TUBERCULOSIS OF THE KIDNEY

A Clinical Study With Special Reference to Renal Function Before and After Nephrectomy.

VOLUME I

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TUBERCULOSIS OF THE KIDNEY

VOLUME I

CONTENTS

CORRIGENDA

Volume I.

Page 8. Smith, H.W. et al (1941,1943) should read Smith H.W. et al (1938,1943)

Page 40. Craik & Macdonald (1958) should read Craik & Macdonald - in preparation.

Volume II.

Fig. 43 M.P. Age 31 should read M.P. Age 46

Fig.47 N.F. should read M.F.

PREFACE

A young female patient, aged 17, who had been known to suffer from the effects of chronic nephritis for several years was admitted to Stonehouse Hospital with chronic renal failure. In order to gain an estimate of the severity of the kidney condition, an excretion and clearance test, using inulin and p-aminohippurate, was carried out with the assistance of Dr. J.E. Craik. The results obtained were most interesting and valuable. As a direct consequence the stimulus to carry out the investigations, which form the basis of this thesis, was created.

There was an opportunity to study tuberculosis of the kidney in Stonehouse hospital. Mr. W.S. Mack and Dr. Alexander Smith permitted me to investigate the patients who had been admitted suffering from suspected renal tuberculosis. Dr. Craik generously made the materials required for the test available, while Dr. Anderson and Dr. Kenny provided the laboratory facilities at the Victoria Infirmary, Glasgow.

An/

An attempt has been made to assess the value of

(1) clinical findings

(2) the ancillary methods of investigation (intravenous pyelography, cystoscopy and retrograde pyelography)

(3) urea clearance tests and

(4) the Inulin/PAH excretion and clearance tests.

As all of the patients studied have undergone nephrectomy the specimens were available for detailed examination. The findings were correlated with those already mentioned and an assessment made of the relationship between them. As the modern methods of anti-tuberculous chemotherapy developed so a further interesting assessment could be made, viz. in regard to the benefit and reaction of the diseased tissue to the drugs being prescribed to the patients under review. Their effect was evident in the histological sections of the kidneys removed at operation.

An incidental finding of considerable interest was that a few cases were hypertensive and that nephrectomy restored a normal blood pressure in most. Special mention will be made of this in chapter XI.

The Inulin/p-aminohippurate excretion and clearance/

clearance test was carried out on three occasions in the twenty two patients who formed this series

(1) prior to nephrectomy

(2) one week after nephrectomy and

(3) six months after nephrectomy.

It was found:-

(1) when a kidney with a minimal tuberculous lesion is removed a large amount of normally functioning renal tissue is lost so that despite hypertrophy of the remaining kidney, the loss is not completely made good.

(2) when a kidney with a moderate tuberculous lesion is removed, a relatively small amount of normally functioning renal tissue is lost. After nephrectomy, hypertrophy in the remaining kidney makes good the surgical loss.

(3) When a kidney with a severe tuberculous lesion is removed practically no normally functioning renal tissue is removed. Hypertrophy of the remaining kidney results in an absolute gain in total renal function.

(4) The presence of a tuberculous kidney inhibits compensatory hypertrophy of the contra-lateral healthy kidney.

CHAPTER I

HISTORICAL REVIEW

In the course of the last 150 years the physiology of the renal tract has undergone considerable investigation. As each physiologist or clinician introduced some new interpretation or discovery a review of the preceding knowledge was inevitably associated with it.

Urea, which is the main nitrogenous end product of protein digestion, and, with water, the chief constituent of urine, was first prepared by Rouelle (1773) by the alcoholic extraction of evaporated human urine. It is also interesting to appreciate that Rouelle extended his investigations to other animals and demonstrated the presence of urea in the urine of the cow, horse and camel. Fourcroy, (1804) wrote that the expulsion of urea, called by him urée to distinguish it from urique (uric acid), is 'the principal and the most necessary, the most remarkable purpose of urinary evacuation'. R. Bright (1827) demonstrated an excessive value of the blood urea in patients who had oedema and correlated this finding with a lowered value of urea in urine which contained albumin./ These

These facts were the basic essential features of the disease - nephritis - which is now given his name as an eponym.

Wohler (1828) is believed to have been the first to create urea artificially from ammonium cyanate. Dumas and Cahours (1842) proved that urea resulted from the combustion of food material comprised of protein. Thereafter the term uraemia became associated with renal insufficiency though, nowadays, it is considered that accumulation of urea in the blood stream is not the precise and specific cause of the symptoms and signs described as renal insufficiency.

At the beginning of the century estimations of blood urea were introduced as clinical tests of effective renal function. Folin (1917) developed further biochemical methods and to them were added the evaluation of non-protein nitrogen, creatinine and uric acid, all of which are appreciably raised in advanced kidney disease.

Ambard and Weill (1912) attempted to create an equation which would give a significant value for kidney function, relating the quantity of urine excreted per unit time to the quantity in each ml. of plasma. Physiologically some difficulty was found in expanding this principal. Austin/

Austin, Stillman and Van Slyke (1921) carried out further investigation on the influence of urine flow on the examination of urea in man and created a more acceptable equation - $\frac{U\ V}{B} \times 1 / \sqrt{V} = K$, which is equal to $\frac{U\sqrt{V}}{B} = K$. Where U is the urine urea (mgms. per 100 ml.) B is the blood urea (mgms. per 100 ml.) and V in the urinary volume (mls. per minute). In all of these calculations V was corrected to body surface area of 1.73 sq.ms. representing the average surface area of adults. When the maximum clearance was more than 2 ml. per minute i.e. above the so called augmentation limit the rate of excretion is at a maximum. It is then simply proportional to the blood urea concentration and is not increased by any addition of urea in the volume of urine. Mohler, McIntosh and Van Slyke (1929) coined the word 'clearance' for this type of formula; accordingly $\frac{U\ V}{B}$ was called maximum clearance. Further when the urine volume is below the augmentation limit of 2ml. per minute, the rate of excretion is slower than at higher urine volumes and diminishes progressively as the urine volume decreases. The rate of excretion of urea is not only directly proportional to the value of the blood urea/

urea but is so changed by the urinary volume that it is proportional to the square root of the urinary volume, V; thus the 'standard' clearance is denoted by the formula $\frac{U\sqrt{V}}{B}$.

More recently, work has proceeded to find other methods of estimating renal function. Smith H.W. et.al(1941,1943) have investigated other substances which could produce a more precise evaluation of renal function. In their tests kidney function was divided into three distinct parts:-

1. glomerular filtration
2. tubular function and
3. the rate of renal blood flow.

In the Homer Smith type of test these three entities are estimated individually but simultaneously. All substances in solution in the plasma are filtered by the glomeruli provided their molecular size is less than that of serum albumin, i.e. a molecular weight of less than 70,000. The glomerular filtrate flows into the tubules and in the passage through the tubules, solutes are dealt with in one of three ways :-

1. they may be reabsorbed by the tubular epithelium. This process may be (a) complete, as for example with glucose; or (b) partial/

partial as with water, sodium, potassium and chloride.

2. more solute may be actively excreted by the tubule cells with the glomerular filtrate, creatinine, diodrast and penicillin being substances of this nature.

3. the tubule cells may have no action on the solute. Only one substance is known which is neither absorbed nor excreted by the tubules, this is inulin; creatinine, thiosulphate, and mannitol undergo tubular excretion in relatively small proportion.

Provided the renal clearance of a substance, such as inulin, in category 3 is known, the clearance of any other substance immediately gives information as to the action of tubule cells in it. If the value is less than that of inulin some of it is reabsorbed by the tubules; if the value is greater than that of inulin some is excreted by the tubules, and if the value is equal to that of inulin it has not been influenced by the tubules.

Glomerular Filtration Rate.

Inulin, which has a molecular weight of 5,200, a starch like polymer of fructose, is:-

Inulin:-

(1) filtered by the glomerulus

(2) neither reabsorbed nor excreted by the tubules

(3) chemically inert

(4) not altered chemically by any blood enzymes

(5) completely excreted in the urine following intravenous injection.

In the search which Smith H.W. (1938) and his associates undertook, many years were spent in proving that the tubule cells had no action on inulin. One or two of their experiments are worthy of mention as illustrations of the completeness of their work.

1. They made tissue cultures of isolated loops of renal tubules and immersed them in solutions containing inulin. No matter how long the loops were left in inulin solution, no inulin appeared in the lumina of the tubules.
2. They injected inulin into the lumina of similarly isolated tubules and showed that the inulin was not reabsorbed.
3. Some of the lower fish, elasmobranchs, have kidneys without glomeruli. Homer Smith showed that these fish were incapable of excreting inulin in their urine.

The following is a table of comparative clearances and illustrates these points:-

GLUCOSE CLEARANCE	NIL	Reabsorbed by tubules.
UREA CLEARANCE	70 ml. per min.	
INULIN CLEARANCE	120 ml.per min.	
EXOGENOUS CREATININE CLEARANCE	170 ml.per min.	Excreted by tubules.
PAH CLEARANCE	600 ml.per min.	

Renal Blood Flow.

Sheehan, H.L. (1931) in the original experiments in the measurement of renal blood flow used the red dye No. 90 which was completely extracted by the kidney from the blood passing through it. As all of the dye is excreted in the urine its clearance is equivalent to the renal plasma flow. This dye is poisonous so it cannot be used in the human subject. Search was made to find some other non-toxic substance. Diodrast was used at the outset but p-aminohippuric acid is mostly used now, and has been employed throughout the present investigation.

Excretion of diodrast and hippuran by the tubules in the rabbit, dog and man was described by Elsom, Bott, Shiels and Walker (1936-7) and Landis, Elsom, Bott and Shiels (1936) who reported that the diodrast ratios in these species/

species are considerably in excess of 1.0 and that the clearance ratios are depressed as the pasma concentration of the solute is increased. Homer Smith and his co-workers re-examined this group of compounds and developed a diodrast clearance at low plasma levels as a means of measuring renal blood flow while a high plasma level was employed to determine the quantity of functional tubular excretory tissue in the kidneys.

P-aminohippurate (PAH) has a clearance identical to that of diodrast at low plasma levels and is used to estimate the renal plasma flow. Its chemical evaluation is straightforward; it is non toxic and can be used to assess the totaltubular excretory tissue. It is less extensively bound by the plasma proteins than is diodrast, and so errors involved in the estimation of the filtrable fraction of the plasma are less important.

In determination of each of these factors, viz., glomerular filtration rate, renal plasma flow and maximal tubular excretory capacity, a combined single infusion method has been devised and will be described in chapter III.

CHAPTER II

THE KIDNEY FUNCTION TEST

On the day prior to the test the patient is informed briefly of its character in order to allay apprehension and obtain his or her co-operation. No special restriction of fluids or diet is necessary. An early light breakfast with tea or coffee is provided before the procedure is commenced. No smoking is allowed after 8.00 a.m.

Procedure at the bedside.

The equipment (fig. 7), having been previously prepared, is brought to the bedside, together with the solutions of Inulin and p-aminohippurate. Within the package there is a specially prepared rubber catheter in that there are extra holes in it to ensure satisfactory and complete drainage of urine from the bladder. The patient is catheterised with it at 9.00 a.m. and a specimen of the bladder urine obtained. It is received into a urine container labelled 'urine blank.' Between 9.15 a.m. and 9.30 a.m. venipuncture is performed; 20 ml. of blood is taken by syringe and put into a heparinised universal container - this specimen being labelled 'blood blank.'

The needle is then attached to the special intravenous infusion set (fig. 6) the filtration funnel of which has been filled with intravenous normal saline. A slow drip infusion of the saline is then instituted and allowed to run slowly to permit the patient to become adjusted to the new condition of intravenous infusion and bladder catheterisation. It is customary to obtain the patient's systolic and diastolic blood pressure readings.

Once the patient has become accustomed to the presence of the drip and catheter, the test proper is commenced. It is divided into two periods of time. In the first period a measurement of renal plasma flow (RPF) and glomerular filtration rate (GFR) is obtained, and from these figures the filtration fraction (FF) RPF/GFR may be calculated. In the second period a measurement of the maximal tubular excretory capacity for p-aminohippurate (Tm_{PAH}) is obtained.

In order that the concentration of the perfusing chemical in the total body water may be rapidly raised to effective levels a priming solution of p-aminohippurate and inulin is prepared. In order that the concentration of the perfusing chemical in the total body water may be consistently maintained at an effective level a sustaining solution is also prepared.

The solutions are made up as follows:-

Priming solution.

(a) 2 ml. of 20% p-aminohippurate

(b) 20 ml. of 20% inulin

Sustaining solution.

(a) 8 ml. of 20% p-aminohippurate

(b) 55 ml. of 10% inulin

(c) 450 ml. of sterile normal saline

The priming solution is given rapidly in less than two minutes, whereas the sustaining sdution is given by slow drip, the rate varying with the severity of renal damage. With a normal kidney function the rate for the sustaining solution is 96 drops per minute. With increasing renal danage the rate is decreased to about 60 drops per minute.

