesion has been confirmed and in spite of the absence of treatment of any kind.

Classification.—No patient was accepted for treatment until a positive guinea-pig inoculation test put the diagnosis beyond all reasonable doubt. At the same time no case, however serious, was refused treatment. The patients were divided in five groups: (1) minor unilateral lesion or subclinical focus; (2) lesion of one kidney with cystitis and nephrectomy; (3) bilateral disease and nephrectomy of the worse kidney; (4) infection of the remaining kidney; and (5) severe bilateral disease. We realize that this is not a perfect classification, but for the purpose of uniformity in assessing the results we have not altered it on this occasion.

Method of Treatment

In addition to the regime described below, the ordinary surgical measures, such as nephrectomy and epididymectomy, were carried out when required, with the proviso that the optimum time was selected for the operation. For example, nephrectomy was often performed during the second or third course of streptomycin.

The whole course of treatment lasted six months, during which time the patient received the usual sanatorium regime at Wrightington Hospital. The three drugs used were: (a) "Ethizone" (*para*-ethylsulphonylbenzaldehyde thiosemicarbazone, or T.B.3), beginning at 50 mg. daily and gradually increasing by weekly increments of 200 mg. daily. Ethizone was given continuously for the six-months course of treat-