

A STUDY

of

RENAL TUBERCULOSIS

WITH PARTICULAR REFERENCE TO THE

RESULTS OF MODERN TREATMENT.

by

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It would indeed have been difficult or even impossible to assess completely the results of chemotherapy in the patients with urinary tuberculosis without the help and skill of Dr. John C. Dick, Pathologist, Stobhill General Hospital. The author has had a long and rewarding association with Dr. Dick and all the histological results and plates he owes to him. He has quoted at length from Dr. Dick's

work and his present régime of treatment logically follows the results of Dr. Dick's histological examination of all the resected specimens.

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Introduction:

From many arguments and discussions with colleagues, who are general surgeons and physicians, the writer has been impressed by their admission of the lack of intimate knowledge and understanding of tuberculosis. There is a tendency to dismiss the disease as a comparatively unimportant one and to assume that its treatment is straightforward and stereotyped, so that what applies to one patient applies to all. Nothing could be further from the truth.

To many physicians, tuberculosis is a disease which affects the lungs, to the orthopaedic surgeons the lesions are confined to bones and joints while neurologists, oto-laryngologists and urologists are concerned mainly with tuberculosis as it affects definite organs which are their interest. To this group may be added surgeons, ophthalmologists, dermatologists and gynaecologists, each of whom may consider himself a specialist in the treatment of tuberculosis. That so many specialists can be mentioned in the treatment of tuberculosis confirms the basic principle that tuberculosis is a generalised disease with

local or focal manifestations. It seems wrong to the writer that the unfortunate patient who suffers from various focal manifestations of tuberculosis should be knocked about like a shuttlecock from specialist to specialist. Rather, there should be clinicians who understand all forms of tuberculosis, who spend time and labour in the study of the disease and in research into its special problems. These people, however, should be ready and willing to use the advice when necessary from specialists in any branch of medicine or surgery.

Robroyston Hospital is rather unique in Britain: and even in America or Europe as far as the writer can find out from literature and from personal contacts. Apart from its many and varied facets, a large part (65 per cent) of the accommodation is devoted to the treatment of tuberculosis in all its forms. There is not a tuberculous lesion which is not treated within the hospital with the sole exception of neurological lesions requiring neuro-surgery. The hospital and its staff can take credit for the fact that as early as 1928

thoracic surgery was being carried out by the late Mr. James Taylor and Dr. M. A. Foulis. In 1934 a genito-urinary unit was started, probably the first in Britain and certainly the largest in Europe then and now, and this unit has been the prototype of many others throughout this and other countries. The year 1945 saw a maternity unit of 80 beds being added to the hospital and those responsible took this opportunity of allocating 10 of these beds to pregnant women who also suffered from tuberculosis and who hitherto had had little specialised attention.

The writer joined the staff of Robroyston Hospital 23 years ago and during that time, firstly as a junior medical officer and then as senior resident medical officer, junior assistant physician and surgeon, senior assistant physician and surgeon and latterly as consultant in clinical charge of wards, among other duties, he has looked after patients with pulmonary, bone and joint, abdominal, glandular and urinary tuberculosis. He was encouraged early on by Dr. John Watson to take an interest in, and

to treat all forms of tuberculosis. Later the writer came under the influence of Dr. M. A. Foulis who further stimulated the writer in medical and surgical aspects of tuberculosis. To Dr. Foulis the writer owes the initial stimulus to investigate patients with tuberculous epididymitis, the results of which were presented to the University of Glasgow for the degree of Master of Surgery. This investigation brought support and further encouragement from Mr. Arthur Jacobs and this encouragement was greatly enhanced by the welcome and tuition in the Urological Department of the Royal Infirmary, Glasgow. The friendship and help thus received made further investigations easy and enjoyable. Numerous publications followed and a climax was reached when the Medical Research Council chose Robroyston Hospital in 1948 as a suitable place for a trial of streptomycin in renal tuberculosis. This was followed by requests from many quarters to give the experience and results and on two occasions Mr. Jacobs and the writer were asked to speak to the Royal Society of Medicine about the results of their trial to that date.

In 1953, Professor Ljunggren of Gothenburg formed a European Group of clinicians who were interested in genito-urinary tuberculosis. A meeting was held that year in Frankfurt and representatives were invited from all the European countries. The writer had the honour of being the Scottish representative. Three years later a second meeting was held in Lucerne and again the writer attended. The next meeting is due in Capri this year and the writer has intimated his intention to attend and to present a communication.

During his years at Robroyston Hospital the writer has not concentrated solely on genito-urinary tuberculosis but takes an active interest in treatment of all forms of the disease. He is a member of the British Tuberculosis Association and its Examination Committee. He is also a member of the Tuberculosis Society of Scotland and its Research Committee and in October 1958 had the honour of being elected the President of the Society.

In the following investigation the writer deals with the records and results of patients whom he knew and treated over the past 20 years. Throughout he tries to

give the results of others and to give credit to the very many writers who have published their findings on this subject. It must be admitted however, that he has found it impossible after 20 years and after treating over 828 patients with urinary tuberculosis, to avoid stressing his own views on many aspects of this disease and that accounts for the omission of some minor references.

It is difficult to compare 50 or even 100 cases with over 800. The investigation seemed necessary to the writer after streptomycin and its successors had been in use for 10 years and he wished to get fact and figures to confirm or abnegate the impression that chemotherapy had made a radical change in the treatment and prognosis of sufferers from genito-urinary tuberculosis. As will be seen, the figures confirm the impression that started to grow in 1948.

Finally must come a frank admission that the writer has fully enjoyed the time spent on the compilation of the following pages. A regret remains. On going over case records of his patients the writer is saddened by

Chapter 1.Sex and Age Incidence:

The series comprises 828 patients, 525 (63.4 per cent) males and 303 (36.6 per cent) females, treated in Robroyston Hospital. This preponderance of males is a constant finding in many other investigations although in at least one of these, where the difference is more marked, Franzas (1952) the figures have been influenced by special conditions as a number of military cases of renal tuberculosis were sent to him for treatment and so accounted for the comparatively large number of men in his series. Figure 1 shows the sex distribution of renal tuberculosis as found by investigators in different countries.

The writer feels that the figures of the sex-distribution of renal tuberculosis in his series are true figures of the real incidence of this disease in Britain. This belief arises from the fact that patients with renal tuberculosis, males and females, are admitted to Robroyston Hospital from the West, South West and North

of Scotland and there is no sex discrimination. Additional support for this view is obtained from an investigation carried out by Ross (J.C. 1953) who was entrusted by the British Association of Urological Surgeons to investigate renal tuberculosis in Britain in two selected two-year periods, one before and the other after the recent war. Questionnaires were sent to all centres dealing with urinary tuberculosis, including Robroyston Hospital and the total number of patients considered was 722.

	<u>Males.</u>	<u>Females.</u>
1937-38:	268 patients. 172 (64 per cent).	96 (36 per cent).
1947-48:	454 patients. 297 (65 per cent).	157 (35 per cent).

From the investigation by Ross it can be seen that the sex distribution throughout Britain is very similar to that found in the patients admitted to Robroyston Hospital.

The ratio of almost two to one in favour of males has been a constant yearly finding since the Unit for the treatment of genito-urinary tuberculosis was established in Robroyston Hospital in 1934. The reason for this is

not obvious. As will be discussed later, renal tuberculosis is often symptom-free and may remain concealed during a greater part of life. In these days patients with tuberculous epididymitis are often examined routinely for renal tuberculosis. Many of the cases in the present series were found to have renal tuberculosis because the patients had sought medical aid for epididymitis. The writer does not feel that such an explanation wholly explains the facts. For many years in Robroyston Hospital it has been realised that renal tuberculosis may be silent and all patients, male and female, suffering from tuberculosis, have had routine monthly specimens of urine examined for abnormal constituents including tubercle bacilli. In a majority of the other hospitals and clinics, particularly in the West of Scotland, dealing with tuberculous patients, the same practice has been adopted. As a result of the increased search for people with renal tuberculosis there has been a marked increase in the total but the sex-distribution has remained the same.

Beskow (1952) maintains that tuberculosis is more common in males than females and he calculated the incidence over a 10-year period and found that the per centage of males was 52.3 and that of females 47.7.

The present writer does not feel that any of these views explains fully the preponderance of renal tuberculosis in males. He feels that other factors must exert an influence on the sex-distribution and so far his efforts to find these have not been successful but his investigations are being continued.

Genito-urinary tuberculosis is found to be comparatively rare in infancy and in old age in the series of 828 patients. Approximately 5 per cent of the males and 5 per cent of the females are under 15 years of age and 12 per cent of the females and 16 per cent of the males are over 40 years of age. Between the years of 16 and 40 the per centage of males and females is approximately 80. (Figure 2.)

The figures in the present series (Figures 2, 3 and 4) lend support to the views of Franzas (1952) who stated

that the incidence was highest between 20-29 years and Riches (1951) who found that the disease was commonest during the 3rd, 4th and 5th decades. Hawthorne and Siminovitch (1949) reported that renal tuberculosis was uncommon in children while Yates Bell (1949) reported 46 cases in children and stressed the possibility of its causing enuresis.

pleuritis 17 per cent; abscess 2 per cent;
other sites 2 per cent.

The high percentage of extra-pulmonary tuberculosis reported by Jackson and Gilbert was due to the fact that these men used the term in its widest sense and included patients with radiologically demonstrable disease of the primary tuberculosis or pleuritis. In the present series the figure was only 45.9 per cent (Figure 3) because only those who had suffered from clinical

Chapter 2.Extra-Urogenital Tuberculosis:

Ljunggren (1957) gave a figure of between 40 to 60 per cent for the number of patients with renal tuberculosis who were suffering from or had a history of extra-urogenital tuberculosis. The figure given by Colby (1940) was 52 per cent which was considerably lower than the 82 per cent reported by Beskow (1952) and 87 per cent by Cibert (1946). Franzas (1952) found his figure of extra-urogenital tuberculous lesions was 60 per cent which was made up by: lungs: 25 per cent; bone and joint: 11 per cent; pleuritis: 17 per cent; glands: 5 per cent; other sites: 2 per cent.

The high percentage of extra-urogenital tuberculous lesions reported by Beskow and Cibert was due to the fact that these men used the term in its widest sense and included patients with radiologically demonstrable signs of healed pulmonary tuberculosis or pleuritis. In the present series the figure was only 46.9 per cent (Figure 5) but included only those who had suffered from clinical

extra-urogenital tuberculosis and no significance was attached to merely technically positive x-ray plates of the chest.

The localization of the lesions is listed in Figure 6.

In the writer's opinion it is important to note that 440 (53.1 per cent) of the 828 patients had no history or clinical evidence of previous tuberculous infection. Evidence of pleurisy with or without effusion prior to the renal investigation should naturally raise the possibility of the renal symptoms being tuberculous in origin. The possibility of a diagnosis of renal tuberculosis however, must never be discounted because of the lack of evidence of tuberculosis elsewhere. In the younger age groups the value of the tuberculin skin test must be emphasized; indeed its importance is probably increasing.

Although there were 388 patients who gave a history of previous tuberculous lesions before the diagnosis of renal tuberculosis was made, accurate records existed in only 235 instances. From these,

Figure 7, it can be seen that renal tuberculosis was diagnosed from 1 to over 10 years after the other manifestations of tuberculosis. These findings lend support to the views given in Chapter 6 that renal tuberculosis is a late manifestation in the chronological course of tuberculous infection.

Since 1948 the follow-up of all patients discharged from hospital has been as complete as possible including patients from Stornoway in the North and Dumfries-shire in the South. Follow-up always included a visit to Robroyston Hospital for examination and careful notes have been taken. In only three instances did a patient have an active tuberculous lesion outwith the urinary tract after the diagnosis of renal tuberculosis and in each case it was due to re-activation of a pre-existing tuberculous lesion. In the years before 1948, the follow-up was carried out at clinics but the number of patients who were later readmitted to Robroyston Hospital because of an extra-urogenital tuberculous lesion was very small and again the lesion was usually due to re-activation of previous disease.

Ustvedt and Wergeland (1949) reviewed 292 cases.

These workers found that the onset of the genito-urinary lesions in two-thirds of the cases was 5 years after the initial pulmonary disease and 15 years in a quarter of the patients. They stated that the latent period was in marked contrast to the onset of disease in bones and joints.

Six of the writer's patients merit further attention, five of whom had a history of tuberculous meningitis and one of acute miliary tuberculosis. In these, there was a marked haematogenous dissemination of tubercle bacilli and renal tuberculosis was diagnosed in one year in 1, in 3 years in 2, in 5 years in 2 and in 6 years in 1.

The writer feels that the time of appearance of the renal tuberculosis in relation to the extra-urogenital manifestations in the present series fits in strikingly well with modern conceptions of the general course of tuberculous infection. (Chapter 6.)

Chapter 3.Symptomatology of Renal Tuberculosis:

The presenting symptom which initiated the urological investigation in the 828 patients can be seen in Figure 8. Obrant (1955) reviewed 303 patients and compared the presenting symptom in his patients with results reported in 1925. (Figure 9.) The writer has added his own results for comparison. This comparison shows that the number of patients who were diagnosed as suffering from urinary tuberculosis but who had no symptoms referable to the urinary tract was between 4 and 10 per cent in 1925 but rose to between 29.6 and 38 per cent in reports published or prepared within the last three years. This difference is due to an increase in the number of patients diagnosed in the pre-clinical stage, before symptoms have developed, and reflects increased awareness and interest in out-patient clinics and hospitals.

The symptoms shown in Figure 8 are all well recognised as symptoms which necessitate a complete

urological examination. Galbraith (1952) in common with those who have reported on this subject, gives increased frequency of micturition as the commonest symptom of urinary tuberculosis. He also stresses, however, that symptomless pyuria is most suspicious of tuberculous infection of the urinary tract. The symptom-free group of 245 patients, almost 30 per cent of the total, forms a most important contribution to the present series and the reason for the investigation in all of these patients is shown in Figure 10.

Colby (1940) reported that renal tuberculosis was present in patients with bone and joint tuberculosis more often than was generally realised and he stressed the importance of a symptomless albuminuria in these cases. Ross (J.C. 1953) stated that recurrent mild urinary upsets were suspicious and he advised a search for tubercle bacilli in young adults with albuminuria and persistent coliform organisms in the urine. A plea to look for tuberculosis of the urinary tract before the appearance of symptoms was made by Ljunggren (1957).

The place of male genital tuberculosis will be discussed in Chapter 7 but it has long been the practice in Robroyston Hospital to carry out a full urological examination in these men and to consider epididymitis as a probable symptom of renal tuberculosis.

The writer feels that this total of 245 patients who were found to have renal tuberculosis but who did not have any urinary symptoms, forms a group of great significance. Probably the most striking feature in his opinion is that it forms almost a third of the total number of patients in the series. The number of patients diagnosed before the onset of symptoms has been increasing year by year and it reflects the increasing awareness that silent renal tuberculosis can exist. Consideration of the total 828 patients shows that renal tuberculosis was unilateral in 548 and bilateral in 280 instances when the condition was first diagnosed. The frequency of involvement of right and left kidneys was practically the same. All stages of development of organ disease were present in these cases.

When the writer examined the symptom-free group of 245 patients, (Figure 11) he found bilateral renal tuberculosis in 83 and unilateral disease in 162 patients. In the 83 bilateral cases, 53 showed moderate to advanced disease while the remaining 30 suffered from tubercle bacilluria without any pyelographic changes being visible. Eighty-two of the 162 unilateral cases were moderate to advanced while 70 showed small lesions and in the remaining 10 no lesion was visible on urography. Medlar (1926: 1932) and Band (1935; 1942; 1943; 1952-53) have proved that tubercle bacilluria indicates renal lesions and their views have been supported by Jacobs (1954) and Ross (J.C. 1953b).

From these results in patients who did not suffer from cystitis and who were completely symptom-free it is obvious that renal tuberculosis may be bilateral and advanced without any urinary symptoms. Silent renal tuberculosis constitutes therefore, a most important group of patients and the very character of urinary tuberculosis must be appreciated. The writer has found

that small renal lesions may exist with moderate or pronounced cystitis while extensive bilateral renal disease may be present without an associated cystitis. In the latter event the patient will not suffer from the generally accepted classical symptoms of urinary tuberculosis mentioned above. The only true symptoms of renal tuberculosis are haematuria arising from the kidney and very occasionally renal pain. The commonest symptom, as quoted, increased frequency of micturition, is not a symptom of renal tuberculosis but a symptom of vesical disease and that develops soon after the start of open renal tuberculosis some years later or not at all. Many writers, particularly in standard books on surgery stress the general symptoms with which one associates an early tuberculous lesion elsewhere in the body. The loss of weight, impairment of appetite and lassitude are all given an important place in the diagnosis of renal tuberculosis. In the writer's experience these symptoms and signs occur as the exception rather than the rule in those patients provided they do not also suffer from

unstable extra-urogenital tuberculosis. Toxaemia from a renal lesion seems to be minimal, perhaps because of rapid excretion of tuberculous toxins or to the fact that some toxaemia may have been present at an earlier phase and has passed by the time the diagnosis is made. When the bladder becomes involved the increasing frequency of micturition during the day and the night, has its effect on the general condition of the patient. Even when epididymitis develops, apart from an initial upset lasting days rather than weeks or months, the patient usually shows little evidence of toxaemia. The writer has long been aware that the view expressed by Foulis (1940) many years ago, that the patients in Robroyston Hospital who are under treatment for urinary tuberculosis, without any other tuberculous manifestations, are by far apparently the healthiest patients in the hospital. Even in progressive renal disease, in the absence of marked vesical irritability this well-being may continue until most of the renal tissue is destroyed and in fact until the patient is approaching an uraemic condition.

Weight, erythrocyte sedimentation rate, appetite, serum urea and general examination may all remain normal until a short time before the onset of the final kidney failure. One obvious exception to this is the pyonephrotic kidney where the secondary infection may give rise to marked systemic upset.

To sum up this section, the writer wishes to stress the importance of a full urological examination in tuberculous patients who have albuminuria or pyuria. Routine examination of the urine for tubercle bacilli will produce surprising results, while epididymitis in the writer's opinion, demands a full examination. haematuria, renal pain or increasing frequency of micturition are all well recognised as symptoms which necessitate a full urological investigation, but the absence of these symptoms should not rule out the possibility of urinary tuberculosis being present.

Chapter 4.Urological Examination:Urine Examination:

In the male, a mid-stream specimen of the first urine passed in the morning and in the female, an early morning catheter specimen are most likely to contain tubercle bacilli. The writer has found these specimens to be of greater value than the more usual 24-hour collection which, in his experience, is often grossly contaminated. The centrifugalised deposit from these specimens may then be stained by the Ziehl-Neelsen method or, as is more usual in Robroyston hospital, examined by fluorescence microscopy. Results are always confirmed by animal inoculation or by cultural methods using Loewenstein-Jaensen medium.

It may be thought that the introduction of chemotherapy has diminished or even removed the need for culturing the organism before instituting treatment, but the reverse is in fact the case. Firstly, it is necessary to identify fully the organism before making a

serious diagnosis and thereby commencing a long course of treatment. Secondly, it is most desirable to have a culture on which to test the resistance of the organism to the various drugs available. It is now generally accepted that a single agent should not be employed in the treatment of any form of tuberculosis but that at least two drugs should be used in combination. Such a technique however, did not always hold and various resistant strains have resulted. In at least 2 of the writer's patients the tubercle bacilli grown were found to be completely resistant to streptomycin and neither patient had been previously treated by chemotherapy. Again even if treatment begins by combined chemotherapy before the patient's organism can be grown and tested, it is desirable to know as soon as possible if there is resistance to any one of the drugs given so that the combination may be altered and the particular drug excluded. It must be realised that culture of the tubercle bacillus from the urine is sometimes not easy and repeated

attempts may be necessary. A negative result, particularly of a single specimen, without confirmation by culture or animal inoculation, is of little value equally in diagnosis and follow-up examination. If, however, three specimens in which tubercle bacilli have been seen by the fluorescence microscopy, or on Ziehl-Neelsen stained slides, are inoculated on a reliable culture medium, treatment need not be delayed.

Intravenous Pyelography:

A straight x-ray of the complete urinary tract should first be made. This may show evidence of calcareous deposits within the renal shadow (Figure 12) and along the ureter. (Figures 12 and 13). Sometimes the whole kidney is seen to be greatly enlarged.

Intravenous pyelography, with or without compression, is of great value in estimating the function of both kidneys. It is often possible to pass one kidney as radiologically normal and to demonstrate an area of disease in the other (Figure 14). The earliest change may be a diminution of renal

function as evidenced by delay in the appearance of the dye and in poor concentration on the affected side. Erosion of a pyramid will produce a little fluffiness in the calyceal outline to which the term "moth-eaten" is often applied. Ulceration accentuates this appearance and makes the calyx rounded or clubbed in contrast with the normal cup shape. With progression of the disease cavitation occurs adjoining the calyx evidenced by a greater amount of contrast medium in it, but with further destruction there is less secretion until finally the kidney fails to secrete at all and no shadow is produced.

Dilatation, irregularity or constriction of the ureter may be apparent and valuable information is obtained about the size and configuration of the bladder. In early renal tuberculosis, however, excretion urography may fail to demonstrate the lesion and more accurate assessment of the calyceal system both in diagnosis and in estimating the progress of the lesion can be obtained by retrograde pyelography. Durand (1954) emphasised the importance

of uretero-pyelography and cystography in patients with tuberculosis of the ureter.

Cystoscopy:

The pathological changes in the bladder resulting from renal tuberculosis will be considered in Chapter 6. The writer has found that except in young people and in patients with a very irritable bladder, cystoscopy may be carried out without anaesthesia in the female and under local anaesthesia in the male, with amethocaine 0.5 per cent. This finding differs from the expressed views of Band (1948) and Riches (1952) each of whom prefers general anaesthesia. The writer feels however, that with gentleness, the procedure may be carried out without causing pain, that overdistension is avoided and full co-operation of the patient is obtained when retrograde pyelography is being carried out. Further, post anaesthetic sickness is avoided and when large number of patients have to be examined, the procedure may be carried out on out-patients.

The bladder urine evacuated through the irrigating cystoscope should be collected in a sterile container and sent for bacteriological examination. Secondly, the capacity of the bladder filled without distress, is estimated and in this procedure a conscious patient will give warning of overdistension which may lead to bleeding and so obscure the field and make visualisation of the bladder difficult. The bladder mucosa is then examined for congestion, haemorrhage, follicles or ulceration. Particular attention is paid to the ureteric openings, their position, edges and shape. If possible, both ureters should be catheterised and separate kidney specimens collected for complete chemical and bacteriological examination.

Retrograde Pyelography:

Once the ureteric catheters are in position and specimens have been collected, retrograde pyelography should be carried out. The writer has found a 50 per cent diluted intravenous preparation greatly superior to sodium iodide as a contrast medium.

Care should be taken to avoid overdistension and he has found that on an average 6 to 8 ml. of fluid for each kidney is sufficient.

Riches (1952) mentions several dangers in ureteric catheterization and pyelography in renal tuberculosis:

- 1) Perforation of the ureter by the catheter with periureteric extravasation of the dye.

The writer feels that this can be avoided if the operator refrains from using force when manipulating the catheter. Also, the use of a stilette in a catheter should be considered only by an experienced operator, and even in his hands great care must be taken to ensure that the stilette does not project beyond the catheter tip. It is another point in favour of local anaesthesia instead of general anaesthesia.

- 2) Transference of tubercle bacilli from the infected bladder into a non-infected kidney.

With proper lavage, the writer feels that this danger is theoretical rather than practical.

In addition, it is his practice to cause forced diuresis before and during the examination which will help to wash away any foreign substance. Chemotherapeutic cover will also be an added precaution, but the writer prefers to withhold drugs in order to obtain viable tubercle bacilli if present in the urine.

3) General dissemination of infection from pyelovenous or pyelotubular back-flow. This danger has been stressed by Steinert (1948).

The author is of the opinion that this complication is unlikely if force is avoided and if the amount injected up the catheter in an average sized adult does not exceed 6 ml.

Opinions still differ on the wisdom of catheterizing the ureter on the unaffected side; Macalpine (1949) has always been apprehensive about it. Wells (1950) considers it unnecessary and he relies on intravenous pyelography while Band (1948) and Emmet and Braasch (1938) feel that it is necessary. The writer agrees with the last named investigators. Often a

tuberculous lesion in a kidney is too small to be seen on excretion urography, (Figure 15), progress can be assessed more accurately by retrograde pyelography and in many thousands of cystoscopic examinations and ureteric catheterizations he has never observed a patient who appeared to suffer any untoward sequelae following retrograde pyelography in renal tuberculosis.

Cystography:

The introduction of an opaque dye into the bladder of a person suffering from urinary tuberculosis is reserved mainly for the contracted bladder to visualise its outline, and to estimate the degree of reflux up a ureter (Figure 16). It is used mainly as a guide to possible surgical treatment but more and more it is now being used to assess results of ileo-cystoplasty, where an x-ray plate is taken with the bladder full and another taken after voiding the fluid to see if there is any residual fluid.

Angiography:

The value of angiography in renal tuberculosis is somewhat limited at the present time, according to Stirling (1956; 1957). He is of the opinion that its main value is in giving further information of the apparently functionless or absent kidney. In such cases, the assessment of the total renal blood supply may be valuable in deciding whether a conservative or ablative procedure should be undertaken. In some cases the extension of the pathological process may be shown to be more marked than is suggested by urography. On the other hand, the early calyceal lesion shown definitely by urography may produce no significant change in the angiographic outlines. It is of practical application and is invaluable in demonstrating the vascular pattern in those cases considered suitable for partial nephrectomy.

In 4 patients this procedure has been necessary to establish congenital absence of a kidney when it seemed likely that the patient suffered from a

non-excreting lesion which might have precipitated an operation, while in a further patient angiography demonstrated the presence of a renal artery when it was thought that the patient had congenital absence of the organ. (Figure 17.)

Chapter 5.Diagnosis of Renal Tuberculosis:

In a patient with or without a history of previous tuberculosis and with symptoms of urinary disease, the diagnosis is made with accuracy by systematic investigations. The condition may be missed because symptoms are absent or slight or because the investigations have not been thorough enough or repeated sufficiently often. Out of the 828 patients in the present series, 245 (about 30 per cent of the total) had no symptoms. Silent renal tuberculosis constitutes therefore a most important group of patients.

The very character of urinary tuberculosis should be appreciated in that small renal lesions may exist with moderate or pronounced cystitis while extensive bilateral renal disease may be present without an associated cystitis. In the latter event the patient will not suffer from the generally accepted classical symptoms of urinary tuberculosis. In Chapter 3 it was noted that of the 245 symptom-free patients when the disease was diagnosed it

was found to be bilateral in 83. Fifty-three of the 83 patients had moderate to advanced renal tuberculosis.

Male genital tuberculosis is a condition which frequently follows renal tuberculosis (Chapter 7.) The palpation of the external genitalia and, in particular the digital examination of the rectum may yield evidence of genital tuberculosis. Nodules in the epididymis, particularly in the globus minor, thickening of the seminal vesicle, and a nodular irregularity and softening of the prostate are more significant of tuberculosis in the young adult than of any other pathological lesion.

When routine examination of the urine reveals albuminuria or pyuria and the cause is not obvious, tuberculosis should be remembered as a possible reason and an exacting search initiated for tubercle bacilli in the urine. This search should include animal inoculation and culture and repeated examinations may be necessary before bacilli are found. Abnormal constituents in the urine of a patient with a previous history of tuberculosis should lead to a full urological investigation.

Such investigations, as outlined in Chapter 4, will give the necessary details to diagnose renal tuberculosis and show the nature and extent of the disease within the urinary tract. That information is necessary to plan adequate treatment.

Finally it should be noted that it is unusual for a patient with urinary tuberculosis to demonstrate any of the signs of tuberculous toxæmia associated with other tuberculous lesions. The absence of malaise, a complete stability in weight, a normal serum urea estimation and erythrocyte sedimentation rate should not therefore influence the clinician against a diagnosis of tuberculosis. The writer cannot too forcibly impress these views, for as already said, in a tuberculosis hospital treating all forms of tuberculosis, those patients with renal tuberculosis form, by and large, the fittest group.

Chapter 6.Development of Renal Tuberculosis:1. Chronological Position of Renal Tuberculosis in the Course of Tuberculous Infection.

The modern conception of the origin of renal tuberculosis and its place in the course of tuberculous infection have received attention from many workers including Cibert, Brun and Fervel (1943) and Ljunggren and Obrant (1952). The primary complex is often situated in the lung and has often healed spontaneously becoming encapsulated and calcified. In the months following the primary infection, tubercle bacilli often enter the blood stream and may settle in various organs, this being the bacillaemic phase or period of visceral spread according to Band (1952-53). Tuberculous infection does not immediately reveal itself clinically in these organs and may never do so. There is often a latent incubation period of varying length depending on the number of organisms, the virulence of the organisms and the resistance of the host. Clinical

disease in many people never occurs. Wallgren (1948) coined the term "The Time-Table of Tuberculosis" and according to him, if the infection develops near the serous membranes it usually manifests itself early, and later if bones and joints are infected. Signs of renal tuberculosis appear later still. His conclusions have been supported by Franzas (1952), Beskow (1952) and the present series and it would seem that clinically genito-urinary tuberculosis is usually the latest of the various manifestations of the same initial tuberculous infection in an individual and that a period of years, average 8-10 according to Gloor (1946) often elapsed between the supposed time of infection of the kidney and the initial clinical symptoms. Ustvedt and Wergeland (1949) reviewed 292 cases and the onset of genito-urinary lesions was 5 years after the initial pulmonary disease in two-thirds of the cases and 15 years after in a quarter of the cases. They stressed that the latent period was in marked contrast to the onset of the disease in bones and joints. The kidneys were probably involved in primary spread but the initial response to infection was of a minimal nature.

As shown in Chapter 3, Figure 7 demonstrates the interval in years in 235 of the 388 patients who had previous extra-urogenital tuberculosis before the diagnosis of renal tuberculosis. Conversely the number of the 828 patients with urinary tuberculosis who can be traced and who subsequently developed extra-urogenital lesions has been only 10 and in at least half of these cases this was the result of progression of a pre-existing tuberculous lesion.

2. The Pre-Clinical Phase:

The Significance of Tubercle Bacilluria:

The importance of the latent period cannot be over-emphasized since although symptoms are absent it is often possible to diagnose urinary tuberculosis in its pre-clinical state. According to Ljunggren and Obrant (1952) the French call this stage "L'étape parenchymateuse", while Thomas, Stebbins and Rigos (1939) use the phrase "The non-destructive stage of renal tuberculosis." Band (1948) on the other hand, has applied the name "The Sub-clinical stage of Renal Tuberculosis",

but the author prefers to describe this period as the pre-clinical phase.

According to Band (1948), Dimtza and St. Kartal in 1932 defined tubercle bacilluria as "the passage of tubercle bacilli in a tuberculous subject through

- 1) a perfectly normal kidney,
- 2) a kidney damaged in any way but not tuberculous, and
- 3) a kidney changed by tuberculous nephritis." The work of Medlar (1926) and later Band (1947) which was supported by Dukes (1948) has shown that this statement is incorrect. Medlar carried out the pioneer work when he studied by serial section the kidneys recovered at autopsy from patients who had died of extra-urogenital tuberculosis. He found microscopic lesions present in both organs of the 30 cases examined. In 1942 Band reported a personal series of 300 cases of extra-urogenital tuberculosis in 21.3 per cent of whom tubercle bacilli were discovered in the urine. Thirty of these patients died later without having developed symptoms or signs of genito-urinary tuberculosis and again serial

sections revealed minute cortical tuberculous foci in every case. All stages of development of the tubercle follicle including epithelioid, giant cell formation and caseation were noted. In many of the cases healed follicles were present. These minute tubercle follicles in the cortex, constantly present when there had been tubercle bacilluria were never visible to the naked eye and were found in relation to the glomeruli.

An important aspect to be appreciated in dealing with this form of renal tuberculosis is that such lesions can and frequently do heal. Band found that tubercle bacilluria in his series was temporary in 23.4 per cent, the disappearance of the infection being associated with the healing of the extra-urogenital lesions. These views of Medlar and Band have received much support, including that from Dukes (1948) who stated that symptomless tuberculous bacilluria resulted from microscopic cortical lesions and was not "excretion without a lesion."

The occurrence of frank renal tuberculosis following tubercle bacilluria occurs in a very low percentage of patients. In a series of 64 cases of tubercle bacilluria Band (1942) found that only 3 developed clinically recognisable renal tuberculosis with positive pyelographic findings and that percentage is comparable to the 6 per cent incidence quoted by Cibert (1946). The writer has had 40 patients who had tubercle bacilluria and not one of these patients has developed clinical renal tuberculosis in a period of from 2 to 6 years. All of these patients however, had the benefit of anti-tuberculosis drug therapy.

The haematogenous dissemination of tubercle bacilli is not limited to the kidneys since renal tuberculosis and bone and joints lesions are frequently associated. Irrespective of the time of onset of these lesions, and the author believes that the orthopaedic lesion usually manifests itself earlier in the majority of cases, the fact must be accepted that miliary tuberculosis is much more common than is generally

realised. Miliary tuberculosis should be regarded as a qualitative rather than a quantitative conception since it follows that miliary tuberculosis not only occurs frequently but that in most cases it is relatively benign in character. Apart from the possibility that clinical miliary tuberculosis may arise, there is the alternative that pre-clinical miliary tuberculosis is either cured or that it passes into chronic tuberculosis of the organs such as the bone, the joint or the kidneys.

3. Pathogenesis of Renal Tuberculosis.

As the author has reported above, it is now accepted that the earliest lesions in the kidneys are usually bilateral and found in relation to the glomeruli of the cortex constituting the pre-clinical phase. These lesions may heal or become encysted. If the former occurs it could account for a later unilateral or "surgical kidney", but if the latter happens, at any time, reactivation may occur under conditions of reinfection or further sensitization from the tubercle bacillus.

The cortical lesions may ulcerate into the renal tubules and discharge tuberculous debris. At this stage pyuria may be absent or slight and urography may demonstrate normal function and outline. The pyramid and papilla are thus exposed to infection by firstly, tubular extension and, secondly, by direct spread from the foci in the cortico-medullary zone. The blood supply of the pyramid, especially in the papilla, is poorer than in the cortex and the chances of healing are not so favourable. Healing foci in the papilla are rare and instead there is a tendency to necrosis and cavity formation. When this has ulcerated into the renal pelvis, the infection can spread to the ureter, bladder, and in the male, to the genitalia.

At this stage, according to Band (1948) the renal pelvis has now become infected and tubercles and ulceration occur in the lining epithelium. Renal function is impaired and the renal pelvis becomes atonic. Residual urine which is present becomes re-absorbed and tubercle bacilli pass in a retrograde manner to

the tubular systems of the neighbouring calyces.

The process of tubular re-absorption is well seen in hydronephrosis and it is well known as a route for the dissemination of infection in pyelonephritis with hydronephrosis and stasis. By this process secondary foci may then appear as a confluence of groups of tubercles in more distant zones of the renal cortex. (Figure 18). Caseation, ulceration and cavitation may follow in the proper sequence.

4. Pathological forms of Renal Tuberculosis.

(a) Ulcerocavernous tuberculosis: This form indicates the process of progressive ulceration of neighbouring calyces which follows a primary active focus with cavitation in the parenchyma. (Figure 18).

(b) Caseo-cavernous tuberculosis: This term is applied when the cavities are mainly within the renal parenchyma. (Figure 19). Types (a) and (b) usually overlap and mixed types are common in the same kidney.

(c) Tuberculous pyonephrosis: In this type there is obstruction to the outflow from the ureter and the whole kidney may be destroyed leaving a shell filled with tuberculous pus. Secondary infection may occur and the condition may then become acute. (Figure 20.)

(d) Putty kidney: The obstructed kidney contains caseous masses which fill the cavities. (Figure 21).

(e) Calcified kidney: (Auto-nephrectomy). Calcification which is one phase of healing of tuberculosis, may extend to the whole organ and render the kidney functionless. (Figure 12).

(f) Tuberculoma: In this lesion there is usually a solid mass of tuberculous granulation tissue forming nodules of large size. (Figure 22).

5. Tuberculosis of the Bladder and Ureter:

The passage of tubercle infected urine down the ureter exposes the ureter and bladder to infection. The spread to the bladder is primarily intraluminal and hyperaemia appears at the ureteric orifice. This may be followed shortly by the appearance of

minute tubercles, greyish yellow pin-head nodules occurring in groups, and these according to Riches (1952) are individually associated with blood vessels. These tubercles tend to become confluent and a characteristic tuberculous ulcer may be so formed. Such an ulcer is irregular in outline and has shallow, shelving and undermined edges. The zone around the ulcer tends to become congested, resulting in a flame-like appearance. Unlike the generalised cystitis due to coliform infections the distant parts of the bladder may be normal, but with progressive disease, congestion, tubercles and ulceration may appear at other sites. Tuberculous ulceration penetrates deeply and leads to irritation and frequent contractions of the bladder muscle. Healing may take place by fibrosis and this results in a permanent contracture of the bladder with diminution in its capacity. The extreme form of this is the so-called systolic bladder.

The ureter, while playing a passive part in the phase of canalicular spread, may itself at the same time

become involved in the tuberculous process. Tubercle follicles appear in the ureteric wall and, according to Band (1948) by means of submucous and adventitial lymphatic plexuses, aggregations of tuberculous granulation tissue appear. Later infiltration with fibrous tissue leads to thickening and the whole ureter may become cord-like. Contraction of the fibrous tissue may then produce shrinkage in the length of the tube and this in turn leads to a retracted and gaping ureteric orifice. This is the well named "golf-hole" orifice which is retracted upwards and outwards on the ureteric ridge.

6. Course of Urinary Tuberculosis:

Untreated urinary tuberculosis is a progressive disease. The systolic bladder with thickened and ulcerated walls causes backward pressure on the healthy ureter and extension of the disease to the opposite ureteric orifice. This raises the possibility of an ascending infection by means of the ureter and its lymphatics to the remaining kidney, which may already be

tuberculous per primam from a haematogenous source. In addition, the systolic bladder with its increased intra-vesical pressure may produce a hydroureter and hydronephrosis on the remaining side with consequent impairment of function on that side, even leading to a fatal issue. (Figure 23).

The writer has had 3 patients each of whom had a contracted or systolic bladder, and each refused operative treatment to alleviate the symptoms of excessive frequency of micturition. After some months in all three cases, the patients reported an improvement in the frequency of micturition usually imparted with a feeling of self-satisfaction that their decision to refuse operation had been a correct one. Examination however, soon revealed that the systolic bladder was being augmented by a dilated ureter and kidney pelvis which made operative treatment all the more urgent. (Figures 23 and 24 a and b.)

In the following chapter it will be seen that urinary tuberculosis may spread to the male genitalia and make further inroads on the individual's resources to combat the disease.

Chapter 7.Male Genital Tuberculosis:

The terms urogenital or genito-urinary tuberculosis indicate the close association of the disease in the urinary and genital systems. This only applies however to the male where there is direct communication between the two systems. In the female, the two systems are separate and tuberculosis in one does not, under normal circumstances, spread to the other.

In the present investigation the number of men suffering from urinary tuberculosis was 525. Nearly 70 per cent of these men also suffered from genital tuberculosis. (Figure 25).

There is general agreement that the two conditions of urinary and genital tuberculosis are very often present in the one patient but there is some disagreement on the exact relationship between the two lesions. The fact that cystoscopy and pyelography are procedures which are not devoid of risk, deters some from carrying out a complete urological investigation

in men with genital tuberculosis, while others believe that the risk to the patient is greater if these investigations are left undone in that a renal lesion may be overlooked. Barney (1936) on the one hand demanded definite indications for a renal investigation stating that "in the absence of symptoms pointing to the kidney, cystoscopy and ureteral catheterisation seem unwise", while, on the other hand, Bumpus and Thompson (1928) believe that tubercle bacilli in the urine indicate renal disease and that unless the urine is negative for tubercle bacilli, cystoscopy should be carried out. A third view is held by Wells (1934) who believes that in tuberculous epididymitis the infection has come from the kidney and that therefore, there has been a renal lesion which might have remained active or it might have healed.

The author (1945-46) reported personal investigations into the pathogenesis of tuberculous epididymitis. He studied the records of 402 men with genital tuberculosis but he also had personal experience of most of them.

He concluded that, in the great majority of patients, the genital lesion was a sequel to the renal one. He also found that tuberculous prostatitis and seminal vesiculitis usually precede epididymitis and from a personal follow-up of men with pelvic genital disease he found that the globus minor of the epididymis was the first part of the superficial genitalia to become involved. With regard to testicular disease it was always, with four exceptions, found to be due to extension from the epididymis and maximal at the mediastinum testis. In the 4 exceptions, the body of the testis was sectioned at operation and was found to be studded with discrete tubercles, a condition which could only have resulted from a haematogenous spread. In addition, the disease in these four men was in the testis with the epididymis practically uninvolved, a clinical state at variance with the usual case of genital tuberculosis.

Later (1948), in a personal series of 500 men with tuberculous epididymitis, the author found that

347 (69.4 per cent) definitely had renal tuberculosis.

The remaining 153 men did not undergo a complete urinary investigation but from the records at least 20 of them had tubercle bacilluria and 10 increased frequency of micturition. In 1952 the author found that the incidence of genital tuberculosis in 125 males with renal tuberculosis was 81.6 per cent.

These patients had all been admitted to Robroyston Hospital within the two years prior to the report when the author and his colleagues were aware of the close relationship between renal and genital disease. In the present series of 525 men with renal tuberculosis, admitted to Robroyston Hospital within the last 20 years, 351 or 66.9 per cent, also had genital tuberculosis.

500 genital cases - renal tuberculosis proved in 69.4 per cent.

525 renal cases - genital disease proved in 66.9 per cent.

The figure of 66.9 per cent of the male patients with renal tuberculosis developing genital tuberculosis seems to be of great importance. That the two conditions

are closely related must be admitted particularly when investigations have shown that 70 per cent of 500 men with tuberculous epididymitis also have renal tuberculosis.

The author believes from his studies that in the great majority of cases the sequence of events in genito-urinary tuberculosis is from the kidney to the pelvic genitalia and from there to the epididymis. Any deposit in the urine would naturally collect in the lowermost part formed in the upright position by the prostate and infective material is brought into contact with the prostatic urethra for a long time. In the prostatic urethra are natural crypts where tubercle bacilli may lodge. Spread of tuberculosis from the pelvic genitalia to the epididymis then takes place in the majority of cases by the lumen of the vas deferens. The incidence of tuberculous epididymitis is highest during the years of maximal sexual potency when the vas deferens would be expected to be most active and with active peristalsis actual shortening

of the vas probably occurs, followed by relaxation with possible resultant suction towards the epididymis.

Kolnick (1925) demonstrated experimentally that when fluid was injected into the vas deferens and the vas was then stimulated, the fluid progressed backwards by gradual stages to the epididymis following each peristaltic wave towards the posterior urethra.

The first part of the epididymis which is involved is the globus minor and from there the disease spreads to the body and head of the epididymis to the vas deferens itself and often to the body of the testis. In only 4 out of 402 patients did the writer believe that there was blood borne infection of tubercle bacilli to the superficial genitalia.

Symptoms and Signs:

Apart from frequent nocturnal emissions which may be blood stained, dysuria and, rarely, the appearance of an abscess in the perineum, there are no symptoms of pelvic genital tuberculosis. This accounts for the fact that it is rarely diagnosed

before the disease has spread to the epididymis and is partly responsible for the belief held by some that the epididymis is the first part of the genital system to become involved. Epididymitis is usually the first visible and palpable symptom as far as the patient is concerned and the one which causes him to seek medical advice. If however, rectal examinations are carried out on all men suffering from renal tuberculosis without epididymitis, over 7 per cent will be found who suffer from pelvic genital disease most of whom will later develop epididymitis unless adequate chemotherapy is given. It must be remembered that in the writer's experience, vide supra, 60 per cent of men with renal tuberculosis were also found to have pelvic genital disease and epididymitis.

Epididymitis is usually subacute in onset producing symptoms of local pain and swelling. In some men, particularly in the older age groups, it may develop insidiously with swelling, while in others the condition may be acute with sudden pain and swelling

and pain radiating to the iliac fossa associated with fever, vomiting, headache and skin redness. The acute variety usually subsides within 7 to 10 days and then resembles the more common subacute variety.

Diagnosis:

The diagnosis of tuberculous epididymitis is usually an easy one to make. If, on examination, the epididymis is indurated and nodular, especially at the lower pole, the condition is very suspicious of tuberculosis. Thickening of the vas deferens and involvement of the prostate and seminal vesicles make the diagnosis certain. Chronicity and bilateral lesions support a diagnosis of tuberculosis while active or healed scrotal sinuses remove all doubt as does the finding of tubercle bacilli in the urine. The presence of a hydrocele in a patient with a history of tuberculosis, past or present, is suspicious that the underlying cause is epididymal tuberculosis and aspiration of its contents may on examination result in the isolation of tubercle bacilli.

Tuberculosis should also be considered a possible cause in a case of undiagnosed acute epididymitis. A history of extra-genital disease, the absence of a urethral discharge and the presence of a hydrocele are more commonly associated with tuberculosis. According to Wildbolz (1928) the acute tuberculous lesion usually occurs in a patient with a high degree of allergy found in patients with an active extra-genital tuberculous lesion and this often helps to differentiate it from a gonococcal epididymitis. In addition an acute tuberculous lesion usually forms an abscess which ruptures through the scrotum and forms a typical sinus.

New growths of the testis may cause some difficulty in differentiation from genital tuberculosis. In both conditions, the man is usually under 30 years but neoplasm is always unilateral, forms a definite mass involving the testis, either a small one or a large heavy mass obliterating all the structure to palpation, and, most important, rectal examination does not reveal any abnormality. Usually there is no history of extra-

genital tuberculous lesions but caution is necessary as the writer has seen four men with seminoma of the testis who had previous clinical tuberculosis. He also had one patient who had a history of unilateral epididymal tuberculosis proved by biopsy and who later developed a neoplasm in the testis on the other side. If there be any doubt regarding the diagnosis between tuberculosis and tumour, operation should be undertaken at once.

Pyogenic infection of the epididymis can be difficult to differentiate from tuberculosis, but a full history and careful examination and observation will help. Syphilis would appear to be rare as the writer has never seen a case but from a study of the literature on the subject, a careful case history, Wassermann reaction and the fact that a tertiary syphilitic lesion is gradual in onset and usually affects the globus major would help to make the diagnosis. In all the records of Robroyston Hospital over a period of 30 years, Foulis (1958) has only seen one syphilitic lesion and that was diagnosed as tumour and operation performed.

Cysts of the epididymis are smooth, tense and non-adherent and a history will exclude trauma and torsion of the testis while a venous thrombosis of the pampiniform plexus can often be palpated.

Chapter 8.Pregnancy and Renal Tuberculosis.

Weber (1939) reported that pregnancy was formerly considered a serious condition for a woman with renal tuberculosis, in that it often caused progression of the renal disease. It was also formerly believed that renal tuberculosis often disturbed the course of pregnancy. In the series of Cibert (1946) there were 23 pregnant women with urinary tuberculosis and apart from those with very advanced renal disease, the pregnancy ran a normal course. Cibert concluded from his study that the prognosis of co-existent renal tuberculosis and pregnancy was not necessarily poor although he felt that his favourable results were due to the fact that in most of his cases the renal tuberculosis was at an early stage.

Beskow (1952) reported 3 cases of certain co-existent pregnancy and renal tuberculosis. He felt the true number was probably higher as in some cases the renal tuberculosis gave symptoms in the form

of dysuria and increased frequency of micturition a short time after parturition and he concluded that the renal disease had probably existed during the pregnancy in these cases. In 2 of the 3 cases fever occurred in relation to parturition and unilateral tuberculous pyonephrosis was found in both; this led to nephrectomy one and two months respectively after parturition. The woman who had the operation one month after parturition died eight weeks later from meningitis. In the third woman renal tuberculosis was discovered during pregnancy and nephrectomy was carried out during the second month after which the pregnancy ran a normal course.

The number of women with co-existent pregnancy and urinary tuberculosis treated by the writer has been small, as all have been treated since an obstetrical tuberculosis unit was established in Robroyston Hospital in 1946. This unit has proved of great value as formerly women with tuberculosis who became pregnant were not welcome patients in maternity wards owing to possible danger of infection and their admission to

tuberculosis wards created difficulties when complications occurred and when the baby was born. With tuberculosis wards and maternity wards in Robroyston Hospital it was an obvious move to reserve a block where women with both conditions could be supervised by an obstetrician and a chest physician. Since 1946 hundreds of women have been successfully cared for in this unit and results have been published by Armstrong (1949) and McIntyre (1949).

The number of women with co-existent pregnancy and urinary tuberculosis supervised by the writer since 1946 has been 5. All of these women had the benefit of specific anti-tuberculosis drugs and in no case was nephrectomy carried out during the pregnancy. In 3 women there was definite disease of one kidney with associated secondary cystitis but in all three cases chemotherapy kept the disease under control until after parturition and in 2 cases nephrectomy was carried out two months later. In the third case, although the disease was initially classified as unilateral renal tuberculosis suitable for nephrectomy, no operation was

considered necessary and observation has been continued in this woman for 2 years without the necessity for interference. In an additional woman, the renal lesions were small and were kept under control by chemotherapy before and after parturition without any operation being indicated.

The last case concerned a woman of 21 years of age, who, in 1953 had a right nephrectomy and a left ureterocolic anastomosis for advanced renal disease and vesical contracture following disease and chemotherapy. In 1956 she was readmitted to Robroyston Hospital because of pregnancy and in due course she was delivered of a live child. This was followed by a normal puerperium. In October 1957, in the course of a further pregnancy, the patient was readmitted and found to be acutely ill with a history of having had no bowel movement and in consequence no obvious excretion of urine for three days. These conditions responded to the use of laxatives and chemotherapy to combat a possible pyelonephritis and resulted in her serum urea falling from 81 mg. per cent to 47 mg. per cent within 10 days. Caesarean section was performed in January 1958 and she was delivered of a live child. Her post natal condition was satisfactory apart from a low alkali reserve which was corrected by the administration of sodium citrate. Her progress to date has been satisfactory.

The writer is convinced that in the majority of cases of women who have urinary tuberculosis and are pregnant, treatment should be by conservative means in hospital, using adequate chemotherapy. Close liaison

with an obstetrician is advisable. No attempt should be made to carry out operative treatment until after parturition, unless pyonephrosis occurs during the early months of pregnancy when removal of the affected organ seems indicated. It seems certain that chemotherapy will protect a normal kidney and may heal a diseased bladder. It may also result in kidney disease becoming quiescent and making operation unnecessary. At the very least, adequate chemotherapy will prevent spread of tuberculosis and complications will not occur so that necessary operative intervention can safely be delayed until the patient has recovered from the birth of her child. In addition, McIntyre (1958) states that from many pregnant women with tuberculosis treated by all the usual drugs, he has not observed any deleterious effect on the child.

The number of cases of co-existent pregnancy and renal tuberculosis in the present series is small but the prognosis of such co-existent conditions appears to be good. On the other hand, in the writer's

experience, the prognosis of pregnancy occurring after nephrectomy for renal tuberculosis is very good, particularly since the introduction of specific chemotherapy. The number of such patients is 30 but that is almost certainly short of the real total as his follow-up records are incomplete. Prior to 1948 he tended to advise a woman to avoid pregnancy, if possible, when she gave a history of urinary tuberculosis within 5 years as so often in these women the disease was still unstable. Now, if advice is sought, permission may be given with safety if the urinary tuberculosis has been under complete control by chemotherapy and in many cases surgery, for a period of 2 years. When there is only one kidney the woman should be kept under close observation and if there is any doubt about urinary infection, tuberculous or pyogenic, the woman should be admitted to hospital.

The writer is convinced that pregnancy occurring after nephrectomy for renal tuberculosis does not, per se,

Chapter 9.Treatment of Urinary Tuberculosis:

Ten years ago Band (1948) wrote that the only curative therapy for urinary tuberculosis was nephrectomy in conjunction with the sanatorium life for six months or a year. He contended that it was only by the surgical removal of the tuberculous kidney that cessation of continued re-infection of the bladder could be brought about. Earlier Jacobs (1945) in a communication on this subject under the heading "Treatment" described at length his indications for nephrectomy. One of his aims was to remove the affected kidney before the bladder was seriously affected. Both these writers stressed the need for general sanatorium treatment because urinary tuberculosis was but a focal manifestation of a generalised infection. The general treatment was given to improve the general health and to rest any other coincidental focal manifestations of tuberculosis but there was little expectation of any improvement in an established urinary tuberculous infection apart from surgical intervention. Ljunggren (1950)

supported the plea for sanatorium care and mentioned that extra-urogenital lesions should be brought under control before any operative intervention was considered.

The treatment of urinary tuberculosis carried out in Robroyston Hospital can be considered under three main measures each of which is complimentary to the other two: general treatment, chemotherapy and surgical treatment. The writer believes that the first two measures should be used in every case and that the third, surgical treatment, should only be carried out when it has been agreed to by both the physician and by the surgeon. For many years he feels that too much emphasis has been placed on surgical removal of the affected organ, the emphasis being misplaced with regard to the timing of the operation, rather than the fact that too many operations were carried out. On the other hand, with the advent of chemotherapy, care must be exercised to ensure that surgery is not entirely neglected or left until it is too late. Surgery should still be considered as an essential part of the treatment in suitable cases and the time for intervention should be a decision made by the surgeon and physician working in close co-operation.

(a) General Treatment:

All writers on this subject were agreed that treatment by a sanatorium regimen was necessary in the days before the introduction of specific anti-tuberculosis drugs. Ross (J.C. 1953) collected information from many centres in Great Britain (including Robroyston Hospital) and he studied the results in 722 patients. He concluded from his work that since the introduction of specific chemotherapy the sanatorium regimen was still necessary. The figures from his collective investigation demonstrated quite clearly that the healing of wounds was more satisfactory in a sanatorium or tuberculosis hospital than in a general hospital. He also found that constant daily supervision of patients taking potent drugs was necessary and the sanatorium permitted the organised treatment and necessary regular and repeated investigations.

The writer is convinced that the tuberculosis hospital, properly equipped to deal with urological patients is the best place for the treatment of patients with urinary tuberculosis. When extra-urogenital tuberculous foci are present it is obviously necessary. Even for the apparently

fit patients with urinary tuberculosis the advantages of initial sanatorium care outweigh its disadvantages.

With complete clinical and laboratory facilities, the modern tuberculosis hospital is well prepared to investigate assess and guide the treatment in urinary tuberculosis.

Chemotherapy properly carried out is more complicated than many people realise. Laboratory facilities should be available at the start and during much of the treatment, since frequent examinations may be necessary the results of which may occasion alteration in treatment.

There is much to be said in favour of having a complete genito-urinary unit in a tuberculosis hospital as there is at Robroyston Hospital. The regular life under good conditions benefits all. The patients learn to appreciate the dangers of untreated tuberculosis, learn to appreciate the importance of drug treatment which may become their own responsibility after leaving hospital and they readily realise the necessity for attendance at follow-up clinics for a considerable time after hospital treatment has finished. With numbers of individuals suffering from the same condition

discipline is good and the great majority accept with equanimity the necessity of the temporary hospital life. The staff in such a unit is accustomed to the care and understanding of the tuberculosis sufferer.

The length of hospital treatment obviously depends on the clinical condition and response to treatment in any one case, but in Robroyston Hospital the average duration of stay of a person with urinary tuberculosis uncomplicated by other active tuberculous lesions is four to five months. Unless surgical intervention is urgent, and that is unusual, the patients after admission, are fully investigated, the extent and localisation of the disease classified and general treatment and chemotherapy started. Rarely is complete bed rest necessary but it has been found advantageous to employ "rest hours" as in pulmonary tuberculosis. Most patients are up for one to three hours each day and this routine is carried on for twelve weeks. At that time the full urological examination is repeated and the patient's response to three months' treatment estimated. The decision to undertake surgical treatment may be made at this time. Post-operative

convalescence usually lasts for four to six weeks after which the patient may be allowed home to continue general and drug treatment as an out-patient. If surgical treatment is not indicated the medical treatment is carried on for approximately two months by which time the patient is usually fit for dismissal to continue treatment as an out-patient. After dismissal, two three-monthly urological examinations are carried out and then the follow-up examinations at intervals of four, six and twelve months for an indefinite period.

(b) Chemotherapy:

Historical: In 1948 an investigation was started in Robroyston Hospital under the auspices of the Tuberculosis Research Unit of the Medical Research Council to determine the value of streptomycin therapy in urinary tuberculosis. At that time no definite evidence existed in this country of the effect of streptomycin in patients with urinary tuberculosis. It was decided that the trial would be a controlled one and selection of the cases for streptomycin treatment was made from a sequence of numbers taken from a statistically prepared list kept at the Medical Research Council's office where the name, age, sex and category of each patient was sent.

It was decided at the outset to group the patients into five categories:

- Group I: Unilateral renal tuberculosis - minor lesion without cystitis. (Figure 26).
- Group II: Unilateral renal tuberculosis - major lesion necessitating nephrectomy; cystitis. (Figure 27).
- Group III: Bilateral renal tuberculosis - nephrectomy for the more advanced lesion. (Figure 28.)

Group IV: Tuberculosis occurring in the remaining kidney subsequent to nephrectomy for unilateral disease. (Figure 29).

Group V: (a) Major bilateral tuberculous lesions (Figures 30 & 31).
(b) Minor bilateral tuberculous lesions (Figure 32).

These categories comprise all varieties of renal tuberculosis excepting tubercle bacilluria where there is no demonstrable renal lesion. It was considered that it would not be possible to draw any conclusions from this type of lesion.

The routine investigations carried out on every patient whether treated by streptomycin or as a control, was the same, and following the lines laid down in Chapter 4. Tests for streptomycin resistance were routine and assays of streptomycin blood levels were carried out. It will be appreciated that an investigation of this nature entailed a magnitude of work which was only possible by the combined efforts of an organised team.

The following were the members of the team:

Dr. M.A. Foulis, Physician Superintendent, Robroyston Hospital, Mr. A. Jacobs, Dr. J.C. Dick, Dr. W.M. Borthwick. Much assistance was also given by Dr. Wimsett and Dr. G. McKinlay, oto-laryngologist.

The patients treated by streptomycin were given 1 gramme daily in two intramuscular injections for ninety days. Controls and streptomycin-treated patients received similar general treatment. In all, 90 patients were included in the trial, 44 of whom were control cases and 46 were given streptomycin. Fifteen months after the start of the trial the preliminary results of six months' observation after cessation of treatment were published (Jacobs and Borthwick 1950). These results concerned 73 patients, 34 of whom had been used as control cases and 39 of whom had received streptomycin for three months. Although these results, as will be demonstrated later, were not completely satisfactory, it was soon obvious that chemotherapy was beneficial and that it was not permissible to withhold it from sufferers from urinary tuberculosis. With the introduction of para-amino salicylic acid (P.A.S.) it was decided to compare the results in patients treated with streptomycin and those after treatment with streptomycin and P.A.S. Wimsett (1952) gave results on the value of this combined chemotherapy.

Later isoniazid became available and initially the writer and his colleagues, like many others, made the mistake of using it alone in a dosage of 200 mg. daily. Dick (1953a and b) reported on the effects of isoniazid on the kidneys of 9 of the patients and following on the clinical results of isoniazid therapy alone supported by Dick's work, this form of treatment was soon given up. With the realisation that none of these drugs should be used singly came a definite planned programme, sponsored by the Medical Research Committee of the Tuberculosis Society of Scotland to determine the effects of the various combinations of streptomycin and P.A.S., streptomycin and isoniazid, P.A.S. and isoniazid and streptomycin, P.A.S. and isoniazid.

Initially streptomycin was given for three months but with experience it was found that the treatment had to be carried on for a minimum of nine months and often 18-24 months depending on the state of the disease.

As mentioned previously, a preliminary report on the value of streptomycin was given by Jacobs and Borthwick (1950).

Later, Wimsett (1952) gave results of combined streptomycin and P.A.S. treatment and in 1957 the writer gave a further account of combined chemotherapy. It is now his intention to review the results of chemotherapy to date, a period of ten years. (Figures 33 and 34). The group of patients in the streptomycin trial who were control cases and therefore were treated in exactly the same way as all the sufferers from urinary tuberculosis in the years before the introduction of anti-tuberculosis drugs, forms a basis of comparison between the results before and after the introduction of chemotherapy.

Group 1: Unilateral renal tuberculosis - minor lesion
without cystitis.

(a) Streptomycin trial:

A total of 15 patients were classified as belonging to Group 1 and of these 7 received streptomycin and 8 were control cases. (Figure 35).

Streptomycin treated patients: Of the 7 patients treated by streptomycin 6 became tubercle negative during treatment. one month after treatment one of these 6 reverted to

tubercle positive; three months after treatment another had reverted and in six months still another had become tubercle positive. Thus in a period of six months after the termination of treatment, 3 of the 6 cases which had become converted to a tubercle negative phase, reverted to a tubercle positive one. The urine of the contralateral kidney became tubercle positive during or after treatment in 3 of the 7 patients and one developed cystitis. With regard to pyelographic changes, it was found that in one case the lesion had increased, whilst in one other the cavity had tended to become shut off.

A.S. Male. Aged 44. Group 1:

The patient was admitted to hospital with a tuberculous elbow and routine examination discovered pyuria with tubercle bacilli in the urine. Urological examination showed that the disease was localised to the upper pole of the right kidney (Figure 36) with the left kidney and bladder free of disease. Three months' treatment with streptomycin was given. One month after cessation of treatment, retrograde pyelography indicated that the lesion had become shut off. (Figure 37). The pyuria had cleared and both kidney urines were tubercle negative on animal inoculation. Four months later, pyelography showed the cavity in the upper pole still shut off (Figure 38) but tubercle bacilli were again isolated in the urine from the right kidney. Eight months after treatment (Figure 39) the left kidney urine as well as the right was tubercle positive and the pyelogram suggested the appearance of a lesion connecting with the upper calyx of the left kidney.

In this case the infundibular opening into the upper group of calyces of the right kidney became constricted but the writer feels, in view of his later experience, that the duration of treatment was insufficient to ensure that the constriction was permanent, and so prevent spread to the other kidney.

Another example of the dangers of a short period of treatment and the lack of follow-up was demonstrated in the following case:

A. McC. Male: Age 27. Group 1:

Early in 1950 this patient was found to have a minimal lesion involving the right kidney without any associated cystitis. Following three months' treatment with streptomycin and P.A.S. the urine was free from bacilli although the pyelographic lesion persisted (Figure 40). The need for maintenance therapy was not appreciated at that time and the patient was dismissed to attend for three-monthly examinations. Unfortunately he changed his address and the writer was unable to trace him. Four years later he was readmitted with advanced disease of the right kidney, ureter and bladder. (Figure 41). Tubercle bacilli were present in the urinary specimens from each kidney. P.A.S. and isoniazid were given and after a month a right nephrectomy was performed. Treatment was continued for eighteen months. His condition four years later was satisfactory with no obvious disease in the left kidney and the bladder free of active disease but with some diminution of capacity.

Control cases: Of the control cases conversion of the urine to tubercle negative occurred in only one patient.

The urine of the contralateral kidney became tubercle positive in 2 of the 8 patients while 4 developed cystitis.

A deterioration of the lesion as shown by pyelograms was manifest in 4 instances.

W. McM. Male. Age 19. (Figure 42).

This patient was admitted to hospital because of tuberculous epididymitis. He had no urinary symptoms but investigation showed a small lesion at the upper pole of the left kidney. (Group 1). His name was submitted to the Medical Research Council for inclusion in the streptomycin trial and he was designated as a control case. After a period of three months it was found that the urine from the left and right kidneys contained acid fast bacilli. The lesion was unchanged in the left kidney and no pyelographic abnormality was visible in the right kidney. As the patient had also developed cystitis a left nephrectomy was carried out.

Consideration of this case some years later after experience with prolonged therapy with at least two drugs, it seems obvious that the decision to remove the whole kidney could be criticised. At the time the patient was under consideration (1949) little was known about specific chemotherapy and partial nephrectomy was not considered as a safe or suitable operation in renal tuberculosis.

Consideration of Figure 35 shows that treatment in both groups gave disappointing results. The fact that half the control cases developed cystitis within six months of observation and half showed a deterioration in pyelographic appearances whereas only one streptomycin-treated case developed cystitis and showed deterioration of the pyelograms, indicated that streptomycin probably had a beneficial effect on urinary tuberculosis. A very significant feature, not fully appreciated at the time, was the fact that 6 of the 7 cases treated by streptomycin became tubercle negative during treatment and reversion took place in half of these in the six months after treatment. It may be argued that obviously the treatment should have been continued for a period longer than three months decided in the protocol, and this would probably have resulted in improved results. Although this is known to be a true assumption on present day results, the writer would like to point out that the trial was arranged without any first hand experience of streptomycin in urological tuberculosis, with the aim of assessing its value. Results would not have been reliable or comparable if the

duration of treatment had been altered at will. Further, streptomycin was found to be a toxic drug and ten years ago the number of patients showing vestibular or cochlear damage was appreciable.

(b) Combined Therapy Results: (Figure 34).

In Group 1 there were 68 patients, 17 of whom received streptomycin and P.A.S., 9 streptomycin and isoniazid, 30 P.A.S. and isoniazid and 12 streptomycin, P.A.S. and isoniazid. The dosage used was one gramme of streptomycin, 10 grammes of P.A.S. and 200 mgm. of isoniazid daily. The duration of therapy was six months in all patients except in a few in the age groups over 45 where streptomycin was limited to four months or given three times a week in conjunction with P.A.S. and isoniazid. This alteration was made because toxic manifestations of streptomycin were more marked in patients over 45. This finding was also confirmed by Ross (J.D. 1958). After six months' treatment the majority of the patients were ready for dismissal from hospital but P.A.S. and isoniazid were continued in combination for at least a further twelve months.

The lesion in the affected kidney was demonstrable by pyelography in every case and in 21 instances it consisted of a localised cavity. These cavities ranged in size from 2 to 5 mm. in diameter. After six months' chemotherapy there was conversion of the urine in 63 of the 68 patients. Sixteen of the 63 patients in whom there was urinary conversion were in the group with definite cavitation and in every case the pyelographic lesion appeared unchanged.

M.R. Female: Age 14. (Figures 43 a and b and Figure 44).

In this girl a small irregular filling defect was exhibited at the lower pole of the right kidney (Figure 43a). Urine from the bladder and right kidney contained tubercle bacilli. The bladder mucosa was normal. (Group 1).

Streptomycin and isoniazid were given and three months later the urine was found to be negative, the filling defect persisted but its walls appeared smoother. After six months' chemotherapy the patient was discharged from hospital and received maintenance chemotherapy, P.A.S. and isoniazid, for a further year.

Six years later the urine remains free from tubercle bacilli but the filling defect persists. (Figure 34b).

Partial nephrectomy was carried out in two instances and histological examination failed to show any active tuberculosis. (Figures 45 a and b). The remaining

14 patients have been kept under observation for up to six years without showing a relapse. (Figure 43).

Five patients in the group with a definite cavity did not show conversion and nephrectomy was carried out. All five had cavities approaching 5 mm. size and histological examination showed active tuberculosis without any bacterial resistance in four but in one the organisms were resistant to streptomycin. In none did the disease spread to the bladder or contralateral kidney.

Summary: Consideration of the results of Group 1 of patients without chemotherapy, patients treated by three months streptomycin and patients treated by combined chemotherapy for six months initially and for 12 months as out-patients, shows conclusively that combined therapy offers results greatly superior to streptomycin for three months which itself is superior to general treatment alone. The chemotherapy should be continued for many months and the results in the streptomycin trial would have improved with longer treatment. Against that however, are the results given in the Medical Research Council's second interim report

on pulmonary cases treated by a single drug (Medical Research Council 1953) where it is shown that bacillary resistance is likely and it is now well recognised that single drugs should never be used.

In the isolated renal lesion without cystitis, it seems reasonable to give a combination of drugs for many months. If conversion of the urine occurs this treatment should be carried on for at least eighteen months with periodic urological examinations. It is the writer's practice to stop chemotherapy for 7-10 days before a check up examination so that reliable culture or inoculation tests may be obtained. Resistance tests are necessary but non-conversion after six months with drug-sensitive organisms usually, in the writer's experience, necessitates surgical intervention which may be limited in extent. The great majority will, however, convert to a negative urine but changes in pyelographic abnormalities seem unlikely. Under adequate chemotherapy - and there was nothing to choose between the various combinations in Group 1 patients - protection of the bladder and the contralateral kidney seems assured.

Group 2: Unilateral renal tuberculosis - major lesion
necessitating nephrectomy; cystitis.

(a) Streptomycin trial:

The affected kidney was removed soon after the initial investigation. (Figure 46).

Streptomycin cases: In the streptomycin group conversion of the urine occurred in 12 of the 14 patients. Cystitis was present in each of the 14 patients before treatment and examination after treatment showed definite signs of improvement in 11 instances. In one patient the bladder mucosa was unchanged and in two patients with severe cystitis, marked contracture of the bladder occurred soon after the start of the treatment and persisted after the prescribed course was finished. Of the 11 patients whose bladder condition improved, the initial examination had shown slight cystitis in 5, moderate cystitis in 5 and severe cystitis in 1. None of the 14 patients developed disease of the remaining kidney during the year of observation.

Control Cases: In the 10 control cases, the initial examination showed cystitis to be slight in 3, moderate in 3 and severe in 4. Conversion of the urine occurred in 2 patients who had an initial slight cystitis. In 2 of the 10 patients the remaining kidney became tuberculous.

The number showing conversion of the urine seems to be significant in the group of streptomycin-treated patients. In addition improvement in cystitis can be expected in most and there also appears to be some protection of the remaining kidney. There seems little doubt that streptomycin for three months is superior to general treatment alone.

(b) Combined Therapy Results:

In this group there were 184 patients (Figure 34) forming the largest single group and the type of lesion most frequently encountered in practice. Forty-nine patients received streptomycin and P.A.S., 28 streptomycin and isoniazid, 78 P.A.S. and isoniazid and 29 streptomycin P.A.S. and isoniazid. When first examined all the patients had cystitis and at the end of the course of treatment there was conversion of urine in all and in none was there any spread of the disease to the contralateral kidney.

When each case was classified at the primary examination it was expected that nephrectomy would be necessary in each patient and in the days before streptomycin that would have been carried out. After three months' treatment however, each patient was re-assessed and the operation was considered necessary in patients whose urine contained tubercle bacilli and where there were (1) ulcero-cavernous lesions in all three poles of the kidney; (2) a pyonephrotic kidney and (3) an apparently non-excreting kidney.

In 9 patients, partial nephrectomy was substituted for total removal of the organ (Figures 47 and 48). In one of these 9 patients wedge resection of the middle segment was carried out one year after the start of treatment because of a marked and persisting deformity. Histological examination however, failed to show any evidence of active tuberculosis and most of the deformity was found to be due to calculus material. No operation was considered necessary in a further 18 patients. Conversion of the urine had occurred in these patients and the

pyelographic appearances had shown marked alteration. (Figures 49a and b). At the initial examination it was thought that disease affected all areas of the kidney, producing marked hydrocalycosis and hydronephrosis. According to Hanley (1957) this was probably due to kinking and oedema which improved with chemotherapy and shows the value of an initial period of three months treatment before any decision regarding surgery is made.

With regard to the effect on the renal lesion no differences were observed between the four combinations but the effect on the bladder disease will be considered later.

Where no operation was carried out, chemotherapy was continued for at least 18 months. In the others the duration of the drug treatment varied between 9 and 18 months depending on the response of the bladder disease.

Summary: Considering all those in Group 2, 208 in number, it is obvious that chemotherapy has benefited greatly the patients and improved the outlook. Although the number of patients who did not receive drug treatment was small, 8 out of the 10 failed to attain urinary conversion within

a period of 6 months and in 2 of the 10 there was spread of tuberculosis to the remaining kidney. The results after three months streptomycin were better than in the untreated group but not completely satisfactory. On the other hand, combined chemotherapy for 9 to 18 months resulted in a urinary conversion rate of 100 per cent, protection of the remaining kidney in every case, reduced the number of operations, reduced the extent of some operations, and, as will be shown later, cleared cystitis in all the patients.

Group 3: Bilateral renal tuberculosis - nephrectomy for the more advanced lesion.

(a) Streptomycin trial: (Figure 50).

Patients in Group 3 had bilateral renal tuberculosis with the disease more advanced on the one side indicating removal of the kidney. The operation was the same in all cases being that of nephrectomy without ureterectomy. Twelve patients were placed in this category and 6 were given streptomycin.

Streptomycin cases: Conversion of the bladder urine from positive to negative for tubercle bacilli occurred in 3 of the 6 patients while in 4 instances conversion of the solitary remaining kidney urine occurred.

Originally the lesion in the remaining kidney was not obvious pyelographically in 3 instances, was visible as a small lesion in 2 and a moderate lesion in the remaining 1. After treatment it was found that there was no alteration in the 3 normal looking kidneys, that a small lesion had apparently disappeared in 1, a small lesion was unchanged in 1, and that the moderate lesion had shown some deterioration.

All 6 patients had cystitis before treatment and improvement after treatment was noted in 5 and unchanged in 1. The improvement amounted to a clearing of the bladder mucosa in 1 with previous slight cystitis, to slight from moderate cystitis in 4, while the 1 patient with severe bladder involvement showed no change after treatment.

Control cases: There was no example of urinary conversion in the 6 patients either in the kidney or bladder urine.

At the beginning of the control period the remaining

kidney lesions were visible by pyelography in 4 instances but could not be seen in 2. On re-examination it was found that in 2 cases an initial small focus had deteriorated and in 1 case where no lesion had been visible there now appeared a filling defect.

Cystitis was slight in 4 patients, moderate in 1 and severe in 1 before the observation period started. After the trial period the cystitis was found to be worse in 3, unchanged in 2 and slightly improved in 1.

(b) Combined Therapy Results: (Figure 34).

There were 37 patients in Group 3 who received combined chemotherapy. Nine received streptomycin and P.A.S., 4 streptomycin and isoniazid, 17 P.A.S. and isoniazid and 7 streptomycin, P.A.S. and isoniazid.

On the initial examination all were considered to have an advanced lesion on one side which necessitated nephrectomy and a smaller lesion on the other side. After three months' therapy 33 patients had a nephrectomy. In 3 instances marked pyelographic changes had occurred and no operation has been necessary so far for a period of

1-3 years. In the remaining case the lesion was found to be localised to one pole of the kidney and a partial nephrectomy was substituted for total removal.

The size of the lesion in the remaining kidney was small in 30 and moderate in 7 instances. In 5 deviation of the urine was necessary and follow-up has been difficult.

In the remaining 32 there was conversion of the urine in all but 2 where partial nephrectomy was necessary to remove a localised infective lesion. (Figure 51).

Pyelographic abnormalities have persisted in 7 patients for 2-5 years without the urine reverting to a tubercle positive result.

Summary:

Again the findings indicate the value of combined therapy over a prolonged period in protecting the remaining kidney, permitting local excisions of diseased kidney tissue and in some instances removing the necessity for operation. In the control group disease of the remaining kidney was progressive in half of the cases over a period of 6 months while in at least 7 patients after combined therapy persistent pyelographic abnormalities have been observed over a period of 2-5 years without any infection returning to the urine.

Group 4: Tuberculosis occurring in the remaining kidney
subsequent to nephrectomy for unilateral disease.

(a) Streptomycin trial: (Figure 52).

The number of patients considered in the streptomycin trial was 6, 4 of whom received streptomycin. These 4 patients all had severe cystitis and advanced disease of the remaining kidney. One man developed uraemia a fortnight after the onset of treatment and died within a week. In 2 of the remaining 3, frequency of micturition was aggravated during the course of streptomycin being sufficiently severe in 1 to necessitate transplantation of the ureter, while in the third patient there was some improvement in the frequency of micturition. In only 1 case did conversion of the urine occur.

The 2 patients who did not have streptomycin showed steady deterioration of cystitis and the pyelographic appearances.

(b) Combined therapy: (Figure 34).

Sixteen patients were placed in this group and 6 received streptomycin and P.A.S., 5 streptomycin and isoniazid and 5 P.A.S. and isoniazid.

The kidney lesions were small but definite in 8 and moderate in 8 patients. In 2 of the latter group there resulted complete occlusion of the lesion (one with streptomycin and P.A.S. and one with streptomycin and isoniazid) and these lesions have remained shut off for nine and six years respectively (Figures 53 a and b, 54 a and b). In the remaining 14 cases, with one exception the kidney lesion at the end of treatment was unchanged but the urine was free of tubercle bacilli. Partial nephrectomy was carried out in the exception and produced conversion of the urine.

Summary: The numbers are very small in this group but comparison of the streptomycin trial cases, where the results were poor, and the patients who had combined therapy for at least one year shows that the latter method offers considerable protection to the remaining kidney and if the lesion is not advanced offers reasonable prospect of control.

Group 5: (a) Major bilateral tuberculous lesions.

(b) Minor bilateral tuberculous lesions.

(a) Streptomycin trial: (Figure 55).

At the start of the investigation it was decided to subdivide Group 5 into two: 5(a) and 5(b). Patients suitable for 5(a) had major bilateral renal lesions for which no active measures were considered possible, while those eligible for 5(b) had small bilateral lesions which were visible on pyelography, thus excluding patients with excretory bacilluria.

The number of patients entered into the trial was 16, 13 in 5(a) and 3 in 5 (b). (Figure 55).

The clinical assessment of patients in Group 5 (Figure 56) presented many problems which make the results difficult to interpret and describe. Catheterisation of the ureters was impossible in many instances because of advanced bladder disease or marked changes in the ureter and moderate to advanced kidney disease often made excretory pyelograms unsatisfactory.

Two of the 8 patients treated by streptomycin died

before the urological condition was re-investigated.

One death was the result of uraemia and the other followed meningitis associated with an intracranial tuberculoma.

Of the 5 remaining cases, 4 had advanced ulcero-cavernous disease of the kidneys and no change was evident after treatment. The remaining case was a patient who, initially suffered from slight cystitis and cavities in the lower pole of one side and in the upper segment of the other. The cystitis cleared and conversion of the urine to negative for tubercle bacilli persisted for the six months follow up after treatment. With the introduction of further agents to combat tuberculosis treatment was carried on by combined drug therapy with a successful result.

The one patient in Group 5 (b) suffered from small pyelographic abnormalities associated with all the major calyces in both kidneys. (Figures 32 and 57). There was in addition slight cystitis. With three months streptomycin all specimens of urine became negative and there was no evidence of cystitis. These findings persisted for six months after cessation of treatment but once again combined

drug treatment was given as a precautionary measure.

Control cases: These numbered 6 with major lesions and 2 with small lesions. Two of the 6 with major lesions died, one due to uraemia and the other following cerebral haemorrhage. The remaining 4 all had severe cystitis with advanced renal disease. No change was evident six months after the start of observation.

Two patients with minor lesions who were control cases did not show any alteration in the cystitis after six months observation but in one the pyelographic appearances became worse.

(b) Combined therapy:

Thirty-seven patients were placed in this Group, 10 of whom received streptomycin and P.A.S., 9 streptomycin and isoniazid, 16 P.A.S. and isoniazid and 2 streptomycin, P.A.S. and isoniazid. (Figure 34).

After an initial period of treatment of six months there were 29 patients with advanced kidney disease unchanged from the first examination. The urine of 16 however, did not contain tubercle bacilli and treatment in

the form of P.A.S. and isoniazid was carried on in these patients for at least two years. In 6 others a moderate lesion on one side improved so that nephrectomy of the contralateral kidney was carried out with a good result. An additional patient had a moderate lesion which improved and became suitable for partial nephrectomy and in one other instance a nephrectomy on one side and a partial nephrectomy on the other side brought about a successful result.

Summary: Group 5 patients, those with major bilateral renal lesions, form a very severe test for any form of chemotherapy. Before the introduction of streptomycin however, the prognosis in this type of case was very poor, as in most of the patients gradual and progressive destruction of kidney tissue led to uraemia and death. A combination of drugs was used in 37 Group 5 patients in the present investigation with the results shown above and these are listed below.

In 16 patients the urine was rendered negative for tubercle bacilli after treatment by P.A.S. and isoniazid for at least two years.

In 6 patients a moderate lesion on one side improved so much that nephrectomy of the contralateral kidney became possible.

In 1 patient a partial nephrectomy, after a period of chemotherapy, was all that was necessary to produce a satisfactory result.

In 1 patient a nephrectomy on one side and later, after prolonged chemotherapy, a partial resection was possible on the other side with clinical success.

From these results it can be seen that the renal tuberculosis in 24 of the 37 Group 5 patients, 64.9 per cent, is at present under clinical control after a period of from 3 to 6 years. It seems possible therefore in over half of the patients with marked pyelographic abnormalities on both sides, to render the urine tubercle negative and keep it so for a period of years, the exact period not yet being determined as far as this series is concerned. Treatment of bilateral cases should always be undertaken and the outcome of adequate chemotherapy supplemented in some instances by surgical treatment may be very rewarding.

In 6 of the 37 patients, 16 per cent, the outcome has been complete clinical control.

Effect of chemotherapy on cystitis: (Figures 58, 59 a and b).

There is no doubt regarding the efficacy of chemotherapy on secondary cystitis. All combinations gave good results and in a patient with slight or moderate cystitis a return to normal can be expected with any of the combinations used by the writer, provided the treatment is continued for a long enough period. Even with an initial severe cystitis there is a prospect of a good result in half of the patients but this can be influenced by the choice of combination.

Figures 60 a and b give the results of chemotherapy in 75 patients who had severe cystitis. Forty-three of these patients had a combination of drugs which included streptomycin but only 12 showed a return to normal bladder mucosa and capacity. Ten of the 43 had a resultant reduction in bladder capacity while 21 of the 43 had severe and persistent bladder contracture. Thirty-two patients with severe cystitis had a combination of drugs which did not

include streptomycin. In 26 of the 32 patients at the end of six months treatment examination showed a normal bladder, while in 4 patients the mucosa was normal but the capacity of the bladder was diminished. In the remaining 2 patients there was severe bladder contracture.

Ross (J.C. 1953) in his review of 722 patients collected from all the British centres treated before the introduction of streptomycin, found that only 44 per cent showed amelioration of bladder symptoms. Practically all of these were in the Group 2 category, that is, a unilateral renal lesion with cystitis suitable for nephrectomy. There was virtually no record of symptomatic improvement in the more severe categories. Franzas (1952) in his monograph on urogenital tuberculosis in Finland before the introduction of streptomycin reported that the percentage of healed bladder tuberculosis was 67.6 (146:126) in the total number of nephrectomized patients. He did not give the figures for his whole series and it must be assumed that his 67.6 per cent was made up of patients in Group 2 since nephrectomy was not undertaken often in patients with

bilateral renal tuberculosis before the introduction of specific chemotherapy. Ljunggren (1950) also reported on the persistence of cystitis even with prolonged treatment and nephrectomy when suitable.

These results obtained in patients most of whom did not have bilateral renal tuberculosis compare very unfavourably with the results after combined chemotherapy, which include patients with all stages of renal disease. The investigation by Ross (J.C. 1953) when he collected information of cases treated before the introduction of streptomycin showed that only 44 per cent had amelioration of bladder symptoms. In the present investigation the writer found that in 251 patients out of 274, 91.6 per cent, the bladder became normal while in the remaining 23 patients, 8.4 per cent, there was severe bladder contracture but in more than half of these the disease in the bladder was later found at operation to be quiescent. From these results the writer feels that he can almost give a guarantee to a patient that the cystitis can be brought under control, but the problem of the bladder contracture must be given

consideration and the writer often warns a patient of such a possibility although he tries to avoid it by his choice of chemotherapy.

Scher (1953) reported that one of the marked complications of streptomycin and P.A.S. was extreme bladder contracture. This view receives marked support from the present series where half of the patients with severe cystitis who received streptomycin developed severe bladder contracture while only 2, or 6.25 per cent, of 32 patients with severe cystitis who did not receive streptomycin were similarly affected. (Figure 60 b). There was return to normal mucosa and capacity in only 12 out of 43 patients treated by streptomycin while 26 out of 32 patients with severe cystitis treated by a combination of drugs which did not include streptomycin became symptom free.

The writer feels that the results shown in Figure 60b are statistically significant and he avoids the use of streptomycin, if possible, for at least a period, in patients who have moderate to severe cystitis when the disease is first diagnosed.

Choice of Chemotherapy:

Reports from Liverpool, Ross et al. (1951) and Ross (J.D. 1953-56) have all been based on alternating chemotherapy. These workers used isoniazid and carbazone for six months along with P.A.S. for 25 days and then streptomycin for 35 days alternating until the end of the six months period. Later, streptomycin and isoniazid were given for two weeks, and carbazone and P.A.S. for the next two weeks. The two combinations were given alternately for two weeks for a period of six months. Band (1955) on the other hand, favoured a programme in which P.A.S. and isoniazid were given when the diagnosis was confirmed. Streptomycin was added daily for 7 days before and 14 days after operation and a combination of P.A.S. and isoniazid in cachets was continued for up to one year. Recently Walsh and Conalty (1958) and O'Flynn (1958) have advocated the use of Hinconstarch which is derived from oxidised starch and combined with isoniazid and thiosemicarbazone. These workers maintain that Hinconstarch is clinically effective, is non toxic and is a powerful anti-tuberculous drug worthy of clinical trial.

The writer has not had any experience of alternating chemotherapy in urinary tuberculosis, nor has he used Hinconstarch. Since 1948, when the controlled trial was started under the auspices of the Medical Research Council, fixed programmes have been used, first of all under the direction of the Medical Research Council, and, in later years, under the guidance of the Research Committee of the Tuberculosis Society of Scotland. By these planned programmes, series of patients in Robroyston Hospital have been treated by drug combinations which were not altered unless complications occurred. Figure 34 shows the number of patients treated by each combination. The results of this treatment have already been given.

The choice of a combination of drugs in the treatment of urinary tuberculosis should depend mainly on two things:

- (1) a knowledge of what each drug will do for tuberculous lesions in general, and
- (2) appraisal of the type of lesion in a particular case.

The latter factor may require re-appraisal after treatment has been going on for 3 to 6 months in view of the results so far achieved.

The various drugs and combinations of drugs have different effects on tuberculous lesions. The writer and his colleagues in Robroyston hospital are greatly indebted to Dr. John C. Dick, Pathologist, Stobhill Hospital, for his detailed examination of all the resected specimens from patients in the present study. Dick (1953a; 1953b; 1954; 1955) and the present writer in collaboration with Dick (1957) have reported on the results of the examination so that knowledge is available on the action of these drugs. The writer, however, is indebted to Dr. Dick for all the histological work and its interpretation.

Streptomycin:

The changes brought about in tuberculous lesions after treatment by streptomycin alone have been described by many writers. These may be summarised as follows: there is absorption of non-specific exudate, for example, in tuberculous bronchopneumonia; diffuse fibrosis, perhaps going on to hyalinisation, occurs in miliary foci and in small follicles round larger lesions; larger lesions and necrotic foci undergo fibrous encapsulation; walls of

cavities become densely fibrous sometimes with a smooth surface and the formation of a lining epithelium. These changes are found in relation to more recent lesions while old foci are not affected. All of these changes have been found in untreated patients in the natural course of the disease. (Figures 61 a and b; 62 and 63). The effect of streptomycin appears therefore to be anti-bacterial and not on the tissues, allowing the regressing processes to occur after the activity of the tuberculous process has been stopped. This results in a contracting fibrosis of the actual lesion, especially if recent, but if the lesion is old with marked fibrosis around, little improvement can be expected. (Figures 64 a and b and 65). Active areas may become quiescent but after chemotherapy has stopped any part may become active again. It appears therefore, that, as will be seen later, unlike isoniazid, no specific changes can be seen or claimed following streptomycin. The following case demonstrates what can happen when single drug treatment is given and when the duration of treatment is short.

P. McM. Male. Age 25:

Admitted to hospital because of genital tuberculosis without urinary symptoms. Investigations showed a filling defect adjacent to lower calyx (Figure 66a). Three months' streptomycin treatment was given and at follow-up examination the filling defect appeared to be shut off. (Figure 66b). Three months later the lesion had reappeared. (Figure 66c). The kidney was removed and histological examination (Figure 66d) demonstrated re-activity of follicles in calyx mucosa, rupturing to the surface. The tubercle bacilli were found to have developed drug resistance to streptomycin.

Isoniazid:

Dick (1953) described changes in tuberculous lesions in the kidneys from 9 patients who had been treated by isoniazid alone. These patients were all in Robroyston Hospital but have not been included in the present series as it was quickly realised that no one chemotherapeutic agent should be used alone. The results from that small series however, are important since they show the effect of isoniazid alone.

In the nine specimens, the macroscopic changes which followed isoniazid therapy were congestion and haemorrhages in relation to the tuberculous lesions. The microscopic changes were absorption of recent caseation, vascularisation

of all stages of tuberculous lesions, including the dense fibrosis round old lesions, and prevention of fibrosis in and around the lesions. Dick also found that open lesions showed the optimal effect after a month's treatment and retrogression was taking place after 3 months' treatment; isolated lesions however, showed more satisfactory effect after the three months' course. The regressive histological appearances in the open lesions after 3 months' treatment indicated at that time that isoniazid should not be used alone for longer than six weeks. This view was supported by the Medical Research Council's second interim report on pulmonary cases (1953) when it was found in a large series of cases, that, of the number of cases under treatment with isoniazid alone, 35 per cent showed drug resistant bacilli after 3 months' treatment.

Mackness and Smith (1952) and Suter (1952) have shown that isoniazid has a more powerful bactericidal action than streptomycin and that it kills intracellular as well as extracellular bacilli.

The following cases and specimens demonstrate the results of isoniazid therapy:

N.R. Male. Age 26.: (Figures 67 a, b, c and d).

After admission investigation showed that there was a non-excreting right kidney and a filling defect at the upper pole of the left kidney (a). After 16 days of isoniazid alone the right kidney was removed (b) and histological examination of an active cavity wall showed narrowing of the epithelioid zone with few individual cells and healthy vascular granulation tissue below. Vacuolation at the edge of the caseation and repaired tubular epithelium were also visible (c). Isoniazid and P.A.S. were then given and a retrograde pyelogram 2½ years later showed that the cavity at the upper pole of the left kidney was unchanged (d).

At present, 5 years later, the urine is still free of acid fast bacilli and the patient is well.

J.H. Female. Age 22: (Figures 68 a, b, c and d).

Renal tuberculosis localised in the upper part of the left kidney (a) without cystitis. Group 1. After 3 months' isoniazid the pyelographic appearance had so altered (b) that nephrectomy was carried out without undue delay. The macroscopic appearances of the kidney were those of extensive ulcero-cavernous tuberculosis of the upper pole with congestion; calyces and ureter showed nodules of tuberculosis, congestion and large areas of haemorrhage (c). Histological section of an epithelioid follicle in the wall of the pelvis showed rounding and absorption of epithelioid cells with increased vascularity. There was also regenerated surface of epithelium (d).

Figure 69 (a and b):

Intravenous pyelogram (a) and section of kidney (b) after 23 days' treatment with isoniazid. The ulcero-cavernous lesion forms a "cyst" at the upper pole and there is intense congestion around the tuberculous lesion.

Figure 70:

After 48 days' treatment with isoniazid, kidney with double ureter. Recent irregular ulcero-cavernous lesion at upper pole with congestion and haemorrhage, also in ureter from this pole, and extensive diffuse disease in parenchyma around it. The middle zone and lower pole lesions drained by lower ureter were more chronic with slight patchy congestion.

Figure 71:

Four weeks' isoniazid treatment. Healing cavity wall with absorption and vacuolation of caseation, epithelioid cells absorbing and no fibrosis or collagen giant cells untouched.

Figure 72:

Three months' isoniazid. Acute caseation recurring in wall already showing attempt at resolution.

Streptomycin and P.A.S.:

According to Dick (1954; 1955) streptomycin and P.A.S. given in adequate dosage cause rapid cessation of activity in spreading lesions. The lesions then proceed to the well recognised process of fibrosing in the way in which tuberculous lesions regressed under favourable circumstances before the introduction of chemotherapy. In small lesions, slight caseation in the centre may be absorbed but more often caseation occurs in larger areas and here the fibrosis of streptomycin therapy traverses this area and aids in the development of hyalinised areas. In active cavity walls fibrosis again occurs and frequently the result of 6 to 9 months' chemotherapy is a smooth-walled dense fibrous cavity in which fresh epithelium grows over the surface in a thin layer from the junction with the calyx and from the mouths of collecting tubules. This process is relatively avascular. This degree of healing occurs frequently over large parts of cavity walls, sometimes all over the affected parts. Such a result was relatively infrequent before the days of chemotherapy.

One serious drawback remains: by the time renal tuberculosis is diagnosed some of the lesions may have been present for a considerable time and are no longer active. Treatment has no effect on shaggy-walled cavities or parts of cavities with rays of epithelioid cells and fibrous tissue running into central caseation. Tubercle bacilli are frequently present in a non-active state in such cavity walls.

Lattimer et al. (1953) reported that streptomycin and P.A.S. slow the process of renal tuberculosis but rarely sterilise a lesion large enough to be visible on x-ray.

Figure 73:

Six months' streptomycin and P.A.S. Old cavity wall with smooth surfaced fibrosis and early epithelial regeneration.

Magnification x 100.

Figure 74:

Six months' streptomycin and P.A.S. Old cavity wall with smooth surface to dense fibrosis.

Magnification x 25.

Figure 75:

Eighteen weeks' streptomycin and P.A.S. Cavity wall with dense fibrosis and nodule of caseation but with renewed cavity in bottom right hand corner.

Magnification x 100.

Figure 76:

Three months' streptomycin and P.A.S. $3\frac{1}{2}$ years previously. Tubercle bacilli in caseation lying in cavity (calyx) in which wall had healed.

Magnification x 100.

Isoniazid and P.A.S.:

As with streptomycin and P.A.S. adequate dosage of isoniazid and P.A.S., according to Dick (1954; 1955), also produces almost immediate cessation of activity in spreading lesions. The active lesion is now converted into a resolving lesion with increased vascularity and small haemorrhages, removal of dead tissue and caseation and, simultaneously, a much more active regeneration of specialised tissue in the neighbourhood. In this process small tubercles completely disappear, leaving only a focus of very loose fibrous tissue and recent lesions in a calyx or small cavity wall can be completely repaired leaving only a slightly dilated calyx. In more chronic lesions if there were activity at the beginning of treatment, there is even loosening and absorption of some fibrosis leaving only a mechanical defect covered by healthy epithelium. Inactive lesions, however, are not affected by treatment.

Figure 77:

Rounding of epithelioid cells to macrophage type at edge of caseating lesion in calyx. After two weeks' isoniazid and P.A.S. Regeneration of epithelium and granulation tissue becoming non-specific.

Magnification x 150.

Figure 78:

Several small follicles, each showing rounding of epithelioid cells. Considerable surrounding round cell infiltration after 15 weeks' isoniazid and P.A.S.

Magnification x 100.

Figure 79:

Loose fibrosis at tip of calyx - ? absorbed follicles. After 5 weeks' isoniazid and P.A.S.

Magnification x 100.

Figure 80:

Fibrosis and epithelial regeneration at tip of calyx ulcer. After 4 months' isoniazid and P.A.S. (3 months streptomycin and P.A.S. previously).

Magnification x 100.

Streptomycin and Isoniazid:

Dick found that with this combination histological examination of specimens resected during the first few months of treatment shows that the isoniazid effect is predominant at this stage. After about 3 months' treatment however, resolution of active lesions has occurred and it is not possible to distinguish between the effect produced by streptomycin on the one hand and isoniazid on the other.

These findings in the kidneys correspond closely to the results found in tuberculous lungs. (Auerbach 1955; Keers, Riddell and Reid 1956).

The main conclusion is that chemotherapy is very effective against recent lesions and not effective in chronic inactive lesions with caseation which may still hold viable virulent tubercle bacilli. This stresses once again the importance of finding cases at the earliest possible stage.

Figure 81:

Four months' streptomycin and isoniazid. Group of epithelioid follicles resolved to loose granulation tissue (nothing indicative of tuberculosis) and good regeneration of tubular epithelium.

Magnification x 100.

Figure 82:

Thirteen weeks' streptomycin and isoniazid. Edge of slough with new epithelium lining healthy granulation tissue.

Magnification x 100.

Figure 83:

Ten weeks' streptomycin and isoniazid. New epithelium covering granulation tissue up to edge of desquamating tuberculous ulcer.

Magnification x 100.

Figure 84:

Four weeks' streptomycin and isoniazid. Sloughing of old caseation with new epithelium covering healthy granulation tissue.

Magnification x 100.

Conclusions:

From the clinical results of 415 patients (Chapter 9) it is obvious that chemotherapy offers a prospect of cure or control of urinary tuberculosis to the majority of patients with that disease. In spite of the great advances in the therapy of urinary tuberculosis by means of these drugs however, it is more than ever necessary to find patients as early as possible and to initiate adequate chemotherapy with the minimum of delay. The drugs must be used in combination and the four combinations under review all appear effective when used for at least nine months and probably as long as 2 years. It must be left to the individual clinician to decide on which combination to use but the writer feels that the extensive investigations of Dick and the clinical results obtained in the present series give indications which may help in that decision. The witer is of the opinion that the most effective drug at his disposal is isoniazid. Whether it should be given with streptomycin or P.A.S. or with both depends on certain

factors which are listed below. His own preference now is to use a combination of two drugs at one time in the majority of cases, the drug omitted being either streptomycin or isoniazid. These two drugs are much more powerful than P.A.S. and it is reassuring to have either streptomycin or isoniazid available if the need arises.

From the report of Dick and Stevenson (1952) on streptomycin serum levels in urinary tuberculosis in the patients treated in Robroyston Hospital, it was learned that there was no obvious rise even in advanced disease.

The choice of drugs to be used in urinary tuberculosis can thus be summarised:

1. If the organism is known to be resistant, or becomes resistant to any of the drugs, the other two will be used.
2. Intolerance to either streptomycin or P.A.S. may modify the treatment. Intolerance to isoniazid is rare.

3. If there is moderate to severe cystitis with or without ureteritis, one should avoid the use of a combination containing streptomycin thus, as far as possible preventing contracture.
4. If it is desired to close off a cavity with a narrow infundibulum, use a combination with streptomycin.
5. It is not advisable to give daily streptomycin for 9 to 18 or 24 months in view of its toxic manifestations, particularly in the older age groups (40 years plus).
6. In the presence of secondary cystitis it should be remembered that P.A.S. and isoniazid are not effective against pathogens, so that streptomycin or some other antibiotic should be used.
7. In hospital it is much easier to give streptomycin than at home and when the patients leaves hospital a combination of P.A.S. and isoniazid is more suitable for continuing treatment.

8. When P.A.S. and isoniazid are being given, it is advisable to give them in a combined form so that the patients take both or neither.
9. If P.A.S. and isoniazid are given separately the patient should be instructed on the necessity of taking both drugs.
10. If P.A.S. and isoniazid are given separately, a simple urine test for P.A.S. should be carried out periodically.

(To 1 ml. of urine add a few drops of normal hydrochloric acid and then drop by drop a ten per cent solution of ferric chloride. When P.A.S. is present (as it should be if the patient has taken the drug within the previous 24 hours) a colour change will be produced, varying from blue-black to reddish-purple according to the amount of P.A.S. present. It is to be noted that salicylates other than P.A.S., for example, aspirin, will also give the colour change.)

11. Dosage: P.A.S.: 10 grammes; isoniazid: 200-300 mgm.; streptomycin: 1 gramme daily. This last is better

than prescribing streptomycin three times a week but this may be used in patients over 40 years if streptomycin therapy is desired for a period of more than 3 months.

12. The toxicity of streptomycin, especially in the older age groups, and its administration by intramuscular injection, emphasises the desirability of using P.A.S. and isoniazid where possible.
13. The duration of chemotherapy depends on the extent and type of disease. A minimum of 9 months is necessary for a Group 2 case where cystitis is slight, but 2 years will be necessary for a lesion which is obvious on pyelography and for which surgery is not indicated.
14. Before every urological examination the drugs should be withheld for 7 days so that culture and/or animal inoculation may be carried out with prospect of a true result. Specimens for culture should be despatched to the laboratory for examination as soon as possible after collection.

Complications of Standard Chemotherapy:Streptomycin:

In a recent publication on modern drug treatment in tuberculosis Ross (J.D. 1958) states that streptomycin is excreted almost entirely by the kidneys and in the presence of renal impairment dosage should be scaled down to prevent dangerously high blood levels and the early appearance of toxic effects. That view is at variance with experience in Robroyston Hospital where special study of that problem was undertaken in the streptomycin trial sponsored by the Medical Research Council. Ninety patients were considered and streptomycin was given to 46 of these for a period of 90 days making a total dosage of 90 grammes to each patient. Dick and Stevenson (1952) reported on the results and these workers found that there was no significant rise in the streptomycin serum level with a dosage of 1 gramme per day in patients with even the most advanced bilateral renal tuberculosis.

1. Eighth nerve disturbance: Since the streptomycin trial in 1948 and up to the present all patients receiving streptomycin in Kbroyston Hospital whether for renal, pulmonary or other form of tuberculosis, are kept under close observation for signs of toxic effects. The earliest toxic symptoms are usually dizziness or difficulty in visual focussing, particularly when the patient turns his head sharply. Balance is disturbed and the patient's walk is unsteady. At that stage the patient is examined by an oto-rhinolaryngologist and if vestibular upset is found the drug is discontinued. Although impairment of vestibular function is usually permanent certain reflex mechanisms come into play to help the patient to maintain his posture. One such measure depends on eyesight so that the patient therefore is only troubled by unsteadiness in the dark. The elderly, however find more difficulty in achieving such compensation and the writer feels that streptomycin should not be used for more than a few weeks in patients over the age of forty if adequate alternate drug regimes are available.

Derangement of hearing is also a possible complication of streptomycin but fortunately it is not a common one. It is usually slow to develop and may be confined to the higher sound frequencies. Usually it does not give rise to much upset if the condition is recognised and the drug discontinued. In isolated instances however, it may be rapid in onset and deafness may be complete. It is necessary for clinicians to be aware of this possibility when using streptomycin and to ask the patient to report any unusual symptoms. The following case occurred within the first year of streptomycin being available in Robroyston Hospital and it left a lasting impression on the author.

M.A. Female: age 24.

Admitted to Robroyston Hospital with a complaint of increased frequency of micturition. After a complete urological investigation the patient was found to have urinary tuberculosis with marked right renal tuberculosis and cystitis. (Group 2). The bladder capacity was 10 oz. and an elongated ulcer $1\frac{1}{2}$ " x $\frac{1}{2}$ " with slight congestion around its edges, was seen midway between the ureteric orifices just above the ureteric ridge. At the time of diagnosis in this case the controlled streptomycin trial under the auspices of the Medical Research Council was being carried out and this patient was designated as a

control case by the Medical Research Council. After her three months' trial period her condition on re-examination was found to be unchanged. Since the allotted time had elapsed, the author was free to give streptomycin to this patient to clear up the bladder ulcer. Streptomycin was given, half a gramme twice a day. Within four weeks the frequency of micturition was very much worse and the patient complained of deafness. The drug was stopped but the increased frequency of micturition, amounting to virtual incontinence, continued and deafness became complete. After many months the contracted bladder showed no alteration and a cystogram showed its size and the reflux up the remaining ureter to the left kidney giving the appearance of a retrograde pyelogram. (Figure 85). Before dilatation of the ureter and pelvis occurred the ureter was transplanted into the pelvic colon.

The deafness has persisted and a hearing aid has had to be supplied. These events occurred during 1949-50 and the condition of the patient in 1958 is excellent. She is fully employed as a clerical worker using her hearing aid and the uretero-colic anastomosis functions very satisfactorily.

In the author's experience the above case is very unusual but it is necessary that clinicians who use streptomycin should be aware of its toxicity and not use the drug unnecessarily.

2. Hypersensitivity reactions: The patient may become sensitive to streptomycin and the common features of this are fever and drug rash. The rash is usually morbilliform or scarlatiniform in type and will disappear slowly if the drug is discontinued.

3. Contact Dermatitis: This may occur in individuals handling streptomycin and manifests itself as a scaly erythema between the fingers. It applies to nurses giving the drug and not to patients who receive it.

In the present investigation the writer excluded from the results of chemotherapy any patient in whom toxic manifestations to streptomycin occurred since that entailed cessation of the drug and the substitution of another one. In his experience with patients suffering from renal tuberculosis not more than 20 have shown vestibular dysfunction and more than half of these, 12 in number, were over 40 years of age. The result of stopping the drugs in each case brought an apparent return to normal except in four instances in people over 50, where dizziness persisted causing a certain degree of disability.

Deafness occurred in only one patient but the outcome was so marked as to impress strongly on the writer the danger of streptomycin.

Para-amino salicylic Acid (P.A.S.):

The main toxic effects of P.A.S. are:

1. Gastric upset and diarrhoea. These effects are frequent but are seldom intolerable and methods of combating them include changing the preparation of P.A.S. and symptomatic treatment.

2. Sensitivity reactions can be severe. These may be high fever and a skin rash resembling rubella. Unless the drug is discontinued the patient may become gravely ill with generalised eczema and sometimes hepatitis with jaundice.

3. Less common side-effects include lowering of blood potassium levels and lowered blood prothrombin. Swelling of the thyroid gland may occur and be associated with features of myxoedema. These features however, usually disappear when P.A.S. is stopped.

Isoniazid:

In the usual dosage of 100 mg. twice a day virtually no toxic effects are seen. With higher dosage, insomnia, muscle twitching and constipation occur. A more serious effect is peripheral neuritis which usually responds to pyridoxine, one of the B-complex vitamin preparations.

The Problem of Drug Resistance:

The potency of the anti-tuberculosis drugs has been proved but the writer feels that there should not be any complacency in their use. The possibility that the tubercle bacillus can develop the power to resist any or all of the drugs available should be borne in mind and this makes the correct use of these drugs all the more important. There are several points the writer feels which need to be re-emphasised:

1. sensitivity tests should be carried out at the beginning and frequently during treatment. Drug resistance ab initio is possible and it may result in a "one-drug" regimen being given unknown to the clinician if sensitivity tests are not done in every new case.
2. Drug regimens where streptomycin is given every second or third day may have the merit of reducing vestibular upset, but these carry a strong risk of resistance developing to the drug with which streptomycin is combined. Intermittent streptomycin therapy is probably

only safe when combined with both P.A.S. and isoniazid.

3. The patient may default in the taking of the drugs, either by carrying out "intermittent therapy" or by cutting out one, usually P.A.S. because of its side effects.

The co-operation of the patient is necessary and in this respect hospital treatment is helpful, including its educational side with regard to tuberculosis and its "talks to patients", which is a feature of some hospitals.

When P.A.S. and isoniazid are prescribed it is advantageous to have them in a single cachet so that the patient must take both or neither.

4. Care must be taken when there is interruption of treatment due to hyper-sensitivity. This need not be a reason for abandoning a drug but each case must receive careful consideration, and if advisable, the individual should be desensitised to the responsible drug.

Side effects may also interrupt treatment.

Alternative Chemotherapy:

There are drugs which are normally employed when a patient's organism is resistant to two or more of the three standard drugs. Ross (J.D. 1958) uses the term "salvage" for these drugs because their principal use is to retrieve a situation which has arisen as a rule through the injudicious use of the standard drugs.

Viomycin: The writer has only had two patients whose organisms were resistant to streptomycin and isoniazid. In both cases the patient originally had suffered from bilateral renal tuberculosis of moderate to advanced lesions. Prolonged chemotherapy with standard drugs was undertaken, followed later by nephrectomy for the worse kidney. Chemotherapy was continued but in both, after two years, bacilli were still being excreted from the remaining kidney. The bacilli were eventually discovered to be resistant to streptomycin and isoniazid. Recourse to the alternative group was then undertaken and Viomycin 1 gm. twice a day on two days per week combined with P.A.S. was given. During this therapy

excision of a localised lesion in the remaining kidney was successfully carried out in one case and is being considered at the present time in the remaining case.

From his experience in other forms of tuberculosis where the problem of drug resistant organisms is very much greater, the writer has encountered the toxic effects of viomycin which include giddiness and deafness similar to those encountered with streptomycin, upsets in body electrolyte balance, liver damage and occasionally hypersensitivity reactions. Such effects are less likely to occur with the dosage described above.

The drugs listed below have all been used by the writer in tuberculous conditions other than urinary tuberculosis.

Tetracycline and Oxytetracycline:

The broad spectrum antibiotics have a weak action on the tubercle bacillus but are capable of delaying or preventing the emergence of strains resistant to the more powerful drugs, streptomycin, isoniazid and viomycin, provided they are used in high dosage of 4 gms. daily. Vitamin B should also be given with the tetracycline group.

Pyrazinamide:

According to Ross (J.D. 1958) the combination of isoniazid and pyrazinamide is effective. The latter drug however, in therapeutic doses of 40 mg./kilo body weight per day is sometimes responsible for liver damage.

Cycloserine:

This is a highly toxic drug sometimes producing personality changes, convulsions, cardiac arrhythmias and congestive heart failure. If however, the dosage is kept at 0.25 gm. twice a day toxicity is less likely and the writer is using this drug at present to treat some patients with pulmonary tuberculosis. He has not however, had any experience of its use in urinary tuberculosis.

Thiosemicarbazone:

Ross (J.C. 1953) has used carbazone with P.A.S. for 2 weeks alternating with isoniazid and streptomycin for 2 weeks.

The writer has used thiosemicarbazone in patients with pulmonary tuberculosis but abandoned its use owing to reports of a wide variety of untoward reactions,

including anorexia, nausea and vomiting, toxic depression of the bone marrow with anaemia, destruction of red blood cells by haemolysis, skin rashes and jaundice.

It follows that the writer has not used this in urinary tuberculosis.

Steroid Hormones:

According to Ross, adrenocorticotrophic hormone (ACTH) and cortisone have many actions some of which may be valuable in the treatment of tuberculosis. Their properties include the ability to suppress the normal connective tissue response to injury, whether mechanical, clinical or bacterial.

It must be emphasised that while these hormones modify the tissue response to the tubercle bacillus they have no direct action on the bacillus itself. They cause suppression of the inflammatory reaction normally incited by the bacillus and new fibrous tissue is not laid down. The hormones, however, are never used in the treatment of tuberculosis without an adequate cover of chemotherapy for tubercle bacilli which are known to be sensitive to the drugs employed.

The writer is at present taking part in a controlled trial under the auspices of the Research Committee of the Tuberculosis Society of Scotland into the use of Cortisone in pulmonary tuberculosis. Some of his cases appear to have benefitted greatly from this combined treatment but the writer is awaiting the final results before any consideration is given to the use of steroid therapy in urinary tuberculosis. Also, he is well satisfied with the results of the present régime and has consequently not used this form of treatment in these cases. As far as he is aware no controlled trials have been reported in current literature.

In Chapter 1 the writer stated that he could not explain why the sex incidence of urinary tuberculosis, males to females, was always in the region of 5:3. He did indicate that his interest in this problem was great and that several lines of investigation were being actively considered. The use of and response to hormones, which is being investigated at the present time, in the treatment

of tuberculosis has made the writer consider the possible role of oestrogen and testosterone in the incidence and localisation of tuberculous infection, at least in some age groups.

In the absence of data from serial skin tests, it is often impossible to assess completely the state of the disease. Several patients have been treated up from 6 to 8 years in whom post-tubercular abnormalities have persisted, but the source from which the

(c) Surgical Treatment:

Introduction:

Before dealing with surgical treatment some points of difficulty may be considered.

The disappearance of bacilli from the urine by no means implies that the tuberculous kidney has healed. An active focus may have been excluded. The writer does not attribute any great significance to occasional negative culture or guinea pig inoculation results. He agrees with Obrant (1955) who uses the term "stable conversion" when the last five examinations over a period of at least four months gave negative results. "Uncertain conversion" is used when the last few examinations were negative but over a period of less than 4 months.

In the absence of acid fast bacilli in the urine after chemotherapy, it is often impossible to assess completely the state of the disease. Several patients have been followed up from 2 to 6 years in whom pyelographic abnormalities have persisted, but the urine from which has not contained tubercle bacilli. Two distinct types of lesion

have been observed. The first is where chemotherapy has resulted in a diseased calyx becoming shut off (Figure 36); in this case prolonged chemotherapy up to 2 years is necessary as in some instances where the duration was 6 months or less, the lesion re-opened and re-activation of the urinary system took place. The second type is the small persisting cavitated lesion where the urine is negative. (Figure 43). The problem here is whether partial nephrectomy should be undertaken. Six patients with this result have been followed up for 5 to 6 years without any re-activation having occurred but this was probably due to adequate and prolonged chemotherapy. Finally, a urine which is persistently positive may be due to drug-resistant organisms or to the presence of small areas of calcification nestling in the apex of a cavity imprisoning colonies of organisms.

Surgical Treatment:

Before the introduction of streptomycin the timing of the nephrectomy in the management of a patient with urinary tuberculosis was a subject of controversy.

Many surgeons endeavoured to diagnose renal tuberculosis at as early a stage as possible so as to be able to carry out nephrectomy without delay - la *néphrectomie précoce* (Chevassu 1947). There were, however, others who believed that when adequate and prolonged sanatorium treatment were available, patients should be treated conservatively for many months. Fey (1950) was convinced that the results from delayed nephrectomy were better and re-activation less likely - la *néphrectomie retardée*.

The introduction of streptomycin and later P.A.S. and isoniazid have brought about a change from these two extremes. Experience has shown that in the majority of patients the decision to operate and the type of operation to be employed, are not decisions which should be taken when the disease is diagnosed, but are more correctly taken after an initial period of conservative treatment usually lasting about three months. By that time changes may have occurred, which may influence the surgeon against operation, or may cause him to modify and lessen the originally anticipated operative procedure. In Chapter 9b the writer reported that

after three months' treatment of 184 patients in Group 2 18 patients did not require operation and 9 patients had a partial nephrectomy in place of removal of the whole organ. Nephrectomy carried out under these circumstances has been named la néphrectomie opportune. (Beaufond 1947).

Nephrectomy:

Jacobs (1945, 1951) stated that the objective of nephrectomy is to remove the focus responsible for the persistent reinfection of the bladder. The operation is seldom a matter of urgency, unless complicating factors arise. Thus a superadded pyogenic infection causing marked toxæmic symptoms or the development of a gross tuberculous pyonephrosis that might rupture or give rise to a perineal abscess would hasten the need for operation. Even under these circumstances adequate chemotherapeutic cover is usually possible. Jacobs felt that it was undesirable to lay down the indications for operation too rigidly but if there were obvious disease on one side and a normal kidney on the other, the diseased kidney or its affected part, if localised, should be removed. In bilateral renal tuberculosis, with one kidney grossly

diseased and a small lesion in the other, it is now the practice to remove the worse kidney and to rely on chemotherapy to control the smaller lesion.

The indications given by Bonnet (1955) for nephrectomy were:

- (1) when medical treatment fails:
- (2) unilateral lesion complicated by bladder involvement, and
- (3) bilateral disease where one kidney is the source of
toxaemia or haematuria.

Ljunggren (1957) reported that he carried out nephrectomy for (1) cement kidney; (2) pyonephrosis; (3) severe damage and lastly, when economic conditions were unsuitable for prolonged treatment. Hanley (1952) was also in favour of removing calcified kidneys and he felt that these were still pyonephroses.

Many surgeons advocate the routine removal of the kidney with the entire ureter down to the bladder, claiming that this hastens the resolution of secondary cystitis. Chemotherapy, in the writer's opinion, has made total ureterectomy, which requires two incisions, unnecessary in all but the few cases in which the whole ureter is

diseased or where ureteric strictures are present in the juxta-vesical portion and associated disease in the uppermost part. The more usual procedure of nephrectomy with subtotal ureterectomy through a lumbar incision gives satisfactory results. When the ureter has been mobilised to the pelvic brim, great care is taken to guard against any spilling that may occur when the ureter is divided between ligatures by the diathermy knife. As an added precaution 1 gm. of streptomycin in solution may be applied to the operation field.

Couvelaire (1952) pointed out that the ureteric stump may give rise to pyuria after the operation and before the introduction of chemotherapy the writer had experience of one such case in which a second operation was necessary to remove a ureteric stump. With proper selection of cases for operation the writer feels that this complication should not occur.

Partial Nephrectomy:

This operation has only been possible as a safe procedure in renal tuberculosis since the introduction of

chemotherapy. Opinions differ greatly on the advisability of the operation. One of the most important published series of records of partial nephrectomy for tuberculous disease was by Semb (1949) who showed that in properly selected patients the operation has a definite place in the treatment of renal tuberculosis. Lattimer (1955) reported that in his opinion 5 per cent of patients were suitable for partial nephrectomy but he felt the operation should only be done if the following conditions were fulfilled:

- (1) that all foci elsewhere were quiescent;
- (2) the lesions were confined to one area;
- (3) that intensive chemotherapy had been carried out before and planned after the operation;
- (4) that there should be minimal handling of the organ to prevent dissemination; and
- (5) that there should be most careful technique.

Band (1952) on the other hand, was not in favour of partial nephrectomy and he felt that chemotherapy offered an improved prospect. Murphy and Best (1957) stressed the dangers of partial nephrectomy, namely, haemorrhage,

fistulae and atrophy of the remaining tissue, while Cibert (1953) stated that it was a serious operation and great care was required especially with a single kidney.

The writer feels that partial nephrectomy has a definite place in the treatment of renal tuberculosis but it should be realised that the operation carries risk to the whole organ and requires skill far beyond that required for removal of the kidney. The patients selected for this operation should have renal disease localised to a segment or sometimes two segments of the kidney as demonstrated by pyelography. (Figures 45 and 47). In addition, the urine should contain drug sensitive acid fast bacilli after four months' treatment with an adequate combination as, when the urine is negative for acid fast bacilli, prolonged chemotherapy appears to be very satisfactory. (Chapter 9b). It may be argued that such patients may have small lesions elsewhere in the kidney which cannot be detected on pyelography, as is sometimes seen after nephrectomy when section of the kidney is undertaken. (Figure 18). It has been the writer's experience that tuberculosis of the kidney which

cannot be demonstrated by pyelography, for example, tubercle bacilluria, responds to chemotherapy.

Jacobs (1953) reported 12 cases in which he carried out partial nephrectomy in Robroyston Hospital. The upper segment was resected in 4 patients; the lower segment in 4, the middle segment in 3 and the upper and lower in 1 patient. Since that report Jacobs has more than doubled that number but the operation is reserved for patients whose lesion is localised and where chemotherapy has failed to bring about urine conversion. It has been of particular value in patients with bilateral renal tuberculosis where the disease has been extensive on one side and localised on the other. (Figure 51).

Vesical Contracture:

From the results of chemotherapy in urinary tuberculosis, it was found that secondary cystitis in the great majority of patients responded to adequate treatment. This response may be a return to normal bladder and function, or to a bladder free from disease but with diminished capacity which does not cause any marked disability. In a small group

of cases healing by fibrosis may lead to a bladder so contracted that the capacity does not exceed 100 mls. under anaesthesia. (Figures 85 and 86). The constant frequency of micturition, amounting in effect to incontinence, gives rise to a crippling disability which makes life intolerable to the patient. Further, the contracture of the bladder wall and the constant systole of repeated acts of micturition lead to an increasing backward pressure to the upper urinary tract, which in most instances, is a single kidney and ureter. Hydroureter and hydronephrosis occur and progressive renal failure may follow. (Figure 23). This condition, according to Band (1952) more often leads to uraemia and death than does bilateral renal tuberculosis. The author is of the opinion that if possible, surgical measures should be undertaken to help the sufferer from a contracted bladder. In his experience the condition is permanent and absolute reliance should not be placed on symptoms alone and apparent well-being of the patients. The author has had three patients who suffered from severe bladder contracture resulting in frequency of

micturition every 15 minutes. Later these patients reported an improvement in the frequency of micturition but a cystogram soon demonstrated that the apparent improvement in the bladder capacity was due to hydroureter acting as a temporary and increasing reservoir. (Figures 23 and 24).

The only methods of relieving these patients are to divert the urine from the bladder or to increase artificially the capacity of the bladder. With a remaining kidney healthy Band (1952) favours uretero-colic anastomosis but with the remaining kidney diseased he carries out cutaneous ureterostomy. Obrant (1953, 1955) prefers cutaneous ureterostomy to uretero-intestinal anastomosis while Riches (1952) favours the latter procedure. Jacobs (1954) on the other hand, reported 52 cases of urinary tuberculosis in which uretero-colic anastomosis was carried out. In 28 of his patients the transplanted ureter was from a kidney which was tuberculous. Many of these patients were treated before the introduction of chemotherapy and the operation was carried out to

relieve symptoms. Over half of the patients are still alive and 7 of them have survived from 6 to 12 years. The operations of ureterostomy and uretero-colic anastomosis do nothing to stay the progress of tuberculosis of the kidney and if the renal lesion is unsuitable for local surgery and too advanced for chemotherapy a fatal outcome is inevitable. The trouble of carrying out uretero-colic anastomosis is well rewarded by the immense relief to the patient for his remaining months or years.

The author has had little experience with patients after ureterostomy. The few he has looked after have all been well nourished and in each case difficulty was experienced in applying a water-tight collecting apparatus. Careful supervision of the apparatus was necessary and even with scrupulous hygiene no case appeared satisfactory. After uretero-colic anastomosis on the other hand, the patients soon learned to have a sufficient fluid intake and stabilisation was not difficult provided that blood electrolyte examinations were carried out at frequent intervals soon after the operation and periodically thereafter.

Cibert (1953) reported that in his opinion the operation of ileo-cystoplasty was better than uretero-colic anastomosis or cutaneous ureterostomy. Hanley (1958) also published a report in which he favoured ileo-cystoplasty while Gilvernet and Gosalvez (1957) showed a preference for using a loop of sigmoid colon in place of the loop of ileum, colocystoplasty. Jacobs (1957) now favours ileo-cystoplasty in patients with vesical contracture where there is no active bladder disease. He isolates a loop of terminal ileum and anastomoses this loop to the contracted bladder. (Figure 87). The results of these operations have been very good and a reservoir of urine of at least 16 ounces is usual, that figure being the amount which the patient holds comfortably and not the amount which can be inserted through a urethral catheter. By the end of 1958 Jacobs had carried out 18 operations of ileo-cystoplasty. To date there does not appear to be any risk of blood electrolytic imbalance.

Strictures of the Urinary Ducts:

In the era before the introduction of streptomycin tuberculous foci healed through the formation of connective

and scar tissue. This tissue showed great tendency to contract and as the author described in Chapter 9b streptomycin appeared to accelerate the formation of fibrous tissue.

If there is a defect in the kidney the most favourable form of repair is that attained when only the area affected by tuberculosis has been excluded. This is possible especially with streptomycin therapy, if one of the necks of the calyx or the communication between some of the calyces and the renal pelvis is changed into cicatricial tissue. This result, the writer feels, is often advisable and as he pointed out in Chapter 9b he would favour a combination of drugs containing streptomycin and not isoniazid in the treatment of such a case with a localised lesion, provided extra-renal lesions in the ureter or bladder did not contraindicate the stimulation of fibrous tissue.

In some cases, with small renal foci, strictures may arise in a peripheral direction, mainly at the lower end of the ureter where the duct is narrowest. (Figure 88). A stricture of the ureter may occlude a tuberculous kidney

and prevent spread to the bladder. The patient, if the contralateral kidney is normal, may be unaware of the process and the condition only diagnosed on routine examination. In others, however, mild infection may occur in the kidney and pyonephrosis may develop before obliteration of the ureter occurs. According to Franzas (1953) the tuberculous process in the kidney seems to be deferred after obliteration of the ureter and cessation of the function of the kidney. If however, the patient has only one kidney and its outflow impeded then severe hydronephrosis occurs. This will occur in a contracted bladder or in a stricture of the ureter and streptomycin may accelerate this contracture. Treatment of the contracted bladder has already been described and surgical intervention may be necessary or desirable for ureteral stricture. Couvelaire (1952A) and Lane (1955) both favour dilatation by bougies to relieve the stricture while Obrant (1955) stated that the process which fully inhibits the function of a tuberculous kidney is not necessarily the tuberculous lesion but frequently the stricture of the ureter. Obrant favoured re-implanting the

lower end of the ureter into the bladder after the stricture had been excised. Jacobs (1958) agrees with this view and he has successfully carried out the procedure in 6 patients who suffered from a tuberculous stricture.

In the author's opinion if medico-conservative treatment is started early in cases of renal tuberculosis before obvious involvement of the ureter, the onset of strictures is prevented, no matter what combination is used. If treatment is started after the occurrence of ulceration there is a great tendency to stricture formation, that tendency being more pronounced when streptomycin is used.

Chapter 10:Management of Patients with Urinary andExtra Urinary Tuberculosis:

It is difficult for the writer to particularise with regard to his opinion on the management of a patient with multiple tuberculous lesions. In general, he feels that progressive pulmonary or active bone or joint disease should have preference over intervention in urinary tuberculosis. As stated earlier the watchword should not be early nephrectomy but nephrectomy during the most suitable period and that is when other lesions are at least under control. There are however, exceptions. The pyonephrotic kidney, even in the presence of progressive pulmonary disease, should be removed as early as possible. A frequency of micturition which disturbs the patient day and night to such an extent that his general condition suffers, should also, if possible, receive treatment.

Disease of the smaller joints does not, as a rule, interfere with the management of a case. The larger joints, especially the hip, should, if possible, receive prior claim,

since instrumental investigation and operative intervention may have a deleterious effect. Spinal tuberculosis should be in a quiescent phase since the position at operation may cause damage, although in the more urgent operations on the urinary tract the writer has never recognised any such damage.

With regard to pulmonary tuberculosis, events can move with such rapidity and with such disastrous results that control of this disease should always be attempted before urological interference is undertaken. Close observation of the renal tract can be carried out without serious upset to a patient with active pulmonary disease.

The writer would not wish to give the impression that he believes renal tuberculosis to be an unimportant incident in a patient with tuberculosis. The advanced stages of this condition cause more upset and discomfort than a similar period in almost any other tuberculous lesion. He does however, feel that in a patient with pulmonary and renal tuberculosis, when both conditions are suitable for treatment, the pulmonary disease should receive prior claim,

always provided that close watch is kept on the genito-urinary condition. It is only advisable to avoid nephrectomy until the lung lesion is under satisfactory control, not to wait until so-called healing has taken place. In the individual with untreatable pulmonary tuberculosis, the author believes that all necessary steps, including major surgical procedures, are justifiable to avoid undue suffering from bladder irritability.

Chapter 11.Prognosis of Renal Tuberculosis:

One of the main reasons for the writer undertaking the present investigation was to attempt to discover whether or not chemotherapy has substantially altered the prognosis in urinary tuberculosis. Two definite periods of time were available to him, 10 years before the introduction of streptomycin and 10 years afterwards. A distinct clinical impression existed in his mind, with which all his colleagues were in agreement, that the number of patients who had died since 1948, when streptomycin was first used, was much smaller than the number of patients who died in the decade prior to 1948. Examination of the literature on this subject most of which deals with the position before streptomycin was used or shortly after it was introduced, is either very general in its facts or very complicated with regard to the number of conditions which affect the prognosis. Nesbit and his associates (1945) estimated that 50 per cent of 153 patients after nephrectomy for tuberculosis, were dead

within 15 years usually from tuberculosis but of 91 patients who did not undergo operation, 80 per cent died in an average of 3 years. Band (1948) on the other hand, reported complete recovery in about 60 per cent of his cases, which, as he stated, was comparable to the figure quoted by Thomson-Walker (1936) and Lett (1936).

Beskow (1952) stated that "the course of the tuberculous infection in a given case will depend essentially upon the natural resistance of the host to tuberculosis. The resistance is hereditary but it may be influenced by various environmental factors." When Beskow published his views in 1952 the writer would have agreed with that statement but with the increasing experience year by year of chemotherapy in all forms of tuberculosis, the significance of the various environmental factors appears to have lessened. Age, sex, heredity and social factors must be considered and taken into account with each patient but more and more does the writer realise that the prognosis in all forms of tuberculosis, including urinary tuberculosis, depends to a very great extent on the

stage of the disease when it is first diagnosed. He assumes that treatment thereafter will be adequate and properly controlled by physicians and surgeons who have experience of anti-tuberculosis chemotherapy. His faith in specific chemotherapy is such that provided destruction is not too marked before diagnosis, the likelihood of stability at least being achieved is great and it is even possible now in some cases to use the word "cure", a word which could not be used prior to 1948. The results of chemotherapy in the present series, chapter 9b, bear out the optimistic views held by the writer. Finally, in Chapter 6 on the chronological order of renal tuberculosis, it was stated that renal disease was probably the last tuberculous incident, apart from the fortuitous occurrence of meningitis, in the time-table of tuberculosis, so that a reliable and definite prognosis is possible on the state of the patient and the state of his urinary disease when it is diagnosed.

In order to determine the influence of chemotherapy on patients suffering from urinary tuberculosis the writer

decided to take two definite periods of six years, one period before the introduction of streptomycin and the other period after it became available. These periods were the years 1940-45 and 1950-55 inclusive. A very much longer follow-up was possible with the first group but it was decided to compare the results of both groups at a similar period of time and in consequence the results of treatment in these cases were assessed in 1948 and 1958 respectively, and these will be given below. The two groups were treated under the same conditions and for the same length of time, the only difference being that all of the second group received specific chemotherapy.

Period 1940-45:

In the years 1940-45 there were 150 patients, 98 males and 52 females, admitted to the Urological Unit of Robroyston Hospital, who were found to be suffering from renal tuberculosis. By 1948, 85 (56.67 per cent) of these patients were dead, 41 (27.3 per cent) were well, 10 (6.67 per cent) were probably well and 14 (9.73 per cent) were untraced. Of the 85 who were dead, 57 were males and 28 were females. The writer found it

an interesting fact that the ratio resembled the ratio of incidence, namely 5 to 3.

Subdivision of 1940-45 Male Deaths:

Detailed consideration of the 57 males who died shows that when the urinary tuberculosis was first diagnosed in hospital it was found to be bilateral in 31 and unilateral in 26.

Males: 31. Bilateral Renal Tuberculosis. (Figure 89).

The cause of death in these patients can be seen in Figure 89. Two of the men were under 20 years of age, 12 were between 20 and 29 years, 7 between 30 and 39 years and the remaining 10 were over 40 years of age when the disease was first diagnosed.

The duration of the renal disease could not be determined with accuracy in all of the patients who died of uraemia but the duration of urinary symptoms before death is shown in Figure 90.

Males: 26. Unilateral Renal Tuberculosis. (Figure 91).

Twenty-six men, who on first examination were found to suffer from unilateral renal tuberculosis, died.

The cause of death in these patients can be seen in Figure 91.

Two were under 20 years, 7 between 20 and 29 years, 10 between 30 and 39 years and 7 were over 40 years of age.

The duration of symptoms at the time of death in the 14 men who died of uraemia can be seen in Figure 92.

Subdivision of 1940-45 Female Deaths:

Consideration of the 28 females who died shows that when the urinary tuberculosis was first diagnosed it was bilateral in 16 and unilateral in 12.

Females: 16. Bilateral Renal Tuberculosis: (Figure 93)

Of the 16 women who had bilateral renal tuberculosis when the disease was diagnosed, 3 were under 20 years of age, 5 between 20 and 29 years, 4 between 30 and 39 years and 4 were over 40 years of age. The cause of death in these patients can be seen in Figure 93 and the duration of symptoms in 12 patients who died of uraemia in Figure 94.

Females: 12. Unilateral Renal Tuberculosis:(Figure 95).

Six of the females who died in this group with unilateral renal tuberculosis on first examination were between 20 and 29 years of age, 1 between 30 and 39 years,

and 5 over 40 years of age. The cause of death can be seen in Figure 95 and the duration of symptoms in 5 who died of uraemia in Figure 96.

Summary of patients admitted with renal tuberculosis 1940-45:

(Figures 97, 98, 99 and 100).

In the patients who were treated before the introduction of chemotherapy, tuberculosis of the kidney was the main cause of death. Fifty-five of the 85 patients (64.7 per cent) were due to destruction of renal tissue by tuberculosis resulting in death. That very high figure shows that tuberculosis of the kidney in the years prior to the introduction of specific chemotherapy, was a progressive disease in the majority of patients. Even with nephrectomy for a diseased kidney, in 38 of the 85 patients, the diseased process in the bladder tended to progress and judging by the duration of symptoms in these patients (Figure 100) this progress was not as slow as many would have expected.

The second highest cause of death was tuberculosis in other systems complicating renal tuberculosis, 23 (27.1 per cent)

and in all these patients the extra-urinary lesion was considered as the precipitating cause of death.

The number of the 150 patients reported well in 1948 either by direct contact or by intimation by letter (probably well) was 51 (34 per cent). In each one of these patients when urinary tuberculosis was diagnosed the renal lesion was localised to one kidney which was amenable to surgical treatment. Involvement of the bladder in each case was slight to moderate and in none was severe cystitis present. In short, they constituted good material apart from their urogenital lesions.

Period 1950-55:

The number of patients admitted to Robroyston Hospital between 1950-55 was 361, 205 males and 156 females.

Males: 205.

An assessment taken at the end of 1958 showed that 149 men (72.7 per cent) were definitely alive and well, 14 (7 per cent) were probably well, 25 (12.2 per cent) were untraced and 17 (8.3 per cent) were dead. Of the 17 patients who were dead, 7 had bilateral renal tuberculosis and 10 unilateral renal tuberculosis when the disease was first diagnosed.

Subdivision of 1950-55 Male Deaths:Males: 7. Bilateral Renal Tuberculosis:

Two of the 7 patients were between 20 and 29 years of age, 2 between 30 and 39 and 3 over 40 years of age. The cause of death and the duration of the symptoms in the 3 men who died of uraemia can be seen in Figure 101.

Males: 10. Unilateral Renal Tuberculosis:

Ten men, who had unilateral renal tuberculosis when the disease was first diagnosed, died and one was under 19

years of age, 2 between 20 and 29 years, 1 between 30 and 39 and 6 over 40 years of age. The cause of death and the duration of symptoms in the 3 men who died of uraemia can be seen in Figure 102.

Females: 156.

An assessment taken at the end of 1958 showed that of the 156 females with urinary tuberculosis admitted to hospital between 1950-55, 120 (76.9 per cent) were definitely alive and well, 15 (9.6 per cent) were probably well, 8 (5.1 per cent) were untraced and 13 (8.5 per cent) were dead. Of the 13 who died 11 had bilateral renal tuberculosis and 2 unilateral renal tuberculosis when first diagnosed.

Subdivision of 1950-55 Female Deaths:

Females: 11. Bilateral Renal Tuberculosis:

Of the 11 patients who had bilateral renal tuberculosis, 1 was under 19 years of age, 3 between 20 and 29 years, 3 between 30 and 39 years and 4 over 40 years of age. Figure 103 gives the details of these deaths.

Females: 2. Unilateral Renal Tuberculosis.

These two patients, aged 25 and 13 years, died of broncho-pneumonia and influenza respectively.

Summary of Details of patients admitted 1950-55.

(Figures 104 and 105.)

In the patients treated by anti-tuberculosis drugs the total death rate was 8.3 per cent within 8 years. Of these 12, or 3.3 per cent, were due to destruction of renal tissue resulting in uraemia and 9 of the 12 patients had bilateral renal tuberculosis before treatment was started. Non-tuberculous conditions accounted for 1.9 per cent of the total but 23.3 per cent of the deaths.

Comparison of the figures shown in Figure 106 amply confirm the clinical impression that since the introduction of chemotherapy far fewer patients with renal tuberculosis die. Even in patients with bilateral renal tuberculosis the outlook is not hopeless provided that all areas of both kidneys are not affected when the disease is first diagnosed. The patient with cystitis in this age of chemotherapy is much more fortunate than he would have been prior to 1948 and in many instances his future recovery may be due to that cystitis which compels him or his medical attendant to have a full urological examination carried out. The writer does not,

of course, wish all his patients to have cystitis but he still considers silent renal tuberculosis a menace to the patient's well being not the least because it may progress to a point when even adequate chemotherapy may be unavailing.

Finally, although it is not proof and follow-up is short, the writer knows that the results in recent years are even better than those quoted. He does not feel it necessary to improve at length the quoted results but many of those who died after chemotherapy had disease so extensive that even streptomycin and isoniazid had no chance of producing stability. In fact circumstances compelled the writer's colleagues to refer cases which only five years ago would have been regarded as poor salvage at the best. That the impression exists that some of these have been saved bodes well for the future.

Chapter 12.Additional Case Records and Examples of Treatment:J. Mc T. Male. Age 26.

This patient was admitted to Robroyston Hospital because of a strained feeling in his right leg causing him to limp for previous two months. Examination in hospital revealed a typical ilio-psoas abscess palpable medial to the right anterior superior spine. Abscess proved by aspiration. Patient had no urinary symptoms.

Complete spinal x-ray failed to show any evidence of bone tuberculosis but the x-ray revealed a calcified right kidney with an enlarged psoas shadow on that side. (Figure 107). There was no excretion from the right kidney and the left kidney appeared normal. The abscess discharged through the skin for six months in spite of streptomycin and isoniazid therapy and eventually a right pyonephrotic kidney was removed. (Figure 108). The skin sinus soon healed after the operation and convalescence was uneventful. (Figure 109).

A.O'H. Male. Age 31:

Unilateral renal tuberculosis, advanced disease of right kidney demonstrated by retrograde pyelography. (Figure 110). nephrectomy carried out and double ureter found on the right side with tuberculosis at the upper pole in relation to the upper ureter. The remainder of the kidney appeared normal as did the lower ureter. (Figure 111).

The danger in this type of case is that the ureteric catheter passes by the lower ureter and gives a normal pyelogram.

J.G. Male: Age 24:

Patient admitted with genital tuberculosis and no urinary symptoms. Investigation demonstrated what appeared to be bilateral normal kidneys but the urine contained acid fast bacilli and two ureter openings visualised on the left side of the bladder. Cystoscopy was repeated and catheters used to ascend both ureters on the left side. Retrograde pyelography demonstrated that there was renal tuberculosis in relation to the uppermost opening and the urine from it contained tubercle bacilli.

A.G. Male: Age 31:

One of the dangers and drawbacks of P.A.S. and isoniazid - tuberculosis of the kidney mixed with acute pyogenic infection. (Figure 114).

Figure 115:

Chronic pyelonephritis in a patient who had extra-urinary tuberculosis and was sent into hospital as a case of urinary tuberculosis. No urinary tuberculosis was found.

R.H. Female. Age 28: (Figure 116).

Intravenous and retrograde pyelograms taken within one day showing what could be fairly normal shadows (Figure 116a) in the one and cavitational disease of the right kidney in the other. (Figure 116b).

The right kidney was removed soon after (Figure 116c) and cavities obvious. Note also discrete tuberculous lesions in the cortico-medullary zone in the middle of the kidney.

D. McD. Male; Age 22. (Figure 117).

Unilateral renal tuberculosis localised to upper pole of left kidney. (Group 1) without cystitis (a). Three months' streptomycin given and urinary specimens negative for acid fast bacilli but pyelographic abnormality persisted. (b). Eight months later, increased frequency of micturition developed and urine from the right and left kidneys contained acid fast bacilli. Retrograde pyelogram showed a persistence of the abnormality in the left kidney (c) and nephrectomy was carried out. Kidney disease much more marked than the pyelograms indicated (d).

This is an example of streptomycin being used alone and for only three months.

Figure 118:

After 52 days' streptomycin: upper calyx irregularly ulcerated; rest of kidney shows scattered white tubercles.

Figure 119:

After 3 months' course of streptomycin alone: ulcero-cavernous lesions at tips of all calyces.

Mrs. C.W. Female: Age 45. (Figure 120).

Apparently well woman investigated and found to have a non-excreting right kidney and hydronephrosis and hydro-ureter on the left side (a). Blood urea was normal until a short time before the patient died of uraemia. Post mortem showed that the amount of kidney tissue remaining in the left kidney was small (b).

Summary:

This work is based on the writer's personal experience of 828 patients with renal tuberculosis treated in Robroyston Hospital over a period of 20 years. It is fortunate that for half of that time the author had at his disposal specific anti-tuberculosis drugs and so it was possible to compare the results of such treatment with the results which obtained in the years prior to the introduction of streptomycin.

Conclusions:

It is not possible to treat adequately patients with genito-urinary tuberculosis other than in hospital at least for a period. A combination of drugs, arrived at in the light of previous bacteriological examinations should be given for a period of nine to twenty-four months depending on the severity and extent of the disease. Hospital stay will only be necessary for part of that time, usually four to five months. Reviews must be periodic and exacting. Surgical intervention may be necessary in some patients to remove the kidney or part of the kidney when the disease has not been controlled by chemotherapy but the decision to

operate should only be taken after the effect of three months' treatment has been assessed, unless in exceptional cases.

In the writer's experience the most potent drug at his disposal is isoniazid and it is possible to give it with P.A.S. for many months without any toxic manifestations. Streptomycin on the other hand, is also a powerful anti-tuberculosis drug but it may sometimes give rise to complications, particularly in people over 40 years of age. It also encourages fibrosis which may or may not be desirable.

Finally, the prognosis in renal tuberculosis has improved immeasurably since the introduction of antituberculous drugs but the most lasting and favourable results occur through early diagnosis.

REFERENCES:

- ARMSTRONG, W. (1949) Edin. Med. J. 56. 612.
- AUERBACH, O. (1955) Amer. J. Surg. 98. 463.
- BAND, D. (1935) Edin. Med. J. 42. 162.
- " (1942) Edin. Med. J. 49. 273.
- " (1943) Post. Grad. Med. J. 19. 266.
- " (1947) 7th Cong. Inter. Soc. Urol. 128.
- " (1948) In textbook Genito Urinary Surgery
ed. by H.P. Winsbury-White. Livingstone. Edinburgh.
- " (1952-53) Trans. Edin. Med-Chir. Soc. 132. 1.
- " (1955) Proc. R. Soc. Med. 49. 1.
- BARNEY, J.D. (1936) In Modern Urology. ed. by H. Cabot
3rd ed. vol. 1. 497. Kimpton. London.
- BESKOW, A. (1952) Acta. Tuberc. Scand. Suppl. 31.
- BONNET, M. (1955) Rev. Med. de Nancy. 80. 281.
- BORTHWICK, W.M. (1945) Glas. Med. J. 26. 173.
- " (1946) Edin. Med. J. 53. 55.
- " (1948) Trans. Brit. Tub. Assoc. and Tub. Soc. Scotland.
- " (1952) Edin. Med. J. 59. 583.
- " (1957) Proc. R. Soc. Med. 50. 869.

- BORTHWICK, W.M. and DICK, J.C. (1957) *Brit. J. Clin. Prac.* 2. 665.
- BULL, P. (1925) quoted from FRANZAS.
- BUMPUS, H.C. and THOMPSON, G.J. (1928) *Surg. Gynec. Obst.* 47. 791.
- CHEVASSU, M. (1947) 7th Cong. Soc. Inter. d'Urol. 123.
- CIBERT, J. (1946) *La Tuberculose Renale.* Paris: Masson et cie.
- " (1953) *Brit. J. Urol.* 25. 89.
- " (1953A) *Brit. J. Urol.* 25. 99.
- " BRUN, J. and FERVEL, J. (1943) *J. d'Urol.* 51. 514.
- COLBY, F.H. (1940) *J. Urol.* 44. 401.
- COUVELAIRE, R. (1952) *Rev. du Praticien.* 25. 99.
- " (1952A) *J. d'Urol.* 58. 612.
- DE BEAUFOND, F.H. (1947) 7th Cong. Soc. Inter. d'Urol.
- DICK, J.C. and STEVENSON, J.S. (1952) *Brit. J. Urol.* 24. 179.
- DICK, J.C. (1953a) *J. Path. Bact.* 66. 365.
- " (1953b) *Lancet.* 1. 808.
- " (1954) *Lancet.* 2. 516.
- " (1955) *Lancet.* 2. 216.
- DIMITZA and ST. KARTAL. (1932) quoted from BAND (1948)
- DUKES, C.E. (1948) *Annal. R. Col. Surg.* 2. 299.
- DURAND, L. (1954) 48 ve. Congres Franc. d'Urol. Paris. 1.

- EMMETT, J.L. and KIBLER, J. (1938) J. Amer. Med. Ass. 111. 2351.
- EMMETT, J.L. and BRAASCH, W.F. (1938) J. Urol. 40. 15.
- FEY, B. (1950) 44th Cong. Franc. d'Urol. Paris.
- FOULIS, M.A. (1958) Personal communication.
- FRANZAS, F. (1952) Acta. Chir. Scand. Suppl. 170.
- " (1953) Acta. Chir. Scand. Suppl. 180.
- GALBRAITH, W.W. (1952) Brit. Med. J. 2. 953.
- GILVERNET, J.M. and GOSALVEZ, R. (1957) J. d'Urol. 63. 466.
- GLOOR, H.U. (1942) Schweiz med. Wchnschr. 23. 1001.
- " (1946) Schweiz. Z. Tuberk. 3. 165.
- HAWTHORNE, A.B. and SIMINOVITCH, M. (1949)
Canad. Med. Ass. J. 60. 276.
- HANLEY, H.G. (1952) Brit. J. Urol. 3. 188.
- " (1957) Proc. R. Soc. Med. 50. 877.
- " (1958) Post. Grad. Med. J. 34. 136.
- JACOBS, A. (1945) Glas. med. J. Dec. 161.
- JACOBS, A. and BORTHWICK, W.M. (1950) Proc. R. Soc. Med. 43. 453.
- " (1951) Brit. J. Tub. & Dis. Chest. Reprint. 416.
- " (1953) Brit. J. Urol. 25. 338.
- " (1954) Brit. Med. J. 1. 1340.
- " (1957) Brit. J. Urol. 3. 307.

- JACOBS, A. (1958) Personal communication.
- JUDD and SCHOLL (1924) quoted from Linden.
- KEERS, R.Y., RIDDELL, R.W. and REID, L. (1956) *Tubercle*. 37. 404.
- LANE, T.J.D. (1955) *Brit. J. Urol.* 27. 45.
- LATTIMER, J.K., LERMAN, F., LERMAN, P. and SPIVACK, L.L. (1953)
J. Urol. 69. 745.
- LATTIMER, J.K. (1955) *J. Urol.* 73. 455.
- LETT, H. (1936) *Lancet*. 2. 1313.
- LINDEN, K. (1950) *Acta. Chir. Scand. Suppl.* 153.
- LJUNGGREN, E. (1950) *Acta. Med. Scand. Suppl.* 246. 125.
- LJUNGGREN, E. and OBRANT, O. (1952) *Trans. Inter. Soc. Urol. U.S.A.*
" (1957) *Brit. J. Urol.* 29. 263.
- MACALPINE, J.B. (1949) *Cystoscopy and Urography*. 3rd ed.
Bristol; Wright.
- MACKANESS, G.B. and SMITH, N. (1952) *Amer. Rev. Tuberc.* 66. 125.
- MEDICAL RESEARCH COUNCIL (1953) *Brit. Med. J.* 1. 521.
- MEDIAR, E.M. (1926) *Amer. J. Path.* 2. 401.
" (1932) *Urol. and Cut. Rev.* 36. 71.
- McINTYRE, J.P. (1949) *Edin. Med. J.* 56. 615.
" (1958) Personal communication.

- MURPHY, J.J. and BEST, R. (1957) *J. urol.* 78. 504.
- NESBIT, R., KEITZER, W.A. and LYNN, J.M. (1945)
 J. Urol. 54. 227.
- OBRANT, O. (1953) *Studies in the Treatment of Urogenital
 Tuberculosis.* Gothenburg.
- " (1955) 27th Meeting Scand. Surg. Soc. Oslo.
- O'FLYNN, J.D. (1958) *Brit. J. Urol.* 30. 29.
- RICHES, E.W. (1952) *Modern Practice in Tuberculosis* ed. by
 T. Holmes Sellers and J.L. Livingstone. Vol 2. 413.
 Butterworths. London.
- ROLNICK, H.C. (1925) *Surg. Gynec. Obst.* 41. 15.
- " (1928) *Ibid.* 47. 806.
- ROSS, J.C., GOW, J.G. and St. HILL, C.A. (1951) *Lancet.* 1. 1033.
- " (1953) *Brit. J. Urol.* 25. 273.
- " (1953b) *Brit. Med. J.* 1. 901.
- " (1956) *Trans. European Symposium Urog. Tuberc.*
 Buergerstock.
- ROSS, J.D. (1958) *Modern Drug Treatment in Tuberculosis.*
 N.A.P.T. Publication. London.
- ROVSING, T. and RYDGAARD, F. (1925) quoted from OBRANT (1955).

- RUNEBERG, B. (1925) quoted from OBRANT. (1955).
- SCHER, S. (1953) Brit. J. Urol. 25. 103.
- SEMB, C. (1949) Acta. Chir. Scand. 98. 457.
- STEINERT, M. (1948) Modern trends in Diagnostic Radiography
ed. by T.W. McLaren. London. Butterworth.
- STIRLING, W.B. (1956) Personal communication.
- " (1957) Aortography. E & S. Livingstone Ltd.,
Edinburgh and London.
- SUTER, E. (1952) Amer. Rev. Tuberc. 65. 775.
- THOMAS, G.J.; STEBBINS, T.L. and RIGOS, F.G. (1939)
Proc. 7th Cong. Inter. Soc. Urol.
- THOMSON-WALKER, Sir J. (1936) Genito Urinary Surgery, London.
- USTVEDT, H.J. and WERGELAND, H. (1949) Acta. Tuberc. Scand. 23. 36.
- WALLGREN, A. (1948) Tubercle. 29. 245.
- WALSH, A. and CONALTY, M.L. (1958) Brit. J. Urol. 30. 25.
- WEBER, H. (1939) quoted from BESKOW.
- WELLS, C.A. (1943) Postgrad. Med. J. 19. 270.
- " (1950) Proc. R. Soc. Med. 43. 462.
- WILDBOLZ, H. (1939) Proc. Staff. Meet. Mayo Clinic. Vol. 3. 169.
- WIMSETT, W.G. (1952) Edin. Med. J. 59. 573.
- YATES BELL, J.G. (1949) J. Urol. 61. 671.

Figure 1.Sex Distribution of Renal Tuberculosis.

<u>Investigator.</u>		<u>Total No.</u>	<u>Males.</u>		<u>Females.</u>	
		<u>of Cases.</u>	<u>No.</u>	<u>Per Cent.</u>	<u>No.</u>	<u>Per Cent.</u>
Franzas (1952)	Finland:	330	229	70	101	30
Linden (1950)	Sweden:			64.5		33.6
Bull (1925)	Norway:			59		41
Judd and Scholl:	America:			63.5		36.5
Emmett and Kibler:	America:	1131		64		36
(Mayo Clinic)(1938)						
Beskow (1952)	Sweden:	228	127	57	101	44
Present Series (1958)		828	525	63.4	303	36.6

Figure 2.Age Distribution (at Diagnosis) of 828 Patients
with Renal Tuberculosis.

Years	-10	-15	-20	-25	-30	-35	-40	-45	-50	-55	-60	Total
Females:	2	13	52	88	54	38	19	17	10	7	3	303
Males:	4	23	85	101	95	76	56	29	27	18	11	525
Total:	6	36	137	189	149	114	75	46	37	25	14	828

Figure 3.

Percentage of Female and Male Patients in Different Age Groups among 828 Patients with Renal Tuberculosis.

	<u>Years:</u>		<u>-15</u>		<u>16-25</u>		<u>16-30</u>	
	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.
Females:	15	5.3	140	46.2	194	64.03		
Males:	27	5.1	186	35.4	281	53.5		
			<u>16-35</u>		<u>16-40</u>		<u>41+</u>	
	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.
Females:	232	76.6	251	82.8	37	12.2		
Males:	357	68.0	413	78.7	85	16.2		

Figure 4.

Number and Percentage of Female and Male Patients in Different Age Groups among 828 Patients with Renal Tuberculosis.

	<u>Years.</u>		<u>16-25</u>		<u>16-30</u>		<u>16-35</u>		<u>16-40</u>	
	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.
Females:	140	46.2	194	64.03	232	76.6	251	82.8		
Males:	186	35.4	281	53.5	357	68	413	78.7		
Total:	326	39.4	475	57.4	589	71.1	664	80.2		

Figure 5.Incidence of Extra-Urogenital Tuberculous Lesions (828 Patients)

	<u>Total</u>	<u>Other Lesions</u>	
		<u>No.</u>	<u>Per Cent.</u>
Females:	303	142	46.9
Males:	525	246	46.9
Total:	828	388	46.9

Figure 6.Localization of Extra-Urogenital Lesion in 388 Patients

<u>Site</u>	<u>Male.</u>	<u>Female.</u>	<u>Total.</u>
Lungs:	129	59	188.
Lungs and Bone:	14	11	25.
Lungs and Joint:	12	6	18.
Pleural Effusion:	4	2	6.
Meningitis:	3	2	5.
Acute Miliary Tuberculosis:	1	0	1.
Bone:	44	32	76.
Joint:	26	16	42.
Lymph Nodes:	10	11	21.
Multiple:	3	3	6.
	246	142	388.

Figure 7.

Interval (in years) between extra-urogenital lesion and
Diagnosis of Renal Tuberculosis in 235 Patients.

Total: Years:	1	2	3	4	5	6	7	8	9	10	10+
235. No:	21	32	32	27	21	21	17	20	1	12	31

Figure 8.

Signal symptom, if any, causing Urological Investigation
in 828 Cases of Renal Tuberculosis

Increased Frequency of Micturition	Increased Frequency & Haematuria	Pain	Painless Haematuria	Pain and Haematuria	Retention	None
434 (52.4%)	20 (2.4%)	36 (4.3%)	61 (7.4%)	27 (3.3%)	5 (0.6%)	245 (29.6%)

Total: 828 (100%)

Figure 9.

Comparison of Symptoms and Per Centage in 5 Investigations

	Bull (1925)	Rovsing & Rydgaard (1925)	Runeberg (1925)	Ravlanda (1955)	Robroyston. (1958)
Symptoms:	Per cent.	Per Cent.	Per cent.	Per Cent.	Per Cent.
Cystitis:	56	62	74	40	54.8
Haematuria:	14	6	6	13	10.6
Renal colic, Pain, retention:	20	25	16	9	5.0
No Symptoms:	10	7	4	38	29.6

Figure 10.Reason for Urological Investigation in245 Symptom-Free Patients.

	Tubercle Bacilli in Urine.	albuminuria.	Pyuria	Epididymitis	Total
Females:	35	7	11	-	53.
Males:	23	7	7	155	192.
Total:	58	14	18	155	245

Figure 11.245 Symptom-Free PatientsBilateral Renal Tuberculosis: 83.

Disease moderate to advanced: 53.

Tubercle Bacilluria: 30.

Unilateral Renal Tuberculosis: 162.

Disease moderate to advanced: 82.

Disease localised and
small extent: 70.

Tubercle Bacilluria: 10.



Figure 12.

Enlargement and calcification of right kidney. The left kidney appears normal.



Figure 13.

R.W. Male. Aged 28. Suffered from genital tuberculosis without urinary symptoms. Pyelogram shows calcification of prostate and seminal vesicles with calcification along ureters. Cystoscopy not possible without force through prostatic urethra but urine contained acid fast bacilli.



Figure 14.

C. McB. Female. aged 17. Pyelogram demonstrates cavitated lesion in left kidney. Urine from that kidney contained acid fast bacilli. Kidney removed and a single large ulcerocavernous lesion found in medulla near a major calyx.

Histology confirmed that cavity was lined by active tuberculous granulation tissue.

Right kidney appears normal.

9.



Figure 15.

Male. aged 27. Lesion at upper pole of right kidney demonstrated by retrograde pyelography. Intravenous pyelograms appeared normal. Patient had no urinary symptoms but suffered from genital tuberculosis.



Figure 16.

M.A. Female. aged 24. Retrograde cystogram showing reflux up left ureter and systolic bladder. Appearances are similar to those of retrograde pyelography.



Figure 17.

W.S. Female. Aged 21. At cystoscopy no right ureteric opening could be visualised and no excretion or kidney shadow found on intravenous pyelography. Angiography showed a right renal artery and at operation a non-excreting pyonephrotic kidney was found and removed.

11.



Figure 18.

Ulcerocavernous lesion
of upper zone; other
lesions in middle-lower
zone.

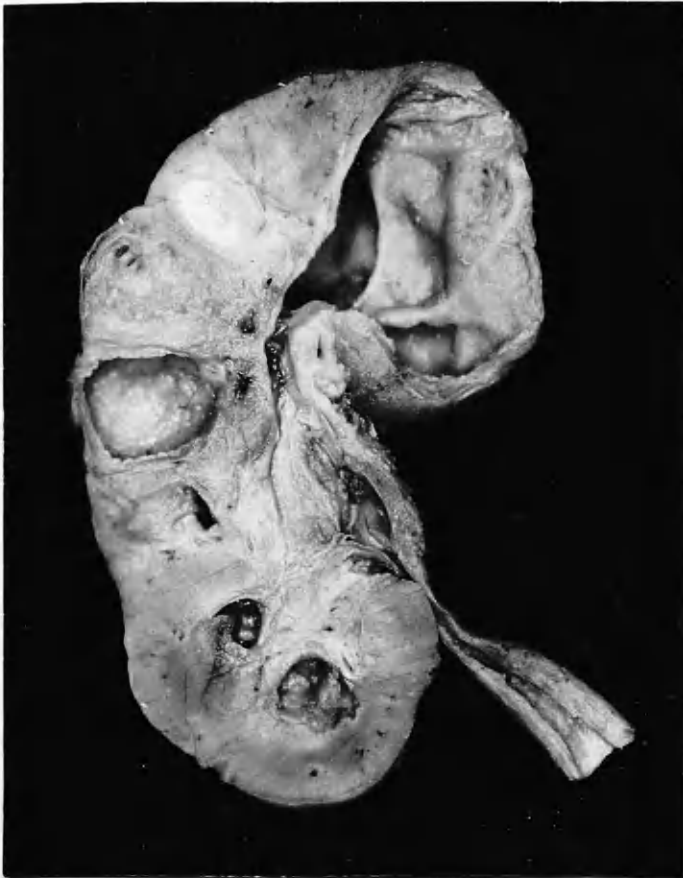


Figure 19.

Large smooth ulcerocavernous
lesion at upper
pole with smaller caseo-
cavernous lesions elsewhere.

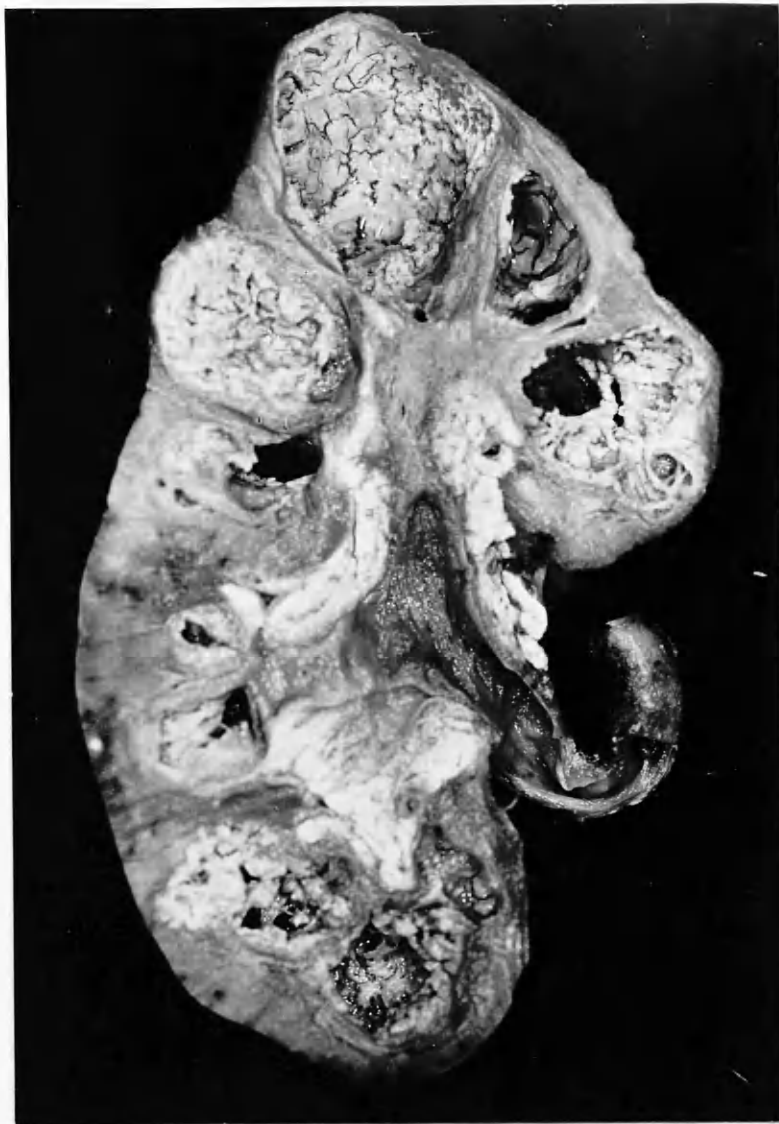


Figure 20.

Non-excreting kidney
on pyelography.
Much of kidney destroyed
and organ greatly
enlarged.

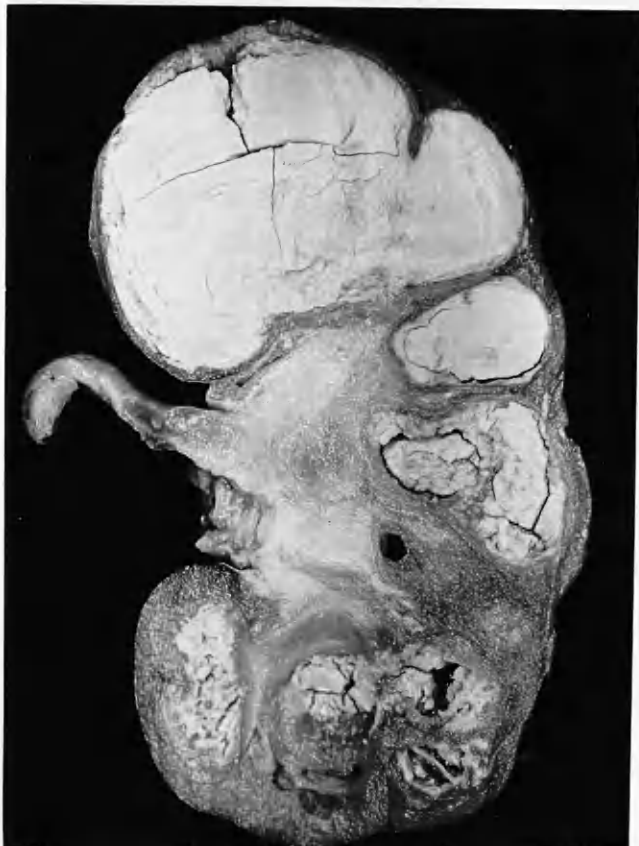


Figure 21.

Advanced lesion; kidney extensively destroyed; ureter reduced to a cord of dense fibrous tissue.



Figure 22.

Atypical moderate lesion. Mass of tuberculous granulation tissue in upper pole.



(a)



(b)

Figure 23.

M.O. Female. Aged 53.
 Bilateral renal tuberculosis;
 left kidney non-excreting
 and urine from right contained
 acid fast bacilli (a).
 Frequency of micturition
 apparently lessened but
 right hydroureter and hydro-
 nephrosis developed (b) and (c).
 Patient refused operation and
 eventually died of uraemia.



(c)



(a)

Figure 24 (a) and (b)

D. McL. Aged 20.

(a) Fairly normal right pyelogram with dilatation of lower end of the ureter.



(b)

(b) Systolic bladder with marked dilatation of ureter in the same patient. Frequency of micturition apparently improved but operation of ileo-cystoplasty considered essential to prevent destruction of kidney.

Figure 25.Genital Tuberculosis in 525 males with Renal Tuberculosis.

Total	No. with Genital Disease.	Pelvic Genital disease and Epididymitis.	Pelvic Genital disease without Epididymitis.
525	351	312	39
100%	66.9%	59.4%	7.4%

Figure 26. Group 1.

Lesion upper pole left kidney.

(No cystitis).

Figure 27. Group 11.

Advanced lesion right kidney.

(with cystitis).



Figure 18: Bilateral renal tuberculosis more advanced on right side.



Figure 29: Tuberculosis in remaining kidney. Group 4.



Figure 30: Intravenous pyelogram showing advanced bilateral renal tuberculosis. Group 5(a).

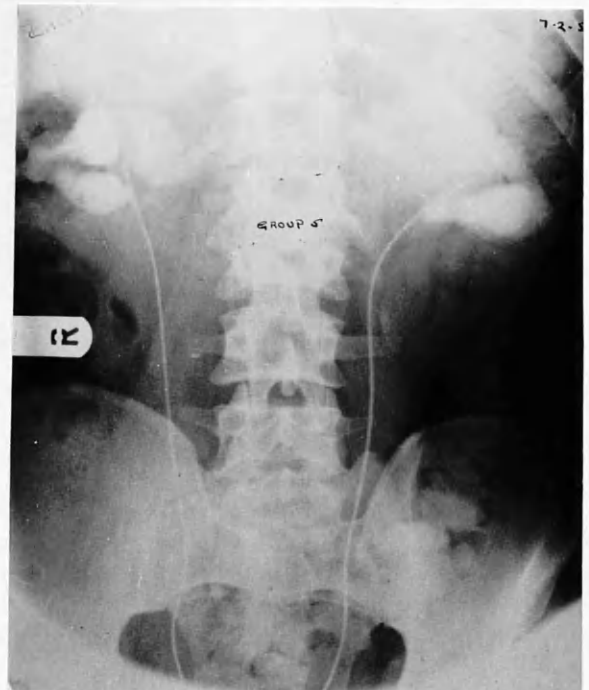


Figure 31: Retrograde pyelogram showing advanced bilateral renal tuberculosis. Group 5(a).

Figure 32.

Bilateral renal tuberculosis;
minor lesions. Group 5(b).



Figure 33.Controlled Streptomycin Trial (73).

	<u>Group 1</u>	<u>Group 2</u>	<u>Group 3</u>	<u>Group 4</u>	<u>Group 5</u>
S:	7	14	6	4	8
C:	8	10	6	2	8
Total:	15	24	12	6	16

S = Streptomycin. C = Control.

Figure 34.Initial Chemotherapy used in 342 patients with Urinary Tuberculosis

<u>Chemotherapy:</u>	<u>Group 1</u>	<u>Group 2</u>	<u>Group 3</u>	<u>Group 4</u>	<u>Group 5</u>	<u>Total.</u>
S & P	17	49	9	6	10	91.
S & H	9	28	4	5	9	55.
P & H	30	78	17	5	16	146.
S.P.& H.	12	29	7	0	2	50.
Total:	68	184	37	16	37	342.

S = Streptomycin; P = P.A.S.; H = Isoniazid.

Figure 35.Group 1.

No.	Conversion of urine for more than six months.	Developed Cystitis.	Involvement of other kidney.	<u>Pyelographic Changes</u>	
				Improved.	Worsened.
S 7	3	1	3	1	1
C 8	1	4	2		4

S = Streptomycin.

C = Control.



Figure 36: (A.S.) Bilateral retrograde pyelogram showing moth-eaten appearance of upper calyces, right kidney.



Figure 37: (A.S.) Bilateral retrograde pyelogram one month after completion of treatment. The lesion in the right kidney has apparently become shut off.



Figure 38.

A.S. Bilateral retrograde pyelogram five months after completion of treatment. The focus in the right kidney is discernible but remains occluded.



Figure 39.

A.S. Bilateral retrograde pyelogram eight months after completion of treatment. The communication with the cavity in the upper calyx is still constricted. There is now evidence of an early lesion connecting with the upper calyces in the left kidney.



Figure 40.

A. McC.: Retrograde pyelogram
after three months' treatment.



Figure 41.

A. McC.: Four years later.
No drugs; no supervision.

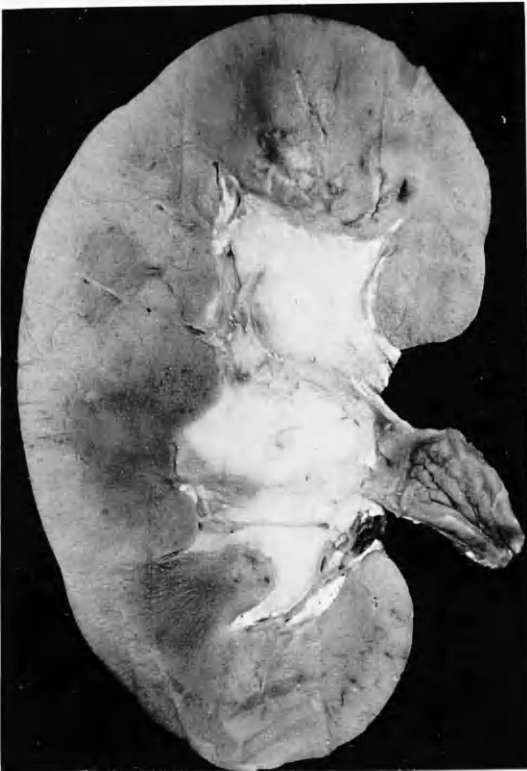


Figures 42 (a) and (b).

(a) W. McM. Group 1: Retrograde pyelogram showing isolated lesion at the upper pole of the left kidney (a).

Kidney of the same patient after removal shows two small tuberculous foci ulcerating into tips of upper calyx (b); rest of organ normal.

No specific treatment.



(b)



Figure 43: M.R. Retrograde pyelograms showing filling defect in right kidney persisting for six years.



Figure 44: Lesion persisting in left kidney although urine negative for tubercle bacilli; after 18 months' treatment.



Figure 45.

(a) Two filling defects at upper pole of right kidney (a) after treatment by P.A.S. and isoniazid. Although the right kidney urine was negative for tubercle bacilli, partial nephrectomy was carried out because of size of lesions (b). Histological examination however, failed to show any active tuberculosis.



Figure 46.Group 2.

No.	Conversion of Urine .	Cystitis			Spread to other kidney.
		Improved	Worsened	Unchanged	
S 14	12	11	2	1	0.
C 10	2	2	1	7	2.

S = Streptomycin. C = Control.

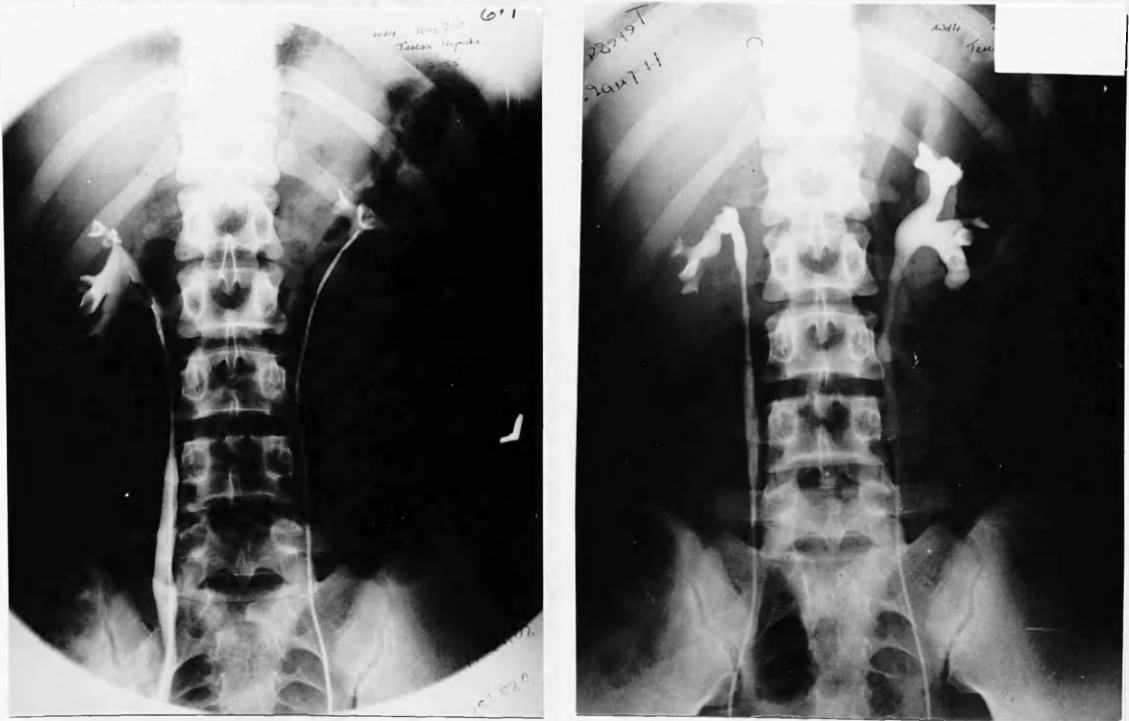


Figure 47: Group 11. Renal tuberculosis upper part right kidney;
before and after partial nephrectomy.



Figure 48: Group 11. Renal tuberculosis lower pole left kidney:
before and after partial nephrectomy.



(a)

(b)

Figure 49: (a) Intravenous pyelogram showing marked hydronephrosis of
left kidney; Group 11. (b) after combined therapy for 3 months left
kidney appears normal.

Figure 50.Group 3.

No.	<u>Conversion</u>		<u>Cystitis.</u>			<u>Kidney Lesion</u>		
	Bladder	Kidney	Improved	Worsened	Unchanged	Improved	Worsened	Unchanged.
S 6	3	4	5	0	1	1	1	4
C 6	0	0	1	3	2	0	3	3

S = Streptomycin. C = Control.

Figure 51.

Bilateral renal tuberculosis. Right nephrectomy was carried out followed later by resection of the lower segment of the left kidney. After treatment by streptomycin and isoniazid there was marked vesical contracture which necessitated uretero-colic anastomosis. Follow-up x-rays difficult to obtain but patient is very well, and working as a nurse.

Figure 52.Group 4.

No.	<u>Conversion</u>		<u>Cystitis.</u>			<u>Kidney Lesion.</u>		
	Bladder	Kidney	Improved	Worsened	Unchanged	Improved	Worsened	Unchanged.
S 4	1	-	1	2	-	-	-	3
C 2	0	-	-	2	-	-	2	-

S = Streptomycin.

C = Control.



(a)



(b)

Figure 53:(a)Tuberculosis occurring in the remaining kidney; prognosis thought to be poor. Streptomycin and isoniazid given and lesion became shut off (b). Lesion has remained shut off for six years and patient very well and working. No abnormality found on blood and general examination.



(a)



(b)

Figure 54: Tuberculosis in the solitary kidney (a). Treated by streptomycin and P.A.S. and lesion became shut off and has remained so for almost 10 years. Patient very well and working.

Figure 55.

Group 5.

No.	Major Lesion		Minor Lesion	
	5A	Died.	5B	Died.
S 8	7	2	1	0
C 8	6	2	2	0

S = Streptomycin. C = Control.

Figure 56.Group 5A.

No.	Conversion of bladder and kidney urine.	Cystitis.		Kidney Lesion	
		Improved	Unchanged	Improved	Unchanged.
S 5	1	1	4	1	4
C 4	0		4		4

Group 5B.

No.	Conversion of bladder and kidney urine.	Cystitis.		Kidney Lesion.	
		Improved	Unchanged	Improved	Unchanged
S 1	1	1	-	-	1
C 2	0	-	2	1	1

S = streptomycin.

C = Control.

Figure 57:Group 5B: Follow-up of plate (Fig.32).

Both kidney urines became negative after streptomycin for three months. Treatment later supplemented by P.A.S. and isoniazid and patient has remained well for about 10 years.

Figure 58.

Number of patients treated by combined chemotherapy (Fig. 34)	342.
Number of Group 1 patients (no cystitis):	68.
Total number of patients with initial cystitis:	274.

Figure 59 (a).Effect of Chemotherapy on Cystitis in 251 Patients.

Group.	No.	Slight cystitis to Normal mucosa.				Moderate cystitis to normal mucosa.				Severe cystitis to normal mucosa.			
		SP.	SH.	PH.	SPH.	SP.	SH.	PH.	SPH.	SP.	SH.	PH.	SPH.
2	174	21	10	34	17	13	9	24	10	8 (6)	7 (3)	19 (2)	2
3	31	4	3	6	3	2	0	6	2	0	0	4	1 (1)
4	15	2	2	1	0	3	1	4	0	1	1	0	0
5	31	6	3	4	1	1	2	5	0	1	1	7 (2)	0
Total:	251	33	18	45	21	19	12	39	12	10	9	30	3

Figures in parenthesis represent number with diminished bladder capacity.

Figure 59 (b).Effect of Chemotherapy on Cystitis in 23 Patients.

Group.	No.	Severe cystitis to severe bladder contracture.			
		SP.	SH.	PH.	SPH.
2	10	7	2	1	0
3	6	3	1	1	1
4	1	0	1	0	0
5	6	2	3	0	1
Total:	23	12	7	2	2

S = Streptomycin; P = P.A.S.; H = Isoniazid.

Figure 60 (a)Effect of Chemotherapy in 75 Patients with Severe Cystitis.

Chemotherapy.	No.	Normal mucosa and capacity after treatment.	Normal mucosa with diminished capacity.	Severe bladder contracture.
SP	22	4	6	12
SH	16	6	3	7
PH	32	26	4	2
SPH	5	2	1	2

S = Streptomycin; P = P.A.S.; H = Isoniazid.

Figure 60 (b)Effect of Chemotherapy in 75 Patients with Severe Cystitis.

Chemotherapy	Condition of Bladder after Treatment.					
	Normal		Diminished Capacity.		Severe Contracture.	
	No.	Per Cent.	No.	Per Cent.	No.	Per Cent.
Combination including streptomycin: (43 Patients)	12	28	10	23.3	21	48.8
Combination not including streptomycin: (32 Patients)	26	81.25	4	12.5	2	6.25

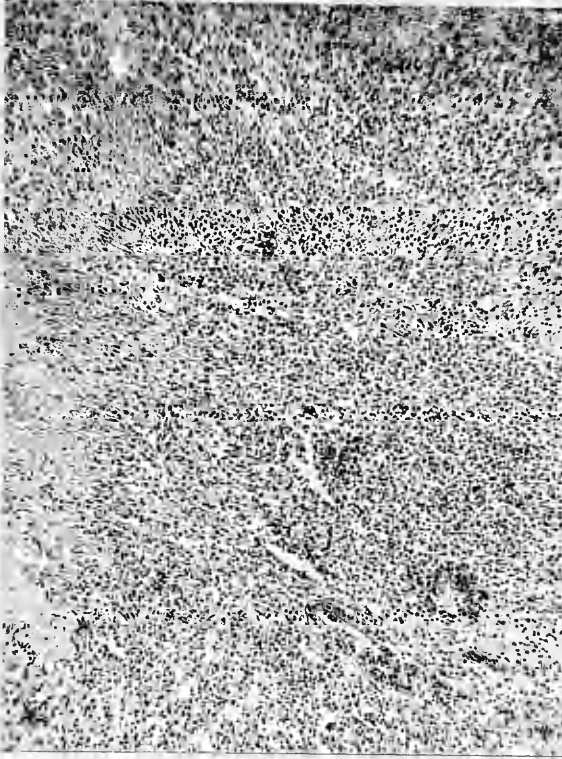


Figure 61(a)

W. McM. (Figure 42).
 Edge of cavity - broad zone
 of acute tuberculous
 granulation tissue with
 caseation to the left and
 some toxic tubules at the top;
 cells are lymphocytes and
 epithelioid - avascular.
 Magnification x 100.
 No specific treatment.



Figure 61(b)

W. McM. (Figure 42).
 Same as above but early
 follicle seen although no
 caseation.
 Magnification x 100.
 No specific treatment.

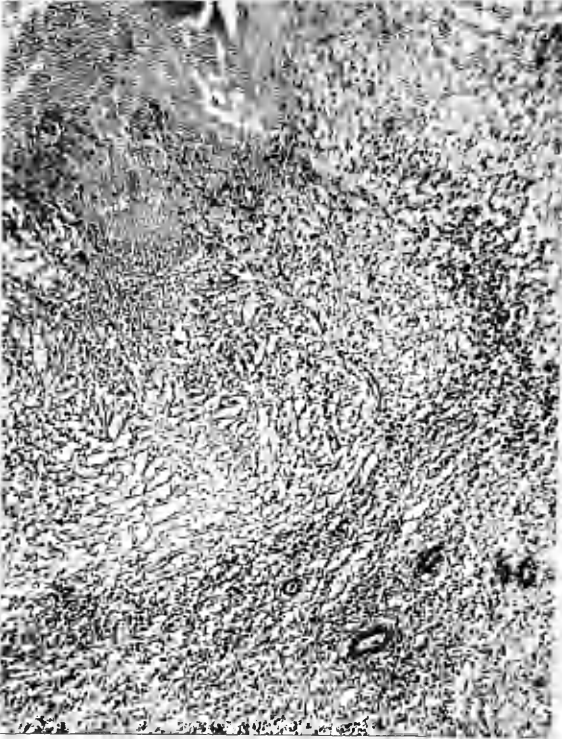


Figure 62.

(Section from specimen
Figure 21).

Fibrosis in tuberculous
granulation tissue, changing
from perpendicular to
parallel to wall of cavity.

Magnification x 100.

No specific treatment.

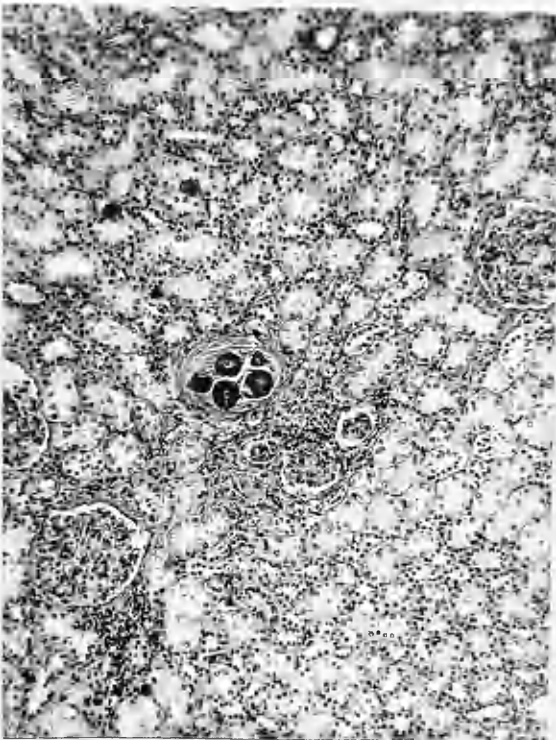
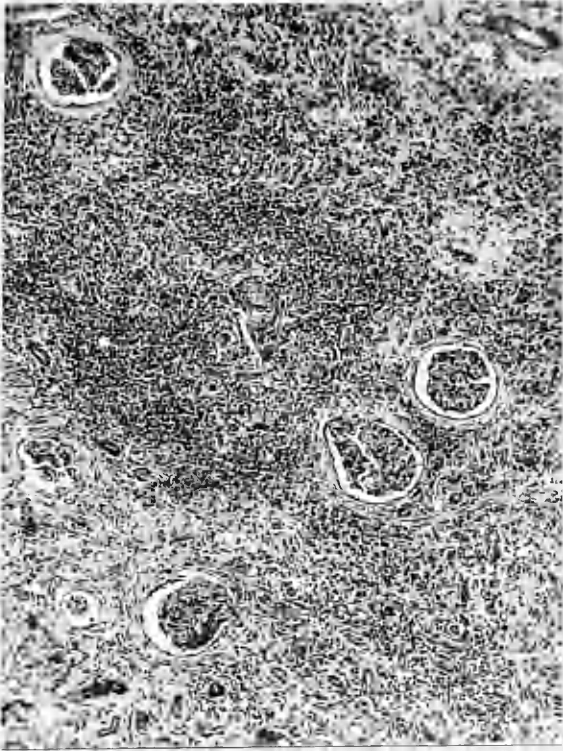


Figure 63.

Densely fibrosed follicle
identified by concentric
laminated bodies;
(many follicles at all stages
from acutely caseating to
this degree of fibrosis found
in the kidney).

Magnification x 100.

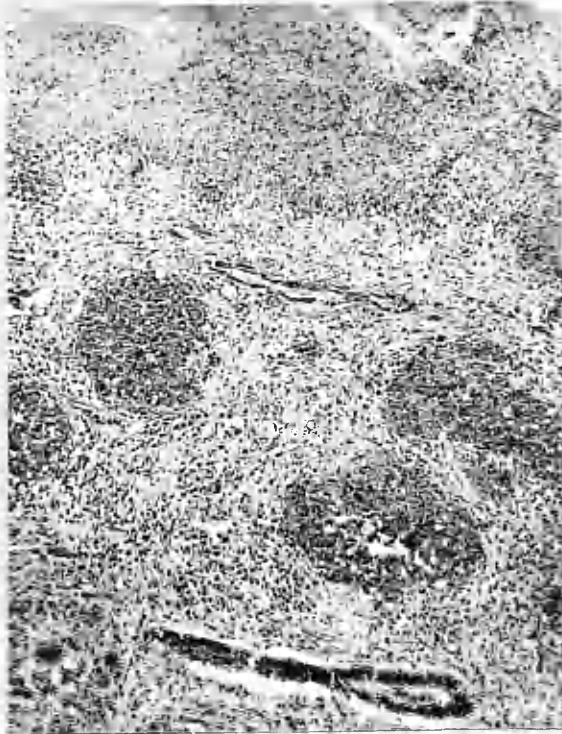
No specific treatment.



(a)

Figure 64 (a)

A.S. (Figures 36-39).
 Follicle almost obliterated
 by fibrosis. Marked round
 cell infiltration from
 secondary pyelonephritis.
 Three months' streptomycin
 2 years previously.
 Magnification x 100.



(b)

Figure 64 (b)

A.S. (Figures 36-39).
 Edge of cavity showing dense
 fibrosis, above, around and
 deep to individual follicles
 which are compressed, one with
 slight absorption of caseation.
 Three months' streptomycin
 2 years previously.
 Magnification x 100.

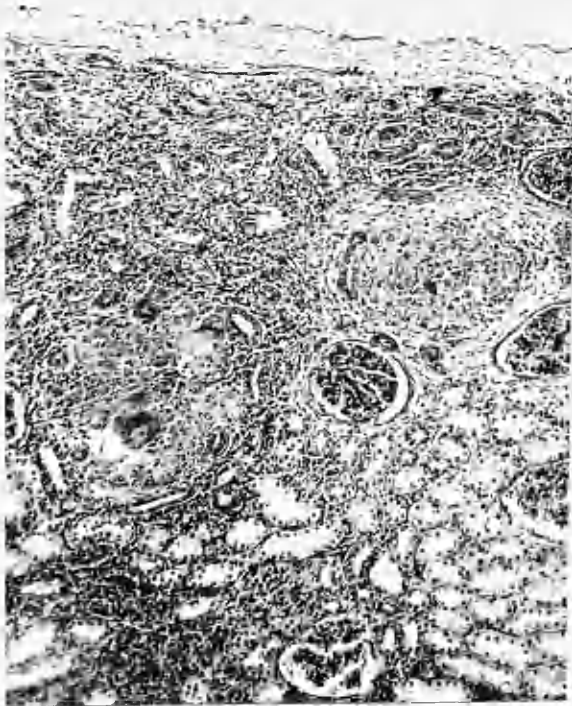


Figure 65.

(X-ray of lesion: Figure 51): Two follicles, one with marked fibrosis and the other with giant cells and slight fibrosis, still easily recognisable as tuberculous.

After six months' streptomycin.

Magnification x 100.

Figure 66



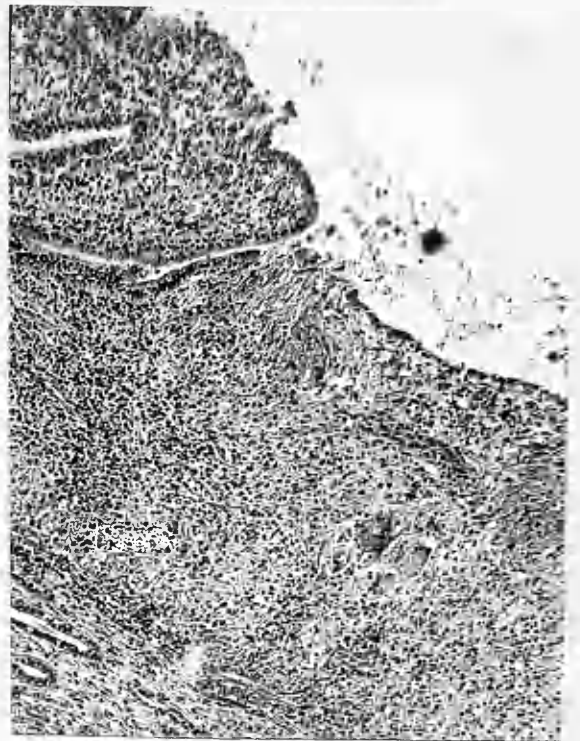
(a)



(b)



(c)



(d)

39.

Figure 67.



(a)



(b)



(c)



(d)

Figure 68.



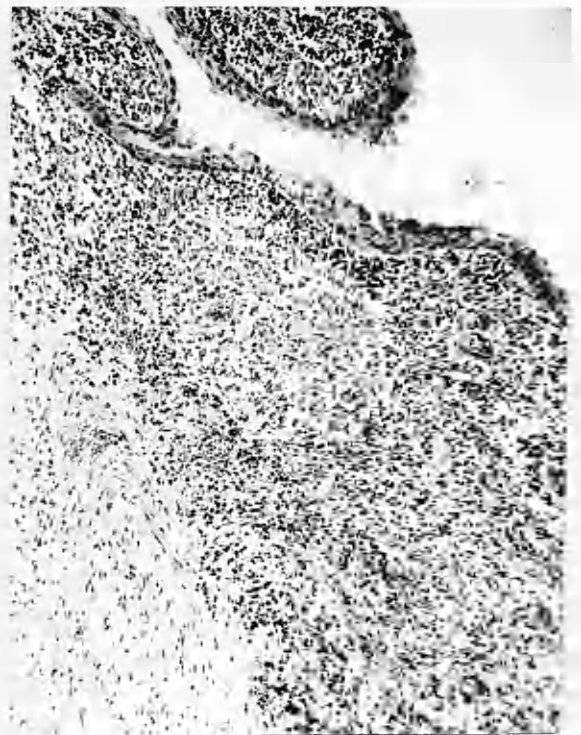
(a)



(b)



(c)



(d)

41.

Figure 69.



(a)



(b)

Figure 70.



Figure 71.



Figure 72.

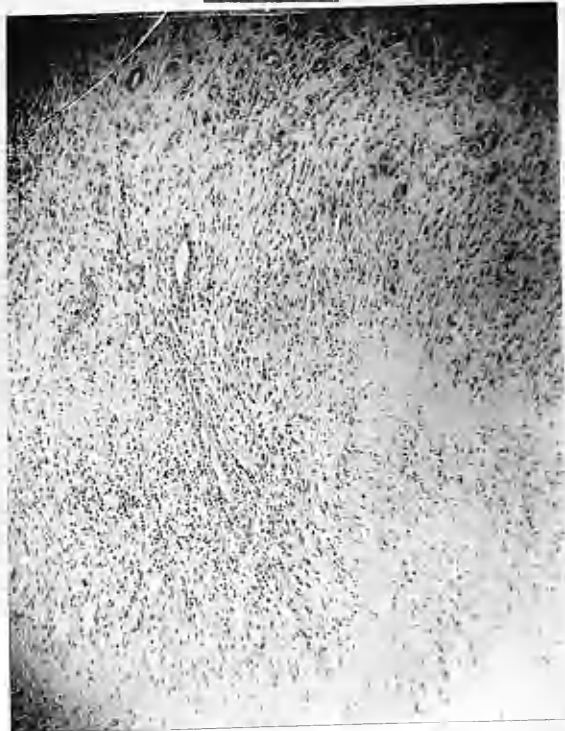


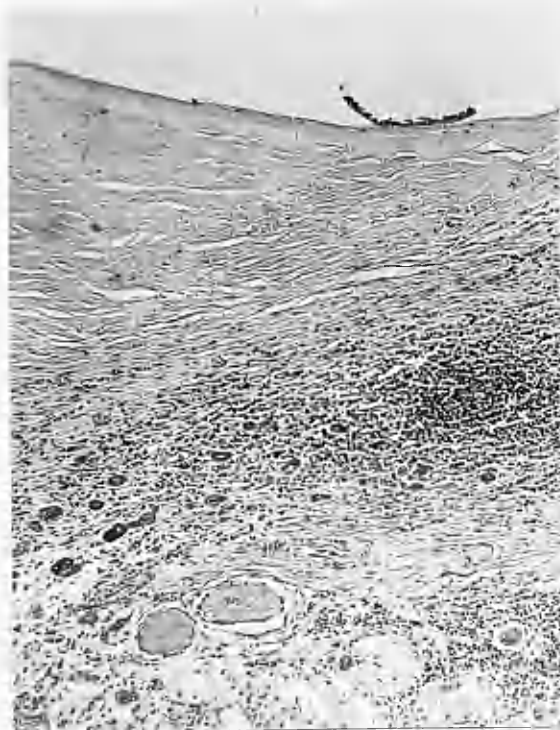
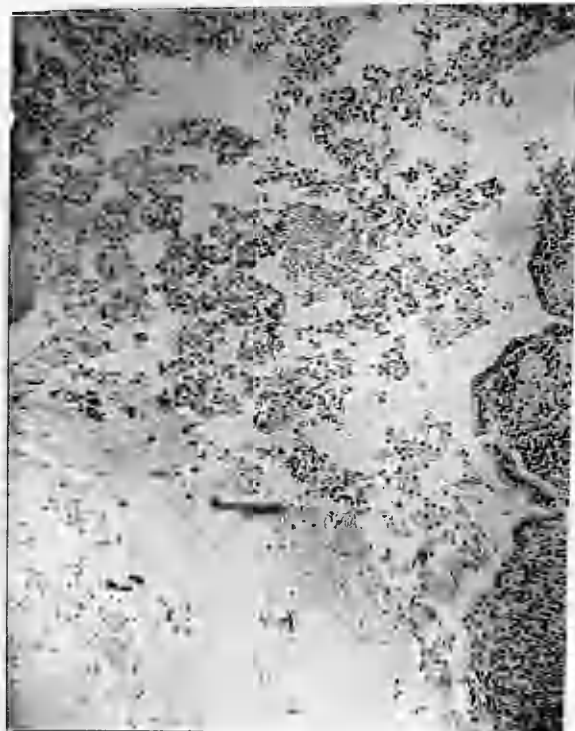
Figure 73.Figure 75.Figure 74.Figure 76.

Figure 77.



Figure 78.

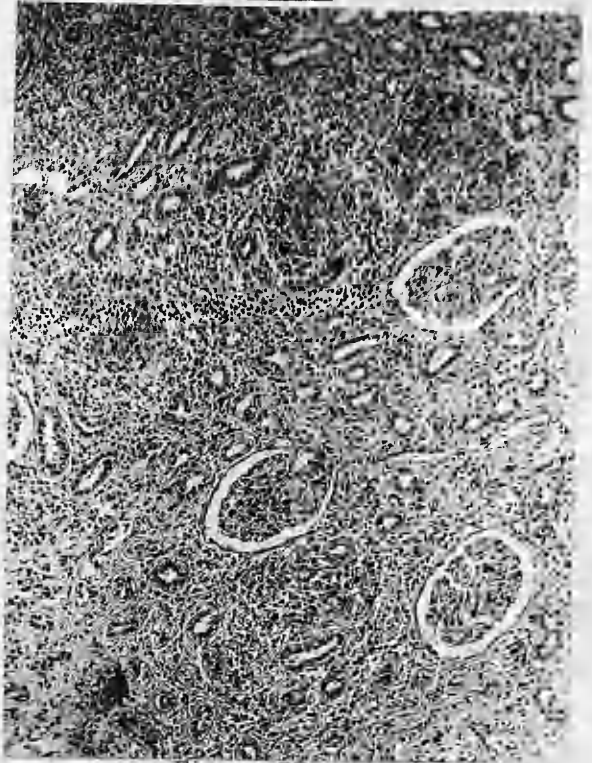


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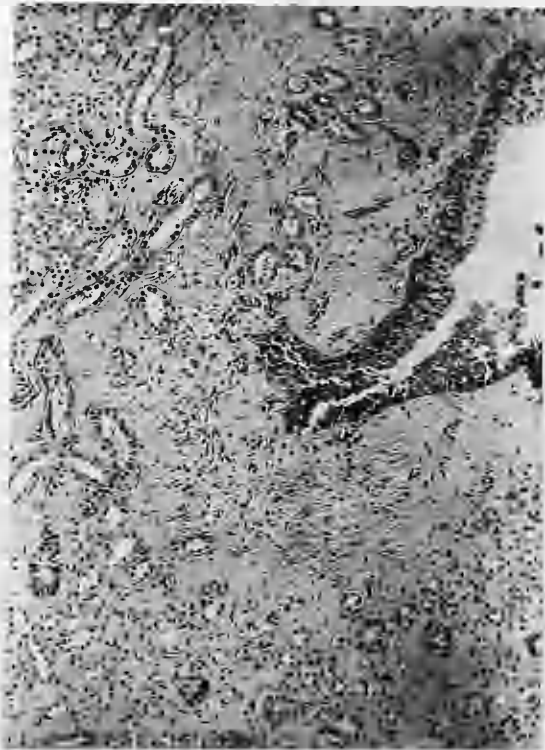


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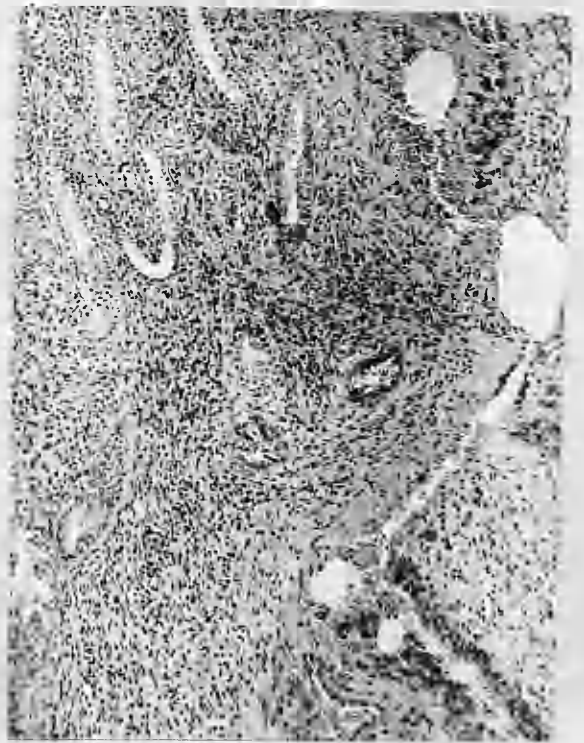


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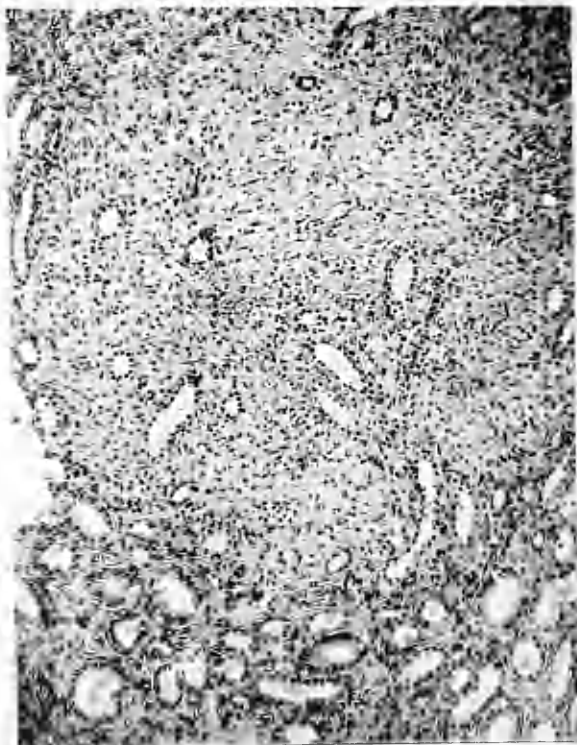


Figure 82.



Figure 83.



Figure 84.





Figure 85.

Cystogram showing systolic bladder and reflux up to left kidney.



Figure 86.

Cystogram showing systolic bladder and reflux up right ureter.

47.



Figure 87.

Cystogram after ileo-cystoplasty.



Figure 88.

Stricture at lower end of ureter requiring nephrostomy when blockage occurred. Later, stricture was excised and ureter re-implanted into the bladder.

Figure 89.Period 1940-45.Cause of Death in 31 Males Suffering from Bilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	24.
Meningitis:	1.
Pulmonary Tuberculosis and Renal tuberculosis:	2.
Pulmonary Tuberculosis: Acute Cardiac Failure:	1.
Pulmonary Tuberculosis: Spinal and Renal Tuberculosis:	1.
Cardiac Disease:	1.
Post-operative Transplantation of Ureter:	1.

Figure 90.Period 1940-45.Duration of Symptoms at time of death in 24 Males who died of Uraemia.

Duration of Symptoms (in years):	1	2	3	4	5	7	9	10
Number:	7	7	2	1	3	1	1	2

Figure 91.Period 1940-45.Cause of Death in 26 Males suffering from Unilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	14.
Pulmonary and Renal Tuberculosis:	4.
Meningitis:	3.
Pulmonary Tuberculosis:	2.
Post-operative Transplantation of Ureter:	1.
Anyloid Disease: Spinal Tuberculosis:	1.
Perforated Gastric Ulcer:	1.

Period 92.Period 1940-45.Duration of Symptoms at time of death in 14 Males who died of Uraemia.

Duration of symptoms (in years):	1	2	3	4	5	6	7	8	10.
Number:	1	3	4	1	1	1	1	1	1

Figure 93.Period 1940-45.Cause of Death in 16 Females suffering from Bilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal tuberculosis:	12.
Pulmonary and Renal Tuberculosis:	2.
Spinal and Renal tuberculosis:	1.
Post-operative Transplantation of ureter:	1.

Figure 94.Period 1940-45.Duration of Symptoms at time of death in 12 patients who died of Uraemia.

Duration of Symptoms (in years):	1	2	3	5	6	7	10.
Number:	4	3	1	1	1	1	1.

Figure 95.Period 1940-45.Cause of Death in 12 Females suffering from Unilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	5.
Meningitis:	1.
Dysentery:	1.
Miliary Tuberculosis:	2.
Pulmonary and Renal Tuberculosis:	3.

Figure 96.Period 1940-45.Duration of Symptoms in 5 Females who died of Uraemia.

Duration of Symptoms (in years):	1	5	10.
Number:	2	2	1.

Figure 97.Period 1940-45.Summary of Details of Patients admitted to Hospital with Renal Tuberculosis between 1940-45.

Total number of admissions:	150.
Combined Deaths within 8 years:	85. 56.67 per cent.
Males:	57. 38 per cent.
Females:	28. 18.67 per cent.

Deaths:

Bilateral renal disease when first diagnosed:	47.
Unilateral renal disease when first diagnosed:	38.

Figure 98.Age (in years) of 85 patients who died.

- 19	20 - 29	30 - 39	40+
7	30	22	26.

Figure 99.Cause of Death in 85 Patients.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	55.
Extra-Urinary Tuberculosis in addition to Renal Tuberculosis:	23.
Non-Tuberculous:	4.
Operative:	3.

Figure 100.Duration of Symptoms in 55 Patients who died of Uraemia.

Duration of Symptoms (in years)	1	2	3	4	5	6	7	8	9	10.
Number:	14	13	7	2	7	2	3	1	1	5.

Figure 101.Period 1950-55.Cause of Death in 7 Males who had Bilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	3. (One man had only one month of treatment).
Post-operative: Ileo-cystoplasty:	1.
Transplantation of Ureter:	1.
Cardiac Disease:	1.
Broncho-Pneumonia:	1.

The duration of the symptoms in the 3 men who died of uraemia was 7, 3 and 4 years respectively.

Figure 102.Period 1950-55.Cause of Death in 10 Males who had Unilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	3.
Tuberculous Meningitis:	1.
Cardiac Disease:	1.
Neoplasm of Eye:	1.
Broncho-Pneumonia:	1.
Post Encephalitic Parkinsonism post-operative nephrectomy:	1.
Pulmonary Tuberculosis:	2.

The duration of the symptoms in the 3 men who died of uraemia was 4, 3 and 2 years respectively.

Figure 103.
Period 1950-55.

Cause of Death in 11 Females who had Bilateral Renal Tuberculosis.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis:	6.
Died at Home: cause unknown:	4.
Post-operative transplantation of Ureter:	1.

The duration of the symptoms in the 6 who died of uraemia was 1 year in 1, 2 years in 2, 3 years in 1, 5 years in 1 and 6 years in 1.

Figure 104.Summary of Details of Patients admitted to Hospital between 1950-55.

Total number of admissions:	361.
Combined Deaths within 8 years:	30. 8.3 per cent of total.
Males:	17. 4.7 per cent of total.
Females:	13. 3.6 per cent of total.
<u>Deaths:</u>	
Bilateral renal disease when first diagnosed:	18.
Unilateral renal disease when first diagnosed:	12.

Figure 105.Period 1950-55.Cause of Death in 30 Patients.

<u>Cause:</u>	<u>Number.</u>
Uraemia: Renal Tuberculosis;	12.
Extra-Urinary tuberculosis in addition to Renal Tuberculosis:	3.
Non-Tuberculous:	7.
Post-operative:	4.
Cause unknown:	4.

Age (in years) of 30 Patients who died.

- 19	20 - 29	30 - 39	40+
3	8	6	13.

Figure 106.Comparison of Death Rates 1940-45 and 1950-55.

Cause of Death:	1940-45 Total (150)		1950-55 Total (361)	
	Number.	Per Cent of Total.	Number.	Per Cent of Total.
Uraemia:	55	36.67	12	3.3
Extra Urinary Tuberculosis:	23	15.33	3	0.8
Non-Tuberculous:	4	2.67	7	1.9
Post-Operative:	3	2.0	4	1.1
Cause Unknown:	-	-	4	1.1
Combined deaths:	85	56.67	30	8.3

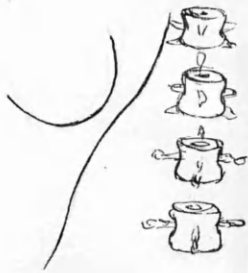


Figure 107.

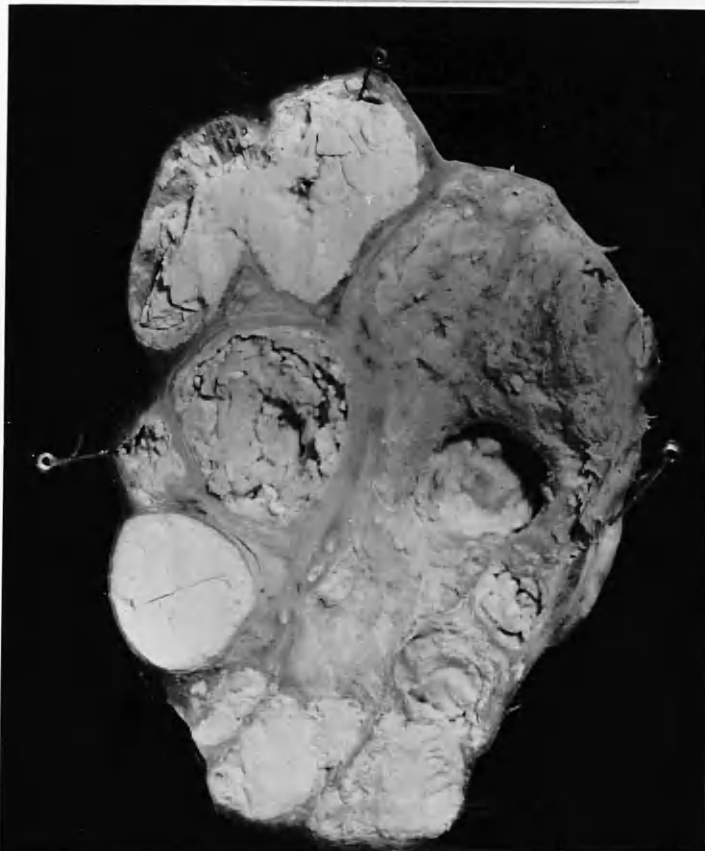
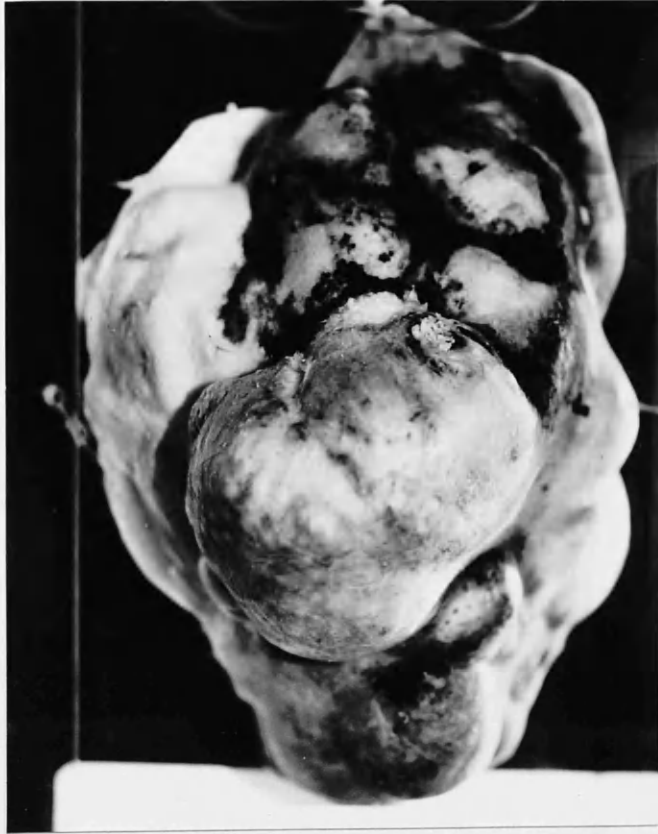


Figure 108.

Tuberculosis of Kidney - loculated tuberculous pyonephrosis associated with psoas abscess.
After 6 months' Strept. + I.N.A.H.609/54

Figure 109.



59.

Figure 110.



Figure 111.

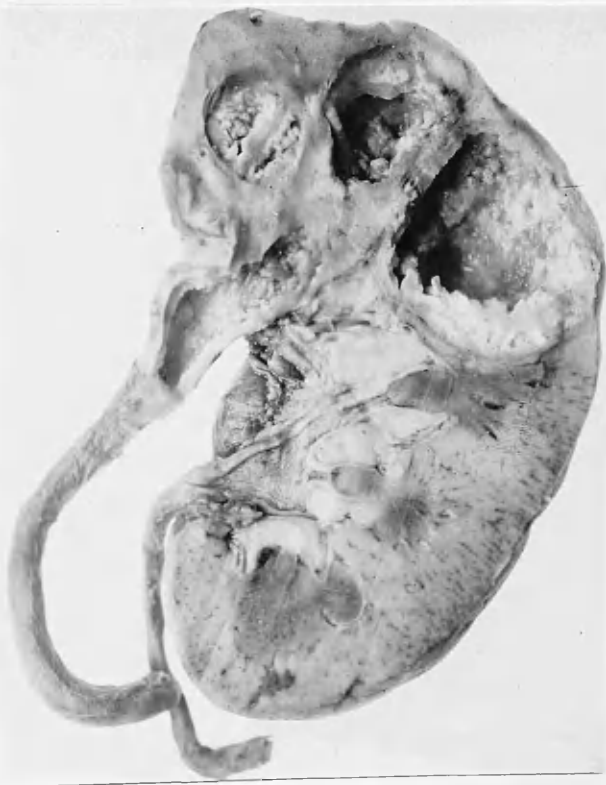


Figure 112.



Figure 113.



Figure 114.



Figure 115.

Figure 116



(a)



(b)



(c)

Figure 117.



(a)



(b)



(c)



(d)

Figure 118.



Figure 119.

65.

Figure 120.



(a)



(b)