Having obtained the specimen of blank urine and of blank blood and prepared the priming and sustaining solutions of the first period, the test is proceeded with as follows:-

The infusion of normal saline is stopped at the needle (fig. 9). The branch of the 'T' tube in the infusion set is opened and the saline remaining in the filtration flask is run off until the neck of the funnel is reached. The branch of the 'T' tube is now closed and the infusion recommenced by opening the clip at the needle. The priming solution is now/

now put into the funnel and allowed to run as quickly as possible. The sustaining fluid is then added to the reservoir and the drip infusion slowed to the optimum rate. In order that complete stabilisation of the inulin and PAH should occur, the infusion is allowed to run for more than twenty minutes. At the end of this time the bladder is completely emptied. This is achieved in the same way throughout all the tests. 15 ml., which need not be accurately measured, of sterile intravenous normal saline are injected into the bladder along the catheter by a sterile 20 ml. syringe supplied in the specially prepared package. Following this injection 15 ml. of air are introduced along the catheter which had been nipped to prevent any loss of fluid.

The time noted as the commencement of the period is taken when the last drop of fluid and the last gurgle of air has left the catheter with suprapubic pressure on the bladder. A stop-watch, which is used as a means of time-keeping, is started at this juncture. The urine obtained up to this point, including that which is removed at the end of the priming period, is discarded and a collection now made of/

of all the urine secreted in a special container. This time is recorded as time zero. After ten to twenty minutes 20 ml. of blood are taken from a vein in the opposite arm to that in which the infusion is being given. This specimen is placed in a heparinised container and labelled 'blood 1.' The time at the 10 ml. mark is noted on the stop-watch and recorded. The infusion is allowed to continue for as long again. The complete specimen of urine, including the bladder washings, is obtained and labelled as 'urine 1.' The time at which this occurs is noted. At the end of this period the urine is then allowed to drain into a receptacle prior to the commencement of period two. The amount of fluid remaining in the reservoir is noted.

For the priming solution in period two, 20 ml. of 20% PAH solution is taken into a syringe from the 100 ml. bottle of 20% PAH. The clip above the 'T' piece is applied to stop the infusion. The 20 ml. of 20% PAH is then slowly injected along the 'T' piece into the patient (fig. 9). As this injection is given the patient may feel somewhat warm and flush in the face and neck. He may also feel a sensation of heat in the bladder. One or two of the patients during the course of this investigation had also abdominal discomfort.

Once the priming solution of 20 ml. of 20% PAH has been given, the remaining 80 ml. is added to the reservoir which contains the residue of the sustaining solution of the first period (fig. 10). The infusion rate is recommenced and adjusted to 96 drops per minute. The stabilising period is about twenty minutes. The bladder is drained at the end of this time in the manner already described, the urine and washings obtained being discarded. The stop-watch is started and time zero for period two established with the collection of urine again being under way. The second blood specimen, labelled 'blood 2', is taken about fifteen minutes after the commencement of the period and the second urine specimen, labelled 'urine 2', collected after thirty minutes in a similar manner to that described for the first period. With the completion of the second urine specimen the test is then concluded. There are now three urine specimens and three blood specimens together with completed chart (figs. 11 and 12).

During the course of this procedure the patient is allowed to drink fluids in moderation and encouraged to spend the time quietly, smoking being forbidden throughout. When the test is completed the catheter is removed from the bladder and the intravenous infusion discontinued. Thereafter he may rise, if/

if permitted, and, as has been done in the course of this series, if the test has been carried out on an out-patient, he or she is allowed home without any ill effects whatsoever.

A list of the apparatus required is appended.

1. Special infusion set with graduated reservoir, drip counter and 'T' tube.

2. Special catheter with extra holes.

3. 20 ml. syringe for washing out bladder.

   These are all supplied dry and sterile in a single paper wrapped package.

4. 3 - 20 ml. syringes, eccentric nozzle, to collect blood specimens 'blank' '1' and '2'.

5. 1 - 20 ml. syringe, central nozzle, for giving priming solution of PAH in period two.

6. Stop-watch.

7. Three universal containers with heparin for blood specimens.

8. Three urine bottles for specimens.

9. 1 - 25 ml. and 1 - 50 ml. ampoule 10% inulin

10. 1 - 10 ml. and 1 - 100 ml. bottles 20% PAH

11. Two bottles of intravenous saline.

12. Special sheet for entering times and results.

Biochemical methods.

Determination of PAH. In order to estimate the renal plasma flow (RPF) i.e. by a low PAH concentration, it is necessary that the serum level should be about 1 - 5 mgms. per 100 ml. For the estimation of the maximal tubular excretory capacity for p-aminohippurate (Tm_{PAH}) the serum level of PAH should be greater than 60 mgms. per 100 ml. The reagents required are:-

1. A specially prepared cadmium sulphate solution.
2. 1.1 N-sodium hydroxide.
3. 1.2 N-hydrochloride acid.
4. 0.1% sodium nitrite (freshly prepared).
5. 0.5% ammonium sulphamate.
6. 0.1% (1-naphthyl) ethylenediamine dihydrochloride.

The urine specimens are diluted so that the concentration of PAH in them is approximately equal to the concentration of PAH in the plasma. Under such an ideal arrangement the clearance in ml/minute would become $U_{dil} \times U_{vol/min}$ With a previous knowledge or estimate of urea clearance as a percentage of average normal function, the following dilutions/

dilutions of urine and plasma are prepared.

In the case of the plasma blank (P_o) and first period plasma (P_1) no dilution is required. For the second period plasma (P_2) a 1:21 dilution is made.

The urine blank (U_o) should be diluted with distilled water so that it gives the same approximate concentration as the first period specimen of urine (U_1) when held up to the light and examined visually. If the urea clearance or blood urea value is not available to give an indication of the patient's renal function, it is usual to assume a 60% renal function value and make dilutions accordingly. If this estimation is found to be far out, twofold or greater, the urinanalysis is repeated at more suitable dilutions.

The dilutions thus made are obtained by reference to the specially prepared nomogram (fig. 13) the dilutions being calculated from the minute volumes of urine of each period. The dilutions of U_o and U_1 are the same.

Once all the dilutions have been prepared and thoroughly mixed, six 50 ml. Erlenmeyer flasks labelled P_o P_1 P_2 U_o U_1 and U_2 have the following added to them:-

1. Distilled water 20 ml.

2. Heparinised plasma, plasma dilution or urine dilution as previously indicated. 2 ml.

3. cadmium sulphate reagent 6 ml.

4. sodium hydroxide reagent 2 ml.

The flasks are shaken after each addition and allowed to stand for five minutes prior to filtration through No.41 9 cm. Whatman filter papers into clean 6" x $\frac{5}{8}$" test tubes. These clean test tubes are labelled P_o P_1 P_2 U_o U_1 U_2 and the appropriate filtrate and reagents are added as follows:-

1. filtrate 10 ml.

2. 1.2 N-hydrochloric acid 2 ml.

3. sodium nitrite reagent 1 ml.

After the addition of the sodium nitrite reagent the solution is thoroughly mixed and allowed to stand for four minutes.

4. ammonium sulphamate reagent 1 ml.

Thorough mixing by inversion of the tube on several occasions in order to decompose the excess nitrous acid is required after the addition of this reagent.

5. N.(1-naphthyl) ethylenediamine dihydrochloride 1 ml.

After the addition of the ethylenediamine thorough mixing is carried out and the solution is allowed to stand for fifteen minutes to allow complete colour developments.

The solutions are then read on a Spekker absorptiometer using the green Ilford filter 605. The figures obtained are later interpreted for absolute values from a calibration curve previously prepared.

Determination of Inulin. To estimate the inulin concentration and thereby obtain a measurement of GFR it is advisable to have a serum level between 18 and 25 mgms. per 100 ml. The reagents required are:-

1. Washed yeast. Bakers' yeast is washed with saline and centrifuged six times in order to remove any soluble carbohydrate. A 1:5 suspension of the packed yeast cells is made in distilled water.
2. cadmium sulphate reagent
3. 1.1N-sodium hydroxide
4. diphenylamine reagent

No dilution of P_o P_1 P_2 is required. The dilution which brought U_o to approximately the same concentration as U_1 is used for U_o. The same dilutions are prepared for U_o and U_1. The dilution required for U_2 is obtained from the nomogram (fig. 13). To seven 12 ml. centrifuge tubes, labelled P_o P_1 P_2 U_o U_1 U_2 and Y.B. (yeast suspension blank) are added the following:-

1.	Distilled water	2 ml.
2.	heparinised plasma, or urine dilution as previously indicated	2 ml.
3.	20% yeast suspension	4 ml.

2 ml. of distilled water is added to the tube Y.B. to make its total volume 8 ml.

The contents of the tubes are thoroughly mixed by inversion and allowed to stand at room temperature for fifteen minutes. The tubes are shaken at intervals during this period. All the specimens are then centrifuged.

4 ml. of the supernatant fluid is taken from the centrifuged specimens into 6" x $\frac{5}{8}$" test tubes, and 6 ml. of the cadmium sulphate reagent is added to each tube. After mixing, 2 ml. of 1.1 N-sodium hydroxide is added, and again the mixture is thoroughly shaken by inversion. The samples are filtered through No.41 9 cm. Whatman filter papers into clean test tubes.

3 ml. of the filtrate are then taken and added to wide bore boiling tubes ($\frac{7}{8}$") to which are then added 10 ml. of the diphenylamine solution. After the contents of the tubes have been thoroughly mixed, glass teats are inserted. The tubes are then placed in a boiling water bath for thirty/

thirty minutes, throughout which time they are agitated frequently to ensure complete mixing of the specimens. After cooling, the solutions are read on the Spekker absorptiometer using the red Ilford filter 609. The figures obtained are then interpreted on a previously prepared inulin calibration curve.

The RPF, GFR and Tm_{PAH} results are calculated and from them are derived the fractions Filtration Fraction (FF) RPF/Tm_{PAH} and GFR/Tm_{PAH}. RBF is obtained from RPF and PCV (packed cell volume) which has been obtained from a haematocrit reading of P_o.

All the results are then converted into percentage of average normal for convenience of clinical interpretation. A completed information sheet is seen in fig. 12.

The principals underlying the method of calculations are described by Bell, Davidson and Scarborough (1957).

CHAPTER III

MATERIAL

The patients who have been investigated because of symptoms and signs indicating the presence of renal tuberculosis were referred to Stonehouse hospital from a number of out-patient clinics and other hospitals in Lanarkshire. At Stonehouse hospital Mr. W.S. Mack, who is consultant urologist, in association with Dr. Alexander Smith, carried out further investigation to confirm the diagnosis and prescribe the necessary treatment. Only four patients in the final group of twenty two presented in this thesis were not at Stonehouse hospital but were seen and investigated elsewhere by kind arrangement with Mr. T.L. Chapman, consultant urologist at the Victoria Infirmary and Hairmyres Hospital.

During the period April 1953 to October 1956 thirty two patients underwent nephrectomy at Stonehouse hospital. Of these, twenty six had clinically diagnosed renal tuberculosis: of the remaining six, one had unilateral polycystic kidney disease, another staghorn calculus whilst in the remaining four the operation was carried out for other surgical reasons viz. (1) chronic infective hydronephrosis, (2) rupture of

of the kidney (3) hypernephroma and (4) non-tuberculous renal abscess.

Thirty patients had the biochemical procedure carried out pre-operatively. The clearance tests were carried out as the decision for nephrectomy was made. The patients were unselected. No specific clinical-feature or other determining feature obtained from the adjuncts of investigation potentiated their inclusion in this series. All the patients underwent nephrectomy and, one week and six months later, with the exception of three patients the test was repeated. In these instances J.A. refused on personal grounds, the second M.McI. succumbed to an acute coronary artery thrombosis whilst the third, F.L. had discharged himself irregularly from hospital and could not be traced, despite every attempt. In five patients histological examination of the kidney did not confirm the diagnosis of renal tuberculosis.

Thus the final completely investigated series comprises twenty two cases of histologically proved renal tuberculosis.

A brief diagrammatic explanation of the theory involved in estimating these factors is given as Figs. 1 - 4 in Volume II.

The initial history in each case was obtained in detail with special reference to the duration of the presenting symptom or symptoms; previous or present infection with tuberculosis and any family history of tuberculosis; home condition, nature of employment and any other details applicable to the social background were also obtained. As a few patients were found to have an elevated blood pressure which did not settle with bed rest, a closer enquiry was made into their family history in order to ascertain whether their parents had suffered from hypertension or had succumbed to a disease process which could have had as its origin increased blood pressure. Complete blood counts were carried out, together with blood grouping.

After the clinical examination was completed, physical, chemical and bacteriological examination of the urine was carried out. Cultures of 24 hour urine collections were made, and later, animal inoculations were also arranged.

Intravenous pyelography, although in many patients carried out prior to admission to hospital, was repeated and followed by cystoscopic examination, when an attempt was made to pass a ureteric catheter into the 'good' kidney/

kidney first of all to obtain some indication of its state. The diseased ureteric orifice was then catheterised if possible, but this procedure failed in many instances because inflammation at the lower end of the ureter and in the bladder mucosa surrounding the ureteric orifice made it impossible. Specimens of urine were obtained if practicable from each kidney and examined chemically and bacteriologically. In patients where ureteric catheterisation had been successful retrograde pyelography was carried out.

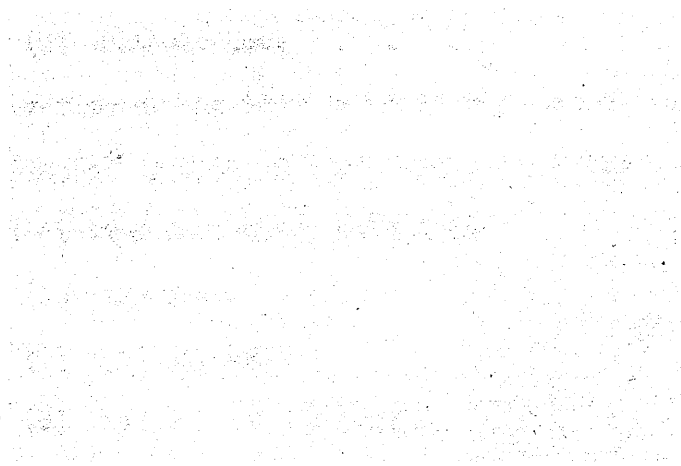
Prior to the initial Inulin/PAH excretion test, in some patients a urea clearance test had been carried out. From it an estimate of the optimum rate of infusion could be obtained. In all the tests a parallel urea clearance was calculated from the specimens.

Once the diagnosis was confirmed, chemotherapy commenced. When the decision to remove the diseased organ was made the Inulin/PAH excretion test was carried out. It was repeated one week after operation and again six months after operation.

It is known that hypertrophy of the remaining kidney commenced shortly after nephrectomy and is significant within/

within a week (see chapters VII and VIII) but as the patients had some reaction following nephrectomy, it was not considered justifiable to carry out these somewhat trying investigations in less than one week after operation.

In six months it was believed that complete compensatory hypertrophy and establishment of the altered renal circulation had taken place and so the test was repeated.



CHAPTER IV

SUMMARY OF RESULTS

A brief annotation is given in this chapter of the lines on which the twenty two patients, who comprise this series, have been investigated. There follows a detailed assessment of the results under three main headings

(1) Clinical

(2) Biochemical

(3) Pathological

The severity of the disease affecting each patient has been estimated by each of these methods and the results of treatment divided into three categories

(a) surgical,

(b) medical and

(c) medical and surgical.

In regard to the clinical findings a resume is given of the main clinical symptoms and signs found, with an opinion in chapter X of their value in the investigation of tuberculosis/

tuberculosis of the kidney.

Intravenous pyelography, cystoscopy and retrograde pyelography which were employed as surgical adjuncts have provided useful information which has been included in chapter V - clinical findings.

The Inulin/PAH excretion test provided a vast amount of useful data which is presented in a concise manner in chapter VII - biochemical findings - together with figs 47 - 59 in volume II.

In chapter VIII an account is given of the interpretation of these results. In addition to the test which is mentioned, a parallel urea clearance test was carried out simultaneously on the specimens obtained for the Inulin/PAH excretion and clearance procedure and comment is made on the correlation between these two types of renal function test.

Bacteriological examination of the urine which is an essential feature of the evaluation of renal tuberculosis provides the findings which are detailed in chapter IX. The opportunity of further identification of the causative organism from the specimen of kidney obtained at operation added to the information already available.

Histological confirmation of the diagnosis revealed not only the pattern of the disease process present in the kidney but also reflected the effectiveness of the anti-tuberculous chemotherapy which had been given prior to extirpation of the affected kidney. A large number of photographs, surface contour and cut surface are presented as figs. 60 - 86 in volume II and in addition, figs. 87 - 99 represent a cross section of the variable photomicrographs of these kidneys. Figs. 102 - 106 are the autopsy material from M.M. who succumbed four years after nephrectomy to cerebral haemorrhage. This feature, which is described more fully in chapter XI under the heading 'Unilateral Renal Tuberculosis with Hypertension' was an interesting corollary discovered pari passu during the main investigation.

Specimens of specially prepared large kidney transparencies are included in volume II as a new method of illustrating the types of tuberculosis of the kidney which occur. In chapter XII there is a discussion of the modern methods of anti-tuberculous chemotherapy and their place in tuberculosis of the kidney.

Some comparison is made with the prognosis which is possible with these methods and the usefulness of the/

the biochemical and other findings as an apparent index of prognosis.

Finally an appraisal is given of the severity of the disease by the various types of procedure which have been employed and their significance in estimating the best therapy to be applied in each instance.

CHAPTER V

CLINICAL FINDINGS

Throughout the clinical aspect of the investigation of renal tuberculosis the pattern of symptomatology was constant. In chapter VI a brief account is given of the prodromal lesions evident prior to the onset of renal tuberculosis. All the patients examined had a good general appearance: in particular their facial appearance and bodily nutrition did not suggest the presence of tuberculosis. Only two patients, R.S and D.O'R. looked ill when admitted to the urological unit and both had active extra-renal tuberculosis.

Increased frequency of micturition which was found in eighteen patients (82per cent) was the most common symptom. It was divided into two distinct categories, viz. diurnal and nocturnal. The diurnal frequency was measured as the average time between successive micturitions and varied from twenty minutes to sixty to ninety minutes. The nocturnal frequency was denoted by the number of times the patient had to rise to pass urine during the night: this varied from four to seven times. The volume voided in those who had the/

the most persistent symptom was two to three ounces. Three patients, V.B., M.B., and A.T had in addition, extreme urgency. In addition to frequency of micturition twelve patients (54.5 per cent) had pain on passing urine. The degree of discomfort varied from a burning sensation during the passing of urine to severe pain at the beginning or on completion of the act. Some relationship between this symptom and the presence of cystitis was noticed and is commented on later. M.M. who had increased frequency of micturition and some dysuria, originally visited a gynaecologist because of stress incontinence. No pelvic abnormality was discovered in explanation of her urinary symptoms and accordingly she was referred for urological investigation, which resulted in the discovery of tuberculous bacilluria.

The passage of blood stained urine was complained of by five patients (22.7 per cent): the amount of blood staining varied. In one patient, A.T., haematuria had been present on only one occasion and appeared to have been associated with a secondary infection which was unsuccessfully treated with sulphothiozole. In the other four patients haematuria was transient and appeared to have been a consequence of a more/

more acute bout of cystitis.

In four patients (18 per cent) there was no history of increased frequency of micturition, dysuria or haematuria.

A.Bk. complained of listlessness and swelling of the ankles which had been long associated with proteinuria. A diagnosis of chronic nephritis had been suggested at the outset of her illness and treatment for this condition instituted. D.O'R who had been suffering from tuberculous epididymitis and was receiving treatment for this condition was found to have a tuberculous bacilluria on routine examination of his urine. There followed more specific examination of his renal tract with the findings which will be mentioned later. R.Y. had been known to have nocturnal enuresis for eighteen months. He was referred to the urological outpatients' department and on bacteriological examination his urine was found to contain tubercle bacilli.

Five patients complained of backache. In V.B's case this complaint was the presenting symptom. In addition he gave a history of typical right sided renal colic. There was nausea and active vomiting with frequency and urgency of/

of micturition during and after an attack. M.B. had had recurrent pain of a cramping character on the left side. This had been present for one year. Each attack had lasted an hour and urgency and dysuria invariably followed. Initially J.M. had pain in the left loin and developed a swelling which was aspirated six weeks later. The pus contained tubercle bacilli. A short history of right lumbar pain occurring shortly after micturition was mentioned as the main complaint by M.P. On cystoscopy she was found to have a sub-acute cystitis. After repeated bacteriological examinations of the urine acid and alcohol fast bacilli were discovered.

Backache developed rather differently in J.P, who had had pain in the right iliac fossa which had travelled up into the right loin region and caused backache. This symptom was mentioned in addition to those of increased frequency of micturition and dysuria. In only one patient (A.T.) was there a history of night sweats, which is a subject of further comment in chapter X. There is appended a table showing the incidence of the main symptoms which occurred and which have been detailed above.

	Inc. Freq.	Dysuria.	Haematuria.	Other Symptoms.	No Symptoms.
No. of patients	18	12	5	4	4
Percentage	82%	54%	22%	18%	18%

As has already been stated the general appearance of the patient was good. Mucous membranes were well coloured, a factor which was confirmed on carrying out examination of the haemoglobin and red cell count. In none of the patients was there any evidence of other than a mild degree of iron deficiency anaemia. Throughout, temperature, pulse and respiratory rates were recorded without any significant alteration being apparent. Occasionally there were small bouts of pyrexia associated with cystoscopic examination or concomitant mild infections of the upper respiratory tract. The lowest value of haemoglobin was 79% (11.7) gms.%. The mean for all patients was 90% (13.3) gms.%. The white cell count was within normal limits, although, when there appeared to be a more intense tissue reaction to the infective process, a leucocytosis (mainly lymphocytic) was present. In addition erythrocyte sedimentation rates were found to be moderately elevated in the pre-operative period although this was not an invariable finding. A more detailed account of these findings is given in chapter X.

Examination of the respiratory system revealed, with X-ray confirmation, that sixteen patients had had pulmonary tuberculosis. This feature is referred to in more detail in chapter VI. In patients who had cough and spit, the sputum was referred for detailed bacteriological examination. In two patients the tubercle bacillus was isolated, whilst in all others the organism was not found in repeated examination of the sputum.

The cardiovascular system was investigated with particular note being made of the blood pressure readings which are presented as fig.42. This table shows the figures before operation, one week after operation and six months after operation. Unfortunately in two patients, A.T. and A.Bt., these records were mislaid. In the other patients it can be seen that thirteen had a normotensive pattern prior to operation, whereas the remaining seven had systolic and diastolic hypertension. Further reference will be made to this in chapter XI and is also the subject of a separate communication (Craik and Macdonald 1958). In no patient was there any evidence of rheumatic carditis, neither was there any clinical sign or symptom to suggest that the patient had previously suffered from tuberculous pericarditis.

Abdominal examination was carried out routinely in all the patients. Tenderness over the affected kidney was an invariable feature. H.McL. had a considerably enlarged right kidney which was freely palpable in the abdomen and appeared to be quite mobile. The presence of previous fistulae was seen in R.S. who also had a firm and adherant mass in the left loin and hypochondrium.

In the female patients detailed menstrual history was obtained from the young age group and in none was there any evidence to suggest the presence of tuberculous endometritis.

All the male patients had the testes examined and rectal examination carried out to note the presence or absence of enlargement of the seminal vesicles. In two patients D.O'R and R.S. who had had tuberculous epididymitis previously, some thickening of the vasa deferentia and the epididymes was felt.

The central nervous system was examined and in particular the fundus oculi to note the presence or absence of any retinal tuberculosis. In the patients suffering from hypertension in association with the unilateral renal disease the findings are commented on in chapter XI.

Urine examination was carried out daily in all the patients in the series and in most protein was found. Pus cells were also present in all patients. Bacteriological examination is referred to in considerable detail in chapter IX.

Once the diagnosis of renal tuberculosis was confirmed bacteriologically, further investigation was undertaken to localise the side of the lesion and assess its severity in order to arrange anti-tuberculous treatment. In respect of this, further surgical investigations were undertaken by means of intravenous pyelography, cystoscopy and retrograde pyelography.

Intravenous pyelography.

Following the intravenous injection of 50% uriodone X-ray examination revealed the opaque shadow which had been produced in the kidney. By this method an indication of the reaction, size, severity, position and distribution of the tuberculous process in the kidney affected was obtained. Further, by serial X-ray, i.e. five to ten minute intervals, concentration of the dye could be judged and the effectiveness of the excretion of the dye into the kidney estimated. In addition the shape of the renal pelvis could be assessed;

assessed; the condition of the ureter and the size and appearance of the urinary bladder gauged. Figs. 14 - 27 in Volume II are representative X-ray photographic reductions of some of the intravenous pyelograms carried out. The different patterns which occurred in tuberculosis of the kidney are very numerous but in the examples included many of the more common features are illustrated.

Fig.14 shows no excretion from the left kidney, with some excretion from the right kidney, which appears reasonably normal, although some hydronephrosis would appear to be present. Fig. 15 shows the bladder of the same patient and reveals a fairly normal sized bladder although some distortion is present at the entrance of the left ureter to the bladder. Fig. 16 shows no function from the right kidney whilst the left kidney appears to be reasonably normal. This figure also shows the distortion present in the lumbar spine, due to spinal caries. The appearance in this photograph is suggestive of right renal tuberculosis. Fig.17 shows dye excretion from both kidneys. On the right side the shadow is less intense but appears to be quite normal. The calyces of the left kidney appear to be somewhat dilated with some fuzziness evident in the middle and lower calyces. The/

The appearances are those of tuberculosis of the left kidney. Fig.18 is an interesting photograph in that the left side appears to be within normal limits though there is some distortion in the calyces of the lower pole. The right kidney is somewhat dilated but there is no other definitive evidence of disease. In this patient the disease is localised to the lower pole of the left kidney. Multiple calcified glands are seen in the abdomen, while the bladder shadow is very small. Fig. 19 shows no excretion from the left kidney. The right kidney shows distortion of the upper pole calyces and little or no excretion from the middle and lower calyces. The kidney appears to be enlarged. The tuberculous lesion is in the left kidney (c/f fig. 58). The bladder shadow is within normal limits. Fig. 20 presents rather an unusual picture in that both kidneys appear to be abnormal in outline; the right kidney shows cavitation and distortion of the calyces of the upper and middle poles of the kidney. No excretion is seen in the lower pole; the left kidney shows some dilatation of the lower pole. In this patient the right kidney is severely damaged; the left kidney also appears to have some mechanical distortion. In fig.21 both kidneys show excretion and generally the appearances are/

are quite normal although on the right side there is some irregularity in the lower pole. The ureter appears to be dilated. Although not clearly seen in the reduction photographs the calyces of the upper pole of the right kidney are somewhat fuzzy and irregular due to tuberculosis. Fig. 22 is a most interesting one in that it shows a completely calcified left kidney with calcification also seen in a thickened left ureter. Fig. 23 from the same patient shows some dilatation of the right kidney with irregularity of the calyces of the upper pole. The left kidney and ureter are calcified as in Fig. 22. Post-operatively fig. 24 shows the remnant of the calcified left ureter; the right kidney shadow shows some slight irregularity of the lower calyces with some slight dilatation of the ureter. Fig. 25 shows an even but reasonably normal pattern from the right kidney which appears to be slightly enlarged. No excretion is visible from the left kidney. Figs. 26 and 27 are at five to fifteen minute intervals after the uriodone injection. The right kidney is rapidly visible in fig. 26 but no excretion can be seen from the left kidney. In fig. 27 there is now a faint shadow seen on the left side whereas the right kidney now appears to be more normal in outline.

These representative intravenous pyelograms indicate the usefulness of this 'surgical' adjunct of renal investigation, although their use is rather limited. It is essential that further methods should be employed to reach a more precise diagnosis. Accordingly cystoscopy was arranged and carried out in each patient.

Cystoscopy.

Cystoscopy was carried out in all the patients in the series by the urological surgeon with or without general anaesthetics. The severity of the symptoms complained of and the patient's general condition being the determining features in the use or otherwise of the anaesthetic.

The bladder capacity was measured; the bladder surface was then examined in detail and the presence or absence of cystitis, tuberculous or non-tuberculous, noted. A brief note is given of the findings in some of the patients as illustrative examples.

In J.McA. who had had a relatively short history of increased frequency of micturition, four weeks only, the examination revealed a normal bladder in which the capacity was small, only four ounces being retained. The right/

right ureter appeared to be normal but the left ureter was likened to a golf hole because of the retraction which was present. The whole bladder was congested but no tubercles were seen. Similarly H.McL. at cystoscopy was found to have a small bladder capacity and on inspection of the mucosal surface a patch of cystitis was evident on which tubercles were visible. The right ureteric orifice was slightly dilated and the left ureteric orifice drawn back considerably. In J.P. the bladder capacity was found to be normal whereas the right ureteric orifice was completely obstructed and obscured.

The extension of the disease from the kidney into the bladder from the ureter can be seen on inspection and if it has been long standing tuberculous cystitis may be evident.

Retrograde pyelography.

Following inspection of the bladder by cystoscopy an attempt was made to pass ureteric catheters first into the more normal or healthy ureter. When this had been achieved and the 10 ml. of 35% uriodone injected along the catheter, a retrograde pyelogram X-ray was carried out. Thereafter an attempt was made to pass the catheter into the ureter on the affected side, but in many cases this proved impossible due to/

to thickening and cicatrization of the ureter. In patients where this procedure was successfully carried out and the dye injected along the catheter, a further X-ray photograph was obtained. In this way a more complete impression was obtained of the character, position, size, severity, location and distribution of the tuberculous process in the kidney affected. A brief note is given of the findings of the retrograde pyelography demonstrated in Volume II as figs. 28 - 41.

In fig. 28 a shaggy appearance of the ureter, due to diffuse fibrosis and granulomatous infiltration, is seen. The renal pelvis is grossly contracted and the normal architecture of the calyces replaced by a number of large irregular cavities which present a 'moth-eaten' appearance. Fig. 29, which is a lateral view confirms the impression given in fig. 28. Fig. 30 shows generalised dilatation of the calyces in the right kidney whereas fig. 31 shows the result of catheterisation of a fairly normal left kidney. The dilated and distorted right kidney calyces are still seen. Fig. 32 shows the left kidney which is normal in outline; there is some dilatation evident in the lower pole of the ureter. The right ureteric orifice could not be catheterised/

catheterised effectively as the catheter did not go beyond 2 cms. It was accordingly withdrawn. Fig.33 shows a somewhat dilated pelvis on the left side with fairly normal cupped lesser calyces. The right ureter in this patient also could not be catheterised and accordingly no dye was injected into the right kidney. Fig. 34 is similar in that the left kidney appears normal, the right ureteric orifice could not be catheterised. Fig. 35 and 36 which were carried out on different occasions show considerable dilatation of the kidney pelvis on the right side with dilatation of the ureter. The left side shows gross distortion of the kidney outline. Cavity formation could be seen in both outer and lower poles. In fig. 37 the right kidney appears to be normal in outline. The left ureter could not be catheterised and accordingly no pyelogram X-ray was obtainable. A normal retrograde pyelogram was obtained in fig. 38 which reveals a slightly dilated renal pelvis. As the left ureter could not be catheterised further than 2 cms. no pyelogram was obtained on this side. In fig. 39 a moderate degree of hydronephrosis is seen on the left side; the ureter shows some dilatation. On the right side the ureter was only partially catheterised and considerable dilatation is seen in it. The kidney is not visualised. A retrograde/

retrograde pyelogram was not possible in the patient J.P. as the right ureter was completely obscured. However the left side was catheterised and a pyelogram obtained. Fig. 40 shows some dilatation of the middle group of calyces and incomplete filling of the upper pole. In regard to R.S. who had been found to have a calcified left kidney and ureter which could not be catheterised, an attempt was made to carry out a retrograde pyelogram on the left side with the result seen in fig. 41. Some distortion of the middle and upper calyces is evident with dilatation of the pelvis.

It can be seen that the retrograde pyelograms obtained are a useful ancillary method of localising the distribution of the lesion in the affected kidney when it can be catheterised. Its value in estimating the appearance and condition of the contralateral kidney is also evident.

It is therefore advisable to make use of all the clinical findings assisted by the surgical techniques of intravenous pyelography, cystoscopy and retrograde pyelography to obtain accurate localisation of the tuberculous lesion or lesions present. It is felt however that a more reliably quantitative estimate of renal damage is required and so the Inulin/PAH excretion and clearance procedures were carried out.

CHAPTER VI

PRODROMAL LESIONS

It has been categorically stated by most authorities in discussing the etiology of renal tuberculosis that the disease is not the initial presenting lesion of tuberculosis.

Thomson-Walker (1937) stated that strictly primary renal tuberculosis does not exist. He goes on to state that there is always a primary focus present in the body though not always discovered clinically. In 193 patients who had renal tuberculosis operated on by him, 48.1 per cent had lesions elsewhere. In 346 patients who had been operated on for renal tuberculosis Braasch (1920) found 71 per cent had had previous evidence of tuberculosis. A further series described by Persson (1925) had prodromal extra renal tuberculosis in 50 per cent of cases. Borthwick (1956) assessed this feature in the course of a review of renal tuberculosis and found that in 48.3 per cent of males there was evidence of extra uro-genital tuberculosis, whereas in females the proportion was slightly lower at 46.3 per cent.

Thomson-Walker (1937) found active pulmonary tuberculosis/

tuberculosis in only 5.3 per cent of his series whereas Borthwick (1956) reports that 47.7 per cent of patients had pulmonary tuberculosis and a further 12.6 per cent had combined lung and bone and lung and joint tuberculosis.

In the present series 16 (72.7 per cent) had evidence of previous pulmonary tuberculosis. Tuberculous epididymitis was found in three patients (13.6 per cent), D.O'R, W.S. and R.S. as prodromal lesions. Thomson-Walker had 23.3 per cent with epididymitis in his series whilst Borthwick had 63.8 per cent.

E.C. in whom there was no evidence of pulmonary involvment had had tuberculosis of the third and fourth lumbar spine seven years prior to the renal disease. M.P. had previously suffered from tuberculosis of the sternum.

It is interesting that the daughter of T.B. had had tuberculous meningitis two years prior to his own illness.

R.Y., who is the youngest patient in this series, had previously suffered from pulmonary tuberculosis and was orphaned by the death of his mother by pulmonary phthisis.

In four patients (18 per cent) no distinctive evidence was found of the presence of a prodromal lesion.

The tubercle bacilli may reach the kidney in one of the following three ways:-

(1) by an ascending route from the epididymis, seminal vesicles or prostate.

(2) by lymphatic channels from neighbouring glands or

(3) by blood spread.

Medler (1926 and 1932) showed that bilateral renal tuberculosis was present histologically in many patients who had died of extra-urogenital tuberculosis.

It was considered that the resistance of the patient and the virulence of the bacilli determined the development of the kidney lesion. Following breakdown of a small quiescent lesion in the kidney, a tuberculous bacilluria may arise and in this way symptoms and signs of the disease develop. The process, once it has invaded the mucous membrane of the renal pelvis and caused ulceration may result in further lesions developing elsewhere in the renal tract with spread occurring into the ureter and thus to the bladder itself.

Fullerton (1927) in a series of 141 cases found evidence of some tuberculous lesions in 26 per cent and added that/

that no doubt hidden foci were present in glands, bones etc. but not sufficiently obvious to arrest attention during an ordinary clinical examination.

In this series the most common precursor of renal tuberculosis was lung involvement. The incidence of prodromal lesions affecting other parts of the genital system - seminal vesicles, prostate and epididymis, - found by Borthwick (1956) was not confirmed in this small series. It is generally recognised however that renal tuberculosis is not a primary disease but is secondary to another focus of tuberculous infection, apparent or latent.

CHAPTER VII

BIOCHEMICAL FINDINGS

The biochemical investigation which has been utilised for the purpose of this series was the combined Inulin/PAH excretion test as described in chapter II. This test was carried out on each patient on three occasions,

(1) prior to nephrectomy

(2) one week after nephrectomy and

(3) six months after nephrectomy.

From the results of the test a value for Renal Plasma Flow (RPF), Glomerular Filtration Rate (GFR), and Maximal Tubular excretion of p-aminohippurate (Tm_{PAH}) was obtained. The maximal excretion of PAH depends on the number and the functional efficiency of nephrons and is little influenced by physiological vasomotor variations in renal blood flow and in glomerular filtration (Smith, (1951). In renal disease the maximal tubular excretion of Tm_{PAH} is a measure of surviving functional kidney tissue, the quantitative accuracy of which is further discussed in chapter X.

If the Tm_{PAH} figures are arranged in descending orde/

order of the pre-operative value (fig.43) the cases can be arranged in mild, moderate and severe groups. It can be seen from fig. 43 that there is an overall loss of functional renal tissue immediately after operation which is not made good in six months time. It is important to note that the values obtained pre-operatively are for the combined functioning ability of the two kidneys, while the post operative figures are for the single remaining kidney, the percentage of average normal figure being calculated on the average normal for two kidneys. In the mild group the Tm_{PAH} value is 75 per cent of average normal or higher; in the moderate group it is 50 - 75 per cent and in the severe group it is less than 50 per cent of average normal.

A review of these groups will now be given, with details of illustrative examples of Tm_{PAH}, RPF and GFR results.

MILD GROUP.

There were five patients in this group in all of whom the pre-operative maximal tubular excretory capacity of PAH (Tm_{PAH}) for two kidneys was more than 75 per cent of average normal. The oldest patient was 35 years, the youngest 23 years and the mean age 28.8 years. (fig.43).

Maximal Tubular Excretory Capacity of PAH.

Maximal Tubular Excretory Capacity of PAH.

The mean value of Tm_{PAH} prior to operation was 63.7 mgm. per min. (80 per cent of average normal): one week after operation there had been a considerable fall to 45.6 mgm. per min. (57.8 per cent of average normal) with a further slight but not significant fall to 42.3 mgm. per min. (53.6 per cent of average normal) after six months. Fig. 44.

In J.P. the Tm_{PAH} pre-operative value was 61.2 mgm. per min. (77.5 per cent of average normal): one week post operatively this figure was 60.4 mgm. per min. (77 per cent of average normal). It is difficult to explain this high value after nephrectomy as the six month's figure was 34.0 mgm. per min. (43 per cent of average normal). In general, at the end of six months the amount of functional renal tissue was within the normal range for a single kidney.

Renal Plasma Flow.

The mean value for the mild group for RPF was 431 ml. per min. (69 per cent of average normal): at one week after operation RPF was 415 ml. per min. (66 per cent of average normal) whilst at six months this figure had fallen to 315 ml. per min. (50 per cent of average normal). Fig. 44.

In fig. 45 the RPF and GFR results are arranged according to the descending value of Tm_{PAH} pre-operatively. It can be seen that the general pattern is similar although the quantitative amount of renal tissue damaged cannot be assessed as accurately as with Tm_{PAH}.

The RPF value for RS pre-operatively was low at 267 ml. per min. (43 per cent of average normal): after one week the figure was 232 ml. per min. (42 per cent of average normal) and remained more or less the same after six months. In this patient there had been some improvement in the RPF after nephrectomy whereas in AC the initial value which had been 527 ml. per min.(84 per cent of average normal) fell immediately after operation to 444 ml. per min. (71 per cent of average normal) and was finally reduced to 277 ml.per min. (44 per cent of average normal) after six months.

Glomerular Filtration Rate.

The mean value for the mild group for GFR was 82 ml. per min. (67 per cent of average normal) prior to operation. Immediately after operation the GFR was 69 ml. per min. (56 per cent of average normal) whereas in six months time there had been some slight recovery and the figure was 72 ml. per min. (59 per cent of average normal). Fig. 44.

The GFR results which have been arranged according to the pre-operative value of Tm_{PAH} results in fig. 45 showed no particular trend other than that there is an associated parallel with Tm_{PAH} and RPF results.

The pre-operative value of GFR in MP was 57 ml. per min. (46 per cent of average normal): after one week the figure had dropped to 52 ml. per min. (42 per cent of average normal) and after six months it recovered to 58 ml. per min. (47 per cent of average normal). Initially RS had a GFR result of 90 ml. per min. (73 per cent of average normal) falling one week after operation to 76 ml. per min. (62 per cent of average normal) and finally rising after six months to 79 ml. per min. (64 per cent of average normal).

In the mild group the Tm_{PAH}, RPF and GFR values pre-operatively indicate that there is a reasonable amount of functional renal tissue, fig. 44. One week after operation there is a reduction in the amount of functional renal tissue present. Six months later there has been a still further slight drop in functional renal tissue but the overall final result indicates that there is still substantial renal function in the remaining kidney.

MODERATE GROUP.

In the moderate group there are eight patients in whom the pre-operative maximal tubular excretory capacity of PAH for two kidneys was more than 50 per cent and less than 75 per cent of average normal. The oldest patient was 45 years, the youngest 12 years and the mean age 27.3 years, slightly lower than but not significantly different from the mild group, fig.43.

Maximal Tubular Excretory Capacity of PAH.

The mean value of Tm_{PAH} prior to operation was 57.7 mgm. per min. (60.5 per cent of average normal): one week after operation Tm_{PAH} was 45.5 mgm. per min. (57.7 per cent of average normal) which indicates that there has been very little loss of functional renal tissue. This result for Tm_{PAH} of 45.5 mgm. per min. (57.7 per cent of average normal) was also found six months after operation. This general result is discussed further in chapter X.

An inspection of individual figures is interesting. TB, RY and MB all showed some increase in Tm_{PAH} after operation although all three reverted to values which were less than those prior to operation. In the case of WN the pre-operative value of 45.5 mgm. per min (58 per cent of average normal) had/

had fallen to 38.5 mgm. per min. (49 per cent of average normal) one week after operation and finally had risen to 46.7 mgm. per min. (59 per cent of average normal) six months after operation, indicating that hypertrophy had occurred in the remaining kidney following removal of the diseased organ. Further reference will be made to this in chapter X.

Renal Plasma Flow.

The mean for the moderate group in respect of RPF results was 597 ml. per min. (79 per cent of average normal) prior to nephrectomy: one week after nephrectomy it was 397 ml. per min. (64 per cent of average normal) and six months later 373 ml. per min. (60 per cent of average normal).

On inspection of fig. 45 it can be seen that the general pattern throughout has been consistent. Only in one, WN, was there an increase in RPF value after operation. It, however, had settled six months after operation. This increase from 385 ml. per min. (62per cent of average normal) was, perhaps, due to some technical difficulty experienced during the execution of the test immediately after operation. VB at six months after nephrectomy had an increase in RPF to 512 ml. per min. (82 per cent of average normal) from an/

an initial value of 437 ml. per min. (70 per cent of average normal) which had fallen to 411 ml. per min. (66 per cent of average normal) one week after operation.

Glomerular Filtration Rate.

The results in this group were in keeping with the other results. The mean value prior to operation was 84 ml. per min. (68 percent of average normal) dropping to 75 ml. per min. (61 per cent of average normal) one week after nephrectomy and recovering to 78 ml. per min. (63 per cent of average normal) six months.

An inspection of the detailed values, fig. 45, shows no specific trend, the figure falling fairly closely between those of RPF and Tm_{PAH}. In JMcA the initial value was 74 ml. per min. (61 per cent of average normal) falling one week after operation to 50 ml. per min. (41 per cent of average normal) and returning to 75 ml. per min. (61 per cent of average normal) six months after operation whereas in DO'R the initial value of GFR was 90 ml. per min. (73 per cent of average normal) falling to 84 ml. per min.(68 per cent of average normal) one week after operation and finally the figure being 65 ml. per min. (53 per cent of average normal) at six months.

The trend generally in the moderate group indicates/

indicates that the amount of functional renal tissue is less than that of the mild group, although the RPF and GFR values remain slightly better. One week after operation there has been a further slight loss in the amount of functional renal tissue as shown by the Tm_{PAH} value but the loss is considerably less than that seen in the mild group. The fall in RPF and GFR has also been correspondingly less than that which occurred in the mild group after one week. Six months later the Tm_{PAH} figure was unchanged whereas in the mild group there had been a further loss at six months.

SEVERE GROUP.

In this group there are nine patients, the pre-operative maximal tubular excretory capacity of PAH (Tm_{PAH}) for both kidneys being less than 50 per cent of average normal. The oldest patient was 62 years, the youngest 25 and the mean age 42.4 years, significantly older than in the other two groups.

Maximal Tubular Excretory Capacity of PAH.

The mean value of Tm_{PAH} before operation was 31.8 mgm. per min. (40.4 per cent of average normal); one week after nephrectomy it had dropped to 30.1 mgm. per min. (38.1 per cent of average normal) whereas in six months time it had risen/

risen to 36.2 mgm. per min. (45.9 per cent of average normal).

In this group the most outstanding feature has been the considerable recovery generally of the Tm_{PAH} values found six months after operation. In WS the pre-operative value for Tm_{PAH} was 29.7 mgm. per min. (38 per cent of average normal); this figure fell to 20.2 mgm. per min. (26 per cent of average normal) one week after operation whereas in six months time the Tm_{PAH} value was 35.0 mgm. per min. (44 per cent of average normal). Fig. 43. The pre-operative value for HMcL was 28.1 mgm. per min. (35.7 per cent of average normal) which had risen slightly one week after operation to 29.1 mgm. per min. (37 per cent of average normal) and made a more significant recovery still to 39.1 mgm. per min. (50 per cent of average normal) six months after operation.

The hypertrophy of the contralateral kidney which occurs on the removal of the diseased organ is well represented in these two examples and will be commented on more fully in chapter X.

Renal Plasma Flow.

The RPF results for this group showed a mean of 240 /

240 ml. per min. (38 per cent of average normal) prior to nephrectomy: after one week RPF was 284 ml. per min. (45 per cent of average normal) whereas in six months the figure obtained was 223 ml. per min. (36 per cent of average normal).

Further reference to fig. 45 shows that the trend which was noted to occur in the mild group and the moderate group so far as the RPF values were concerned has been maintained in the severe group. In AT the pre-operative value for RPF was 416 ml. per min. (67 per cent of average normal) a figure which, after one week, had fallen to 260 ml. per min. (42 percent of average normal) and was reduced to 215 ml. per min. (34 per cent of average normal) six months after operation. In WS the pre-operative value for RPF was 170 ml. per min. (27 per cent of average normal) which rose slightly one week after operation to 213 ml. per min. (34 per cent of average normal) but six months after nephrectomy had fallen again to 184 ml. per min. (30 per cent of average normal).

Glomerular Filtration Rate.

The GFR results in this group follow a similar pattern to that seen in the mild group and moderate group. The mean value for GFR before operation was 51 ml. per min. /

min. (41 per cent of average normal): one week after operation was 53 ml. per min. (43 per cent of average normal) with reversion to the original value six months after operation, 51 ml. per min. (41 per cent of average normal).

In the severe group WS had an initial GFR value of 42 ml. per min. (34 per cent of averagenormal) which improved to 47 ml. per min. (38 per cent of average normal) one week after nephrectomy and remained at 47 ml. per min. (38 per cent of average normal) six months after operation. In HMcL the pre-operative value for GFR was 42 ml. per min. (34 per cent of average normal) rising one week after operation to 53 ml. per min. (43 per cent of average normal) but finally returning to a lower figure of 44 ml. per min. (35 per cent of average normal) six months after nephrectomy. Fig. 45.

In the severe group, as has been stated, there has been a considerable loss of functional renal tissue, the mean value of Tm_{PAH} RPF and GFR being less than 50 per cent of average normal in each case. One week after operation there has been a slight improvement in RPF and GFR group figures, though the Tm_{PAH} results have been still further lessened. In regard to this, comparison with the other two /

two groups, mild and moderate, shows that there has been a slight increase in the RPF and GFR values in the severe group whereas in the other two groups there had been a fall in RPF and GFR after one week. Six months later the outstanding feature has been the recovery of Tm_{PAH} with a maintenance of the GFR value though the RPF result has fallen to a value lower than that existing pre-operatively.

Comparison with the mild and moderate groups at six months after nephrectomy reveals that the general trend of reduction in RPF and GFR values has been consistant in the three groups but that the Tm_{PAH} value has shown recovery. The significance of this feature will be discussed in chapter VIII.

CHAPTER VIII

INTERPRETATION OF RESULTS

In chapter VII reference has been made to the tables prepared from the results of the excretion and clearance tests. It is now proposed to assess the significance of these results.

The maximal excretion of PAH depends on the number and the functional efficiency of nephrons and is little influenced by physiological vasomotor variations in renal blood flow and in glomerular filtration, Smith (1951). In renal disease the maximal tubular excretion of PAH is a measure of surviving functional kidney tissue.

The Tm_{PAH} results have been arranged in descending order of their pre-operative values. It has been found that a convenient though arbitrary arrangement of these results can be made by which the patients are divided into three distinct groups:-

(1) a mild group in which the pre-operative values of Tm_{PAH} were 75 per cent or more of average normal. There are five patients in this group.

(2) a moderate group in which the pre-operative value of Tm_{PAH} was from 50 - 75 per cent of average normal. There are eight patients in this group.

(3) a severe group in which the pre-operative value of Tm_{PAH} was less than 50 per cent of average normal. There are nine patients in this group.

Mild Group.

In the mild group, as has already been seen, the diseased kidney still contains a considerable amount of functional renal tissue and this is lost when surgical removal takes place. That this is the case is seen in the Tm_{PAH} values pre-operatively and post-operatively, fig. 44.

From the group means it can be seen that the pre-operative value for Tm_{PAH} was 63.7 mgm. per min. (80.7 per cent of average normal): one week after operation the value was 45.6 mgm. per min. (57.8 per cent of average normal) with the final result six months later being 42.3 mgm. per min. (53.6 per cent of average normal). It is also noted that compensatory hypertrophy of the remaining kidney is maximal by the end /

end of the first post operative week. Six months later there is no significant alteration of renal function, though the renal plasma flow has shown some decrease from 415 ml. per min. (66 per cent of average normal) one week after operation to 315 ml. per min. (50 per cent of average normal).

Moderate Group.

In the moderate group the amount of functional renal tissue remaining in the diseased kidney pre-operatively is considerably less than that remaining in the affected kidney in the first group. The mean value for Tm_{PAH} for the moderate group is 47.4 mgm. per min. (60.5 per cent of average normal) as compared with 63.7 mgm. per min. (80.7 per cent of average normal) in the mild group. One week after operation there has been some slight loss of functional renal tissue, the Tm_{PAH} figure dropping from 47.7 mgm. per min. (60.5 per cent of average normal) to 45.5 mgm. per min. (57.7 per cent of average normal) and in six months time there is no further hypertrophy of the remaining kidney to make good the loss resulting from the removal of the diseased organ, the TmPAH figure being unaltered from that found one week after operation, 45.5 mgm. per min. (57.7 per cent of/

of average normal).

Severe group.

The most interesting finding is, that in the severe group there is a significant increase in the Tm_{PAH} values six months after operation. A week after operation hypertrophy of the contralateral kidney has almost made good the loss of functional tissue following operation. Unlike the mild and moderate groups compensatory hypertrophy is not maximal in a week and progresses until, in six months, renal function is better than before nephrectomy. This is a most intriguing situation and can only be interpreted by suggesting that the presence of a severely diseased kidney has inhibited compensatory hypertrophy of the contralateral kidney and possibly also depressed its functional capacity. As soon as the diseased kidney is removed this influence no longer exists - function is recovered and in fact is improved further by the occurrence of some hypertrophy in the remaining kidney. These facts have been represented diagrammatically in fig. 100.

Arataki (1926) carried out experimental researches on the compensatory enlargement of the surviving kidney/

kidney after nephrectomy in albino rats and found that the increase in renal mass was attributed to hypertrophy and hyperplasia of the tubules and their epithelium, but not to increase in the number of glomeruli. Jackson and Shiels (1927/28) confirmed these findings and made detailed observations of the rate at which the compensatory hypertrophy took place. They have stated that this is much greater when nephrectomy has occurred in young rats (first month) than in adolescent or mature animals. They also state that there was no evidence of pseudo-hypertrophy due to renal congestion.

Moore (1929) found that there was no increase in the number of glomeruli in the kidney of the adult white rat which had had nephrectomy in early life. He followed this with a further paper in 1930 in which he reported an interesting case in which there had been hemi-hypertrophy. He took the opportunity to study in detail the two kidneys. He found that each kidney contained essentially the same number of glomeruli in spite of the notable difference in the size and weight of the two organs.

Rollason (1949) in his paper on the role of cellular hyperplasia in the compensatory hypertrophy of the kidney/

kidney of the young rat concluded that the hypertrophy began immediately after the recovery from the operation and had reached its maximum within twenty days. He found that both cortex and medulla increased in size. The tubules became enlarged within twenty four hours as a result of hypertrophy occurring in the cells whilst increase in this mitotic figure was present within four to eight hours in most of the tubules.

Saphir (1927) mentioned that the glomeruli became enlarged in rats and also in rabbits primarily because the capsular cells increased. Sulkin (1949) also studied the cytological alterations which took place after operation and found that mitosis was most active between the third and tenth days. Malm (1949) described a series of studies which referred to the recovery of renal function after nephrectomy for renal tuberculosis. Malm found that on the twenty sixth day after nephrectomy there had been considerable recovery of function in the remaining kidney.

I have not been able to find a report of hypertrophy of the remaining kidney following nephrectomy, for unilateral renal tuberculosis, in man. All the evidence quoted above has been from the results of experimental studies mainly/

mainly in the albino rat.

Another aspect of the experimental study in this problem has been the assessment of the effectiveness of diet. A high protein diet has been found to accelerate hypertrophy and cause a greater increase in the mass of renal tissue. McKay et al (1938), Smith, A.H. and Moise (1927) have commented on the effectiveness of diet in the achievement of hypertrophy of the surviving kidney in animals. No special arrangement was made to ensure that the patients in my series had a particularly enriched diet in so far as protein was concerned. The diet was arranged to provide sufficient nutrition for the patients' general needs and not particularly to encourage hypertrophy of the remaining kidney.

The RPF results have been arranged in descending order according to their pre-operative value, fig. 48 and although an arbitrary arrangement similar to that which has been made for Tm_{PAH} would result in a suitable division into two groups:-

(1) above 50 per cent of average normal value

(2) below 50 per cent of average normal value

no advantage would be achieved.

The GFR results have similarly been arranged in descending order according to their pre-operative value, fig. 49 and the same comment applies to this table.

A division into two groups could be made but once again the information gained would not be of any further advantage.

The three principal groups have been inter-related as follows:-

(1) GFR and RPF have been arranged in tabular form according to the descending order of the pre-operative value of Tm_{PAH} Fig. 45.

(2) GFR and Tm_{PAH} have been arranged in tabular form according to the descending order of the pre-operative value of RPF. Fig. 50.

(3) RPF and Tm_{PAH} have been arranged in tabular form according to the descending order of the pre-operative value of GFR. Fig. 51.

In group (2) the closest pair of correlations are given. This suggests that loss of tubules and glomeruli/

glomeruli is much more dependent on diminished blood supply than is the loss of glomeruli and diminished blood supply with destruction of tubules or loss of tubules. It thus appears that the diminished blood supply results in the destruction of glomeruli, indicating that intimal proliferation of the arterioles is the most important change in renal tuberculosis.

In order to confirm statistically the correlations of:-

(1) Tm_{PAH} with RPF

(2) Tm_{PAH} with GFR

(3) UCT with Tm_{PAH}

(4) UCT with GFR

(5) RPF with GFR

tables have been prepared and are presented in Volume II as figs. 53 - 57.

The correlation co-efficient obtained with RPF and GFR is + 0.79 indicating that there is statistical significance in this relationship. The regression equation for RPF and GFR has also been derived and is $x = 5.40 (y - 73.0) + 374$ where x is RPF and y is GFR. This curve is shown in fig. 51. Fig. 59. and fits very well with the plotted results.

It is suggested that the close relationship between RPF and GFR in renal tuberculosis is due to the pathological effect of the disease on the arterioles which become the seat of endarteritis - figs. 94 and 95. As a result of the intimal proliferation the lumina of the vessels are narrowed and the blood flow through the glomeruli is diminished. As a further consequence of the lowered intra-glomerular blood pressure the glomerular filtration rate decreases in proportion to the fall in blood supply.

That the tubular function is less directly related to blood flow suggests that there are considerable reserves of oxygen carrying capacity to compensate the loss in total blood supply, thus tubular function diminishes with blood supply but is not quite so directly dependent as is the filtration rate.

The slight dilatation of the afferent arteriole combined with slight constriction of the efferent arteriole will increase the filtration fraction and thus compensate in the same degree for the reduction of blood flow.

Nineteen patients had intimal proliferation of the smaller arterioles amounting to endarteritis. In three/

three patients no evidence of this was seen in the sections examined.

In regard to the correlation coefficient obtained between UCT and GFR which was 0.80, fig.56 and between UCT and Tm_{PAH} which was 0.32, fig.55 it is evident, as is to be expected, that there is a closer correlation between the two filtration factors, UCT and GFR, than there is between UCT and Tm_{PAH}. The urea is filtered by the glomeruli but some of it is reabsorbed on its passage through the tubules.

The regression equation has been prepared from the UCT and GFR figures which is $x = 0.66 (y - 76) + 56$ where x is UCT and y is GFR. The curve of this equation, as seen in fig. 58, fits in satisfactorily with the actual plotted results.

Perhaps the most significant figures are found in fig. 46 in which the derived values i.e. fractional figures, (FF) RPF/Tm_{PAH} and GFR/Tm_{PAH} have also been arranged according to the pre-operative descending value of Tm_{PAH}. In primary renal disease there is, as a rule, vaso-dilatation of the post glomerular arterioles lowering the effective glomerular filtration and thus producing a low filtration fraction. In/

In hypertension, on the other hand, there is peripheral vaso-constriction affecting, in the kidney, the post-glomerular arterioles thus raising the effective glomerular pressure and producing a high filtration fraction.

The filtration fraction is the fraction of the blood plasma that is filtered in the glomeruli and passes from the capillaries into the glomerular capsule. It is principally dependent on the hydrostatic filtration pressure which in turn is controlled by:-

(1) pre-glomerular vasospasm, i.e. increased resistance to the flow of blood before it enters the glomerulus.

(2) post glomerular vaso-dilatation, i.e. diminished resistance to the outflow of blood from the glomerulus.

RPF/Tm_{PAH} represents relative proportions of plasma flow and tubular function. If it is high there is hyperaemia of remaining functional renal tubules. If it is low there is ischaemia of the remaining functional tubules.

GFR/Tm_{PAH} represents the amount of glomerular filtrate that is acted on by each unit of functional renal tissue. If high the tubules are being relatively overloaded, and if low, /

low, they have to elaborate less than their optimum amount of urine.

It can be seen that there are two general patterns of renal function in the present series:-

1. primary renal disease and
2. hypertensive nephrosclerosis

In (1) the filtration fraction was low while the RPF/Tm_{PAH} was slightly raised. In (2) there was a high filtration fraction and a lowered RPF/Tm_{PAH}. Illustrative of the first group is JP, fig 46, who pre-operatively had a filtration fraction of 0.157 (80 per cent of average normal) and RPF/Tm_{PAH} of 10.68(134 per cent of average normal) which would suggest that there is a simple primary renal disease. Post-operatively the filtration fraction had fallen still further to 0.137 (70 per cent of average normal) whilst the RPF/Tm_{PAH} remains much the same at 10.40 (131 per cent of average normal). In six months however the filtration fraction is raised to 0.198 (100 per cent of average normal) and the RPF/Tm_{PAH} increased to 13.20 (167 per cent of average normal) showing an alteration from the primary renal disease pattern to a pattern which is midway between primary renal disease and hypertensive nephrosclerosis.

From the clinical findings there has been no apparent alteration in the blood pressure. Fig.98 shows that JP whose blood pressure was 128/86 prior to nephrectomy had a reading of 130/80 six months after operation.

As an example of the second type of functional pattern MP had an elevated filtration fraction at 0.233 (118 per cent of average normal) pre-operatively and a lowered RPF/Tm_{PAH} of 3.70 (47 per cent of average normal). One week after operation there is not very much alteration in either of these fractions although the RPF/Tm_{PAH} value has been elevated slightly to 5.33 (66 per cent of average normal) which remains lower than the average normal figure of 7.92. The six months post operative values of 0.296 (138 per cent of average normal) for FF and 4.88 (62 per cent of average normal) for RPF/Tm_{PAH} confirm the continued hypertensive nephrosclerotic pattern seen in the derived figures in this patient's case. Reference to fig. 42 shows that MP had a pre-operative blood pressure of 160/100 although in six months time this had dropped to 128/84. It had become somewhat elevated to 170/106 after four years. Fig.98.

An attempt has been made to arrange the mean values of the derived figures in groups. The arrangement shows /

shows the general pattern in patients who have a Tm_{PAH} value

(1) greater than 75 per cent

(2) between 50 and 75 per cent

(3) less than 50 per cent

It is seen that in the pre-operative phase in the mild group the values for all three fractions are less than normal, that is the simple primary renal disease pattern whereas six months after operation there has been an alteration to the hypertensive pattern. In the severe group the initial pattern resembles that of hypertension - high filtration fraction and lowered RPF/Tm_{PAH} and six months after operation this has been further intensified. It is interesting to note that the older patients tend to be in the latter group with the most severe lesions.

The derived fraction GFR/Tm_{PAH} is closely allied to that of RPF/Tm_{PAH}, the information which is given by each being similar in every instance.

CHAPTER IX

PATHOLOGY

Twenty two kidneys were examined which had been surgically removed from patients who were considered clinically to be suffering from renal tuberculosis. There were eleven right kidneys and eleven left kidneys and of these specimens twelve (55 per cent) were obtained from males and ten (45 per cent) from females.

BACTERIOLOGY.

Isolation of the causative organisms is necessary to confirm a diagnosis of tuberculosis. The Koch's bacillus, which is an acid and alcohol fast organism is sometimes difficult to isolate but if the satisfactory routine of bacteriological search is practised and culture and biological techniques carefully employed the results should be appropriately successful. In this series direct examinations were carried out at Stonehouse and Hairmyres Hospitals. The patients who were seen at Stonehouse Hospital had the direct examination carried out in the laboratory at the hospital whereas those seen at Hairmyres Hospital had their examination carried out at the laboratory at Hairmyres Hospital. Cultures and animal/

animal inoculations were carried out from both hospitals at the Central Laboratory, Hamilton.

The presence of ulcerative lesions in the pelvis or abscesses in the cortex or medulla, which have direct access to the renal pelvis, seem to be the determining factors in the production of tuberculous bacilluria. Repeated and detailed examination of the urine obtained casually and in 24 hour collections was carried out in every case. Out of 116 urines from twenty patients who were examined bacteriologically, 54 were positive and 62 negative for tuberculosis. In two patients, A.Bk. and J.M., no tubercle bacilli were discovered by any of the methods mentioned. In J.M. five specimens of urine were examined pre-operatively whilst in A.Bk. five were examined.

The figures just mentioned include the total results from the different methods of bacteriological examination of urine, direct examination, culture and animal inoculation. Dr. Gow Brown of the Central Laboratory, Hamilton, carried out typing of some of the specimens and found them to be of the human variety. In the post-operative phase five specimens of urine contained tubercle bacilli, three of these were from/

from one patient, A.Bt, who, on cystoscopic examination was seen to have persistent chronic cystitis. A second patient, M.M. also had a small area of persistent tuberculous cystitis and from her, on two occasions post-operatively, urine was found to contain tubercle bacilli. Another three of the remaining twenty patients were found to have secondary urinary infection after operation. In those three patients a coliform pyelonephritis was present which responded to treatment.

All the kidneys removed at operation underwent a similar examination. They were bisected sagittally, one half was retained for photography while from the other half, blocks were taken for histological examination. The remainder of this tissue was digested and concentrated. It was then examined microscopically and culturally for tubercle bacilli. From fourteen of the kidneys acid and alcohol fast bacilli were found on direct film and four on culture. The remaining eight were negative on concentration and on culture. It is pointed out that repeated examination of urine may often be necessary in order that the causative organisms can be identified with certainty and thus effectively establish the bacteriological diagnosis of tuberculosis.

MACROSCOPIC APPEARANCES.

Examinations of the kidneys obtained at operation included a linear measurement of the specimen together with its weight; the length of the ureter attached was also noted. Photographs of most of the kidneys are shown in Volume II, figs. 60 - 86.

After the kidney has been bisected sagittally the detail of the macroscopic appearance of the pelvis, medulla and cortex is noted, the presence of tuberculous abscesses detailed, and, as mentioned already, smears obtained of any purulent material present. A brief note is now given of the kidneys which are illustrated in Volume II. All the kidneys photographed are actual size except figs. 74 and 75 which are 4/5ths of life size.

Figs. 60 - 61. A.Bk. The surface of the kidney is lobulated and there are five large abscesses on the cut surface. Urine culture was not positive but was negative on eight occasions.

Fig. 62. A.Bt. This is a small kidney which had foetal lobulation on its surface. The cut section revealed a dilated pelvis which was lined by granulation tissue. Multiple tubercles are scattered throughout the medulla/

medulla and cortex; a few foci are caseous. Urine culture was positive on two occasions and negative on two occasions.

Fig.63. T.B. This was a moderately large kidney on the surface of which there was evidence of abscess formation. On cut surface a large lobulated abscess is present in the mid zone of the kidney. The lower calyces are dilated; granulation tissue is seen on the mucosal surface of the calyces of the lower pole. Urine culture was positive on two occasions and negative on two occasions.

Figs. 64 - 65. V.B. The surface contour shows gross foetal lobulation. On cut surface the kidney is a bag of caseous pus. There is a small amount of relatively normal tissue present in the upper pole. Urine culture was positive on one occasion and negative on one occasion.

Fig. 66. M.B. The contour of the kidney is normal. On cut section the primary calyces and pelvis are dilated. A tuberculous cavity is seen in the mid zone. Petechial haemorrhages are seen in the pelvic mucosa. Urine culture was positive on two occasions and negative on two occasions.

Figs. 67 - 68. A.C. The contour of this kidney/

kidney is normal but the surface is irregularly lobulated. No scarring or abscess formation is seen. On cut surface however, there is coalescing tuberculosis confined to the medulla. There is no caseation. Urine culture was positive on two occasions and negative on two occasions.

Figs. 69 - 70. A.F. This is a very large lobulated kidney of rather cystic appearance. There is considerable thickening of the ureter. On cut surface there is gross hydronephrosis with distension of the pelvis primary and secondary calyces. Urine culture was positive on two occasions and negative on one occasion.

Figs. 71 - 72. M.F. This kidney is of normal size and contour but on cut surface there is gross dilatation of the primary and secondary calyces. Abscess cavities are seen in the lower pole. The pelvic fat is increased. The ureter is not unduly thickened. Urine culture was positive on one occasion and negative on five occasions.

Figs. 73 - 74. M.M. Several small retention cysts are seen on the surface of the kidney, which, on cut surface, reveals that they are confined to the cortex. Numerous tuberculous cavities are present, particularly at the poles. The adjacent calyces show some mucosal ulceration. The pelvic/

pelvic fat is increased. There is no thickening of the ureter. Urine culture was positive on two occasions and negative on one occasion.

Fig. 75. H.McL. This is a large lobulated kidney with a smooth surface containing tubercles up to 8 mm. in diameter. On cut surface the pelvis and all the calyces are grossly dilated being filled with caseous pus. Multiple small tubercles are scattered in groups throughout both cortex and medulla. The ureter is somewhat thickened. Urine culture was positive on two occasions and was not negative.

Figs. 76 - 77. J.McA. The kidney is of normal contour. There is some increase in pelvic fat. On cut surface the pelvis, primary and secondary calyces are dilated, being filled with caseous pus. Small tubercles are seen in groups in both medulla and cortex. Urine culture was positive on two occasions and was not found negative.

Fig. 78. D.O'R. This is a kidney of normal shape and size which on cut section reveals dilated pelvis, primary and secondary calyces. Multiple tubercles are present on the mucosal surface of the upper calyces. The ureter is not thickened. Urine culture was positive on one occasion and/

and negative on two occasions.

Fig. 79. H.P. The kidney appears to be normal but on cut surface there are two small areas of fibrosis together in a pyramid on the lower pole. The mucosa of the pelvis is ulcerated and shows petechial haemorrhages. The ureter is normal. Urine culture was positive on one occasion and negative on one occasion.

Figs. 80 - 81. J.P. This is a normal shaped kidney with two groups of tubercles seen at the upper pole and another larger group present in the mid zone. On cut surface the pelvis is slightly dilated but no ulceration of the mucosa is evident. There are tiny coalescing tubercles underlying the superficial lesion. Urine culture was positive on one occasion and negative on one occasion.

Figs. 82 - 83. W.S. This is a small kidney of normal shape with a finely granular surface and a few depressed scars. On cut surface the pelvis is slightly dilated but the primary and secondary calyces are more dilated. In the upper pole there are large numbers of small abscesses in the pyramids and in the cortex. The serous surface of the pelvis and ureter are covered with punctate haemorrhages. Urine culture was positive on three ocasions and negative/

negative on one occasion.

Figs. 84 - 85. A.T. The kidney is small but unusually thick with some foetal lobulation. Depressed scars are present but no abscesses. On cut section there is gross dilatation of the primary and secondary calyces which contained caseous pus. The cortex is reduced to a narrow rim. Innumerable punctate haemorrhages are seen. The ureter is thickened. Urine culture was positive on four occasions and was not found negative.

Fig. 86. R.Y. This is a small kidney with two isolated large abscesses visible on the anterior surface near the lower pole and in the middle of the posterior surface. On cut section hydronephrosis is present. All the calyces are dilated. They are lined with tuberculous granulation tissue containing caseous material. The ureter is slightly thickened. Urine culture was positive on two occasions and was not found negative.

Seventeen patients (77 per cent) have evidence of tuberculous granulation in the mucosa of the renal pelvis. In the two patients, J.M. and A.Bk. in whom no tubercle bacilli were found on culture, tuberculous lesions were walled.off.

It is evident from the selection of kidneys seen that the outward appearance gives no indication of the extent of the lesion within the kidney substance. It is, however, evident that the extent of the tuberculous process histologically cannot be fully gauged from the macroscopic findings alone.

In the next section a description is given of the histological appearances which are seen in renal tuberculosis together with the results of modern anti-tuberculous chemotherapy.

HISTOLOGICAL APPEARANCES.

A few representative photomicrographs are included in Volume II, figs. 87 - 99 to demonstrate the types of lesions which are present in renal tuberculosis. It is proposed to discuss the histological appearances as they were affected by the various chemotherapies employed.

Streptomycin and PAS. Figs 87 - 88.

In fig. 87 characteristic tuberculous pyelitis is seen in which caseating tubercles are being walled off by reactive fibrosis which has been stimulated by streptomycin and PAS. The giant cell systems, showing multi-nucleated epithelioid cells surrounded by lymphocytes, are seen in the lower part of the section. In fig. 88 a/

a section of the ureter is seen. Chemotherapy has caused reactive fibrosis as a result of which the tuberculous ureteritis is being confined. Tuberculous giant cell systems are seen in both these sections.

Streptomycin and Isoniazid. Figs. 89,90,92 and 96.

In fig. 89 a large area of caseation is seen surrounded by reactive fibrosis which is attempting to wall off the tuberculous process and confine it. A destroyed glomerulus is seen in part of the section. In fig. 90 a larger area of caseation is present but the reactive round cell infiltration is more active than in the previous section. In fig.92 active tuberculosis is present with giant cell systems being seen in the lower part of the section. There is also considerable coalescing tubercles evident. In addition to that the section shows nephrosclerosis. A very active invading type of caseating tubercles is seen in fig. 96 with evidence of active round cell infiltration occurring in the neighbourhood of the caseating tubercles.

Streptomycin, Isoniazid and PAS. Fig.91.

In this figure the section reveals considerable reactive fibrosis taking place in an active renal tuberculosis. Multiple giant cell systems are seen in the centre of the section.

Isoniazid. Fig.97.

The outstanding feature in this section, in which multiple giant cell systems are seen, is the considerable round cell infiltration which is taking place to control the tuberculous process which is very active.

Untreated. Figs. 98 - 99.

As a means of comparison to the sections described above, two sections are included, figs. 98 and 99, which demonstrate untreated renal tuberculosis. The sections show widespread renal tuberculosis without any evidence of active control taking place. There is some round cell infiltration but the round cell reaction which is present is not as active as that which is seen in the sections described above.

Effects of Renal Tuberculosis.

(a) Healing. In fig. 90 staisfactory evidence is present of the healing reaction produced by the streptomycin and isoniazid. The confining influence of the round cell infiltration, stimulated by chemotherapy, is evident also in figs. 89, 96 and 97.

(b) Nephrosclerosis. In figs. 92 and 93 there are typical signs of nephrosclerosis showing destruction of /

of glomeruli and other renal elements.

(c) Endarteritis. In figs. 94 and 95 examples are presented of sections showing characteristic intimal proliferation occurring in renal tuberculosis, a feature which has already been mentioned in chapter VIII and which was confirmed on review of the histological sections.

LARGE KIDNEY SECTIONS.

In Volume II, as specimens 1 - 5 there are presented whole kidney sections from patients who are known to have had tuberculosis of the kidney. The method of preparation of these sections is given as an appendix to this chapter.

Specimen 1. J.McA. The kidney, which is of normal contour, reveals scattered tubercles of small size throughout the medulla. There are very small tubercles also seen in groups in the cortex. There is some dilatation of the pelvis and primary and secondary calyces. The ureter is not thickened.

Specimen 2. D.C. The kidney, which shows an indentation in the mid zone, shows hydronephrosis with three abscess cavities in the upper pole. There is also evidence of haemorrhage in this area. In the mid zone/

zone and in the lower pole there are areas of fibrosis. The ureter appears to be somewhat distorted.

Specimen 3. R.McN. A single large caseous abscess containing caseous pus is occupying the renal pelvis. There is a small abscess cavity in the lower pole. There is thickening of the ureter.

Specimen 4. M.J. A small kidney showing indentation of the surface. There is hydronephrosis of the upper pole with small areas of punctate heamorrhage. The ureter appears to be slightly thickened. This specimen shows healed renal tuberculosis.

Specimen 5. G.R. In this kidney there are three abscess cavities with an area of fibro-caseation in the upper pole. The ureter is somewhat thickened. There are also small tubercles seen in the lower pole.

Specimen 1 is that of J.McA, whose kidney is also seen as figs. 18, 37, 76 and 77. The other four specimens are from patients who were undergoing a further investigation which is being reported as a separate paper. All these specimens have been included as a practical method of demonstrating the lesions in renal tuberculosis.

Band (1935) used whole sections of kidney to demonstrate/

demonstrate the presence of microscopic bilateral renal tuberculous lesions in kidneys which, on naked eye appearance had revealed no evidence of tuberculosis though there had been tuberculous bacilluria.

DISCUSSION.

The histological appearances which have been described above are indicative of the effectiveness of the modern method of anti-tuberculous chemotherapy. Dick (1953a) described the effects of isoniazid when given alone in the treatment of renal tuberculosis. It was found to cause disintegration of the epithelioid cells and prevented development of fibrosis of isolated parenchymatous 'epithelioid' lesions. There was some absorption of recent caseation with re-vascularisation of all stages of tuberculous lesions including the dense fibrosis which surrounded old lesions and furthermore prevented the development of fibrosis in and around new lesions. It was stated at that time that a combination of various methods of treatment would probably produce a better effect than that produced b isoniazid alone. Dick (1953b) described the effects of streptomycin with and without p-amino-salicylic acid (PAS) on the histopathological processes in renal tuberculosis. In it he stated that tuberculous/

tuberculous lesions in the specimens from patients who had been treated with streptomycin and PAS showed a greater degree of fibrosis than after streptomycin alone. Also in this paper it was suggested that the best results from the histological viewpoint were obtained after a double course of streptomycin and PAS. The same author (Dick,1954) later compared the effects of streptomycin and PAS with those of streptomycin and isoniazid.

The main difference appeared to be that isoniazid had a more fundamental anti-tuberculous action by which epithelioid cells reverted to macrophages, highly vascular granulation tissue was produced without fibrosis and healing was more complete, with greater absorption of necrotic tissue. Dick (1955) is of the opinion that a combination of drugs, including isoniazid is more effective, as the toxic factor present is dealt with more expeditiously and real healing appears to occur more rapidly.

From these papers and the photomicrographs, figs. 87 - 99 it is apparent that a single drug therapy does not produce the maximum benefit but rather creates a condition in which the metabolism of the tubercle bacilli is so altered that it develops resistance to the drug which is being employed.

From the histological appearances it would appear that the best combination would be streptomycin and isoniazid. The improvement in the patients treated in this way would suggest that the drugs are synergistic in action. Borthwick (1956) in a review of genito-urinary tuberculosis has confirmed these findings and has added his opinion that the most effective combination of anti-tuberculous chemotherapy is obtained with streptomycin and isoniazid. Further reference to this aspect as it applied in this investigation is made in chapter XII.

APPENDIX

Method for cutting whole kidney sections employing the M.S.E. Large Section Microtome.

The kidney specimens are fixed in formol-acetate for two weeks, and then washed in running water for twelve hours. They are then transferred to a special solution of gum arabic and immersed for twenty four hours.

At the end of this period the specimens are orientated on the object table of the microtome in a four sided wooden box, which has sufficient gum arabic solution to cover them. The object table is placed in the deep freeze at -20°C for four to six hours, by which time the gum arabic solution should be frozen. The four sides of the wooden box are then removed and the sections cut at 100 - 150 μ/thickness.

The sections are collected in a flat dish in tap water (if sections are rolled up they should be flattened out) and the water changed to get rid of any surplus gum arabic. The specimen thus obtained is placed flat on a sheet of perspex over which has been poured a warm solution of 10 per cent gelatine, the whole is then covered with a sheet of No.1 filter paper, and arubber roller squeegee is run over it lightly to squeeze out surplus gelatine and air bubbles./

bubbles. The perspex sheet is suspended for a few seconds to drain, and then laid flat until the gelatine is set. It should be hung up at room temperature until no damp patches can be seen. The paper with the section mounted on it is peeled off the perspex and examined on an illuminated viewing box.

CHAPTER X

ASSESSMENT OF THE CASE

In this chapter an attempt is made to correlate the extent of the damage found on pathological examination of the extirpated kidney with the

(1) clinical findings

(2) surgical findings and

(3) biochemical findings.

CLINICAL FINDINGS.

Routine enquiry was unrewarding in the establishment of any precise symptom which would give an indication of the pathological state of the patients' functional renal tissue. Many patients when presenting their symptoms for the first time appeared to be very well. A common complaint given by eighteen out of the twenty two patients investigated was increased frequency of micturition at night and occasionally by day. Four of these patients were in the mild group, six in the moderate group and eight in the severe group, the grouping having been determined from the Tm_{PAH} values obtained pre-operatively - chapter VII. The degree of increased frequency was difficult to assess as many patients had been instructed by their doctor to/

to increase the amount of fluid taken. This hydrotherapy accordingly had increased the frequency and volume of micturition. The remaining four patients, one in the mild group, two in the moderate group and one in the severe group, did not give any history referable to the urinary tract and made no mention of difficulty in urination as they had apparently become accustomed to their symptoms. On questioning they admitted that they had some increase in the frequency of nocturnal micturition.

Painful micturition, which was not expected to be a common complaint was found in nine patients, two in the mild group, three in the moderate group and four in the severe group. The dysuria was normally associated with the commencement and completion of micturition and was most evident in patients who had a small bladder capacity. There was no suggestion however that the presence of this symptom gave any indication of the severity of the renal lesion but was more likely to be associated with the presence of cystitis and urethritis.

Six patients had backache which was found to vary somewhat in description. In five there was specific reference to the loin and in all of them the lesion was found on the side in which/

which the pain had been felt. In the remaining patient, backache was more generalised but eventually a swelling on the affected side which, on examination by aspiration, revealed the presence of acid and alcohol fast bacilli. Two patients had no symptoms referable to the urinary tract but on routine testing of the urine, protein and pus were discovered. Specially obtained specimens of urine from these patients was examined bacteriologically and the presence of acid and alcohol fast bacilli determined.

The erythrocyte sedimentation rate was carried out repeatedly in the patients under review and showed a wide variation. An attempt has been made to relate the findings to the histological findings of the kidneys obtained at operation. A brief note of some of these patients is given to demonstrate the usefullness of this test in the assessment of the case. All the readings are for the first hour and are given in millimetres. The method used was the Westerglen method. The results have not been corrected for any mild associated anaemia.

J.P. who had readings of 38 mms. and 54 mms. within a few days prior to operation had an increase to 76 mms. which fell to 70 mm. within two weeks and finally, the last reading/

reading available five months after nephrectomy was 29 mms. This patient had an active but very localised tuberculosis of the kidney which showed small areas of caseation which were undergoing re-active organisation. A.Bt. had ESR values of 40 mml. and 30 mm. prior to operation and immediately after operation the reading was 36 mm, eventually falling to a normal value of 10 mm. four months after operation. This patient had multiple scattered tubercles with associated caseation. Gross interstitial fibrosis of the kidney had also occurred. There was caseating tuberculosis with evidence of organisation in the tissues surrounding the active lesion. A.Bk. had a considerably elevated ESR value of 106 mms. This feature persisted although improved with chemotherapy. After operation a value of 80 mms. was obtained and in three months time this patient's ESR returned to normal. The post operative elevation was associated with a discharging nephrectomy wound. The kidney contained five large caseous abscesses: there was considerable fibrosis and glomerular sclerosis. This was a caseous kidney which was undergoing generalised fibrosis.

M.B. had more normal values for this test, 9 mms., 16 mms and just prior to operation 17 mms. Six weeks after operation/

operation the value had risen to 47 mms. settling in a further three months to 19 mms. This patient had a very early lesion, the appearance being that of tuberculous pyelitis. This was a non-caseous lesion with evidence of organisation taking place in the wall of the single tuberculous cavity present. M.F., prior to operation, had readings of 17 mms. and 11 mms. The kidney showed multiple tiny tubercles with associated abscess formation containing caseous pus. There was considerable re-active organisation taking place. After operation the findings were 12 mm., 8 mm., and 10 mm., 4 mm. and 5 mm. This patient had shown no evidence of the activity of the disease in the values obtained for the sedimentation rate. H.McL. prior to operation had a reading of 16 mm. Histologically he had a widespread lesion with multiple caseating abscess cavities. There was some re-active organisation taking place. The values after operation were 12 mm., 8 mm., and 2 mm. In this patient the readings did not indicate the extent or type of lesion present. D.O'R. before nephrectomy had readings of 2 mm. and 4 mm. Histologically he had an unusually widespread tuberculosis of the kidney with large areas of caseation. The values obtained prior to operation gave no indication of the /

the severity of the kidney lesion.

J.M. had a pre-operative reading of 13 mms. Microscopically the appearances were those of extensive fibro-caseous tuberculosis. In this patient also the near normal value of the reading gave no hint of the severity of the lesion. V.B. had a pre-operative reading of 18 mm. On examination histologically the diseased kidney was a bag of caseous pus. The reading in this patient gave no suggestion of the severity of the tuberculous process. The pre-operative valuesof M.M. were 37 mm. and 13 mm. The kidney removed at operation was the seat of widespread renal tuberculosis. There was associated fibrosis. The readings obtained after operation were 35 mm., 16 mm., 12 mm. and 13 mm. In this patient also the pre-operative values gave no indication of the type or severity of the lesion.

It can be seen from a review of these figures and the histological findings stated briefly that the sedimentation rate can not be employed as a means of assessing either the severity of the lesion existing in the diseased kidney or the type. In several of the patients mentioned above, normal values were obtained and at operation the kidneys were found/

found to be severely diseased with active renal tuberculosis.

To summarise I have taken the highest ESR recorded in each patient prior to medical and surgical treatment. The mean for this figure in the mild group of cases is 18 mm., in the moderate group 23 mm. and in the severe group 41 mm. Thus it is seen that the ESR gives little indication of the severity of the renal lesion, though the highest mean value was found in the severe group.

A review of all the patients from the history viewpoint appeared to give a loose arrangement of the severity of the disease into two categories

(1) mild to moderate and

(2) severe.

On closer examination of the features which would tend to place them in these categories, viz. general appearance, severity of symptoms, loss of weight, the assessment was far from accurate once the offending kidney had been removed surgically and its condition estimated. As an exception to this general statement one patient, R.S. had had severe discharging sinuses in addition to his new complaint of increased frequency of micturition. It was thought clinically that this patient would have a severe renal lesion.

Investigation revealed the presence of a completely non-functioning and calcified left kidney.

It is also noteworthy that the duration of symptoms could not be employed as a measure of assessing the severity of the tuberculous process in the kidney. As an example W.S. had a very short history, which was increased frequency of micturition, and yet was found to have had severe renal tuberculosis.

In regard to a past history of tuberculous disease affecting other tissues, such as lungs, bones or epididymes no indication could be given of the severity of the new lesion affecting the kidney.

SURGICAL FINDINGS.

The localisation of the tuberculosis in the renal tract depended almost entirely on the surgical investigations, intravenous pyelography, cystoscopy and retrograde pyelography. A rough estimate of the functional capacity of the kidney could also be made in most instances.

Intravenous Pyelography.

There appeared to be four groupings possible in this investigation, which was dependent upon the success of the dye excretion by the kidney, provided the technique of the/

the injection had been satisfactory.

1. Apparently normal. The dye was well concentrated in both kidneys and the X-ray photographs revealed two normally functioning kidneys.
2. Poorly functioning. The dye was poorly concentrated in the pelvis of the diseased kidney producing only a very faint shadow on the X-ray plate.
3. Apparently non-functioning. In this group the dye was not sufficiently concentrated by the diseased kidney to produce even a faint shadow on X-ray examination.
4. Functioning but abnormal. This goup occurred when there was reasonable concentration of the dye in grossly distorted and damaged calyces.

From the appearances obtained in these dye excretion photographs it is possible to localise the disease of the kidney affected and in some instances to give an assessment of the size, position, character and extent of the tuberculous process in the kidney affected. It is important/

important to realise that the assessment given must be governed by all the circumstances applicable to the case under review. Gryspeerdt and Thomas (1954) reported a case of renal tuberculosis which masqueraded as a simple renal cyst.

In the assessment of the case accordingly intravenous pyelography plays an important part but one which should be utilised only in association with the other procedures undertaken in the investigation of the patient's renal state.

In the first group J.P. was found, as appearances revealed, to be quite normal, the only abnormality detected was a slight degree of faintness on the right side with dilatation of the ureter, fig. 40. The appearances at the upper pole were somewhat irregular but in view of the wide variation in the normal pattern this pyelogram could be read as normal. Nephrectomy was carried out and the tuberculous process present in the kidney was quite mild, figs. 80,81. It is realised that small lesions occurring in the medulla or cortex of the kidney would not be shown on intravenous pyelography.

In the second group M.M. was placed. The right/

right kidney appeared to be functioning normally but on the left side the shadow was that of poorly functioning kidney, fig 17. The kidney obtained at operation showed widespread renal tuberculosis and nephrosclerosis with retention cysts, figs 73,74. In this patient, the X-ray appearances had confirmed the side on which the lesion was present but did not accurately denote its extent and severity.

In the third group were placed A.Bk. and H.McL. both of whom showed no excretion from the left kidney whereas the right kidney appeared to be normal. A.Bk. was found to have an advanced renal tuberculosis in the non-functioning side, figs. 60.61, whilst H.McL also had widespread renal tuberculosis with considerable dilatation of the pelvis and calyces which were filled with caseous pus, fig.75.

In the fourth group D.O'R showed good excretion in both kidneys. All the calyces of the left kidney were dilated as was the pelvis in the right kidney, fig.20. The specimen obtained at operation was the right kidney which appeared to be more particularly damaged and it had widespread renal tuberculosis with dilatation of the primary and secondary calyces. There were multiple tubercles on the mucosal surface/

surface of the calyces, fig.78.

Intravenous pyelography, whilst a useful adjunct in the investigation of renal tuberculosis, giving as it does an indication of which side is mainly implicated in the tuberculous process and also some indication of the situation of the lesion, does not give an assessment of the severity of the parenchymatous lesion in the kidney.

Cystoscopy.

This surgical procedure was carried out by the urological surgeon in every patient who was believed to be suffering from renal tuberculosis. Its purpose was fourfold:-

(1) to measure the capacity of the bladder

(2) to inspect the mucous membrane and the ureteric orifice of the bladder

(3) to attempt ureteric catheterisation of the 'normal' kidney and

(4) to attempt ureteric catheterisation followed by retrograde pyelography of the diseased kidney.

The bladder capacity, though reduced in many of the patients because of secondary involvement of the mucosa by invasion from the ureter on the side affected, was not/

not invariably so. When it was reduced as in R.S. and H.McL. to four ounces and two ounces respectively it could not be employed to give an assessment of the severity of the renal lesion present, but was an indication that the tuberculous process in the kidney was probably an ulcerative one, causing extension down the ureter to the bladder mucosa.

Inspection of the bladder mucosa in all of the patients showed a variable picture. In many of them there was very little abnormality but in others, e.g. A.Bk., cystoscopic examination revealed evidence of secondary infection as well as the tuberculous cystitis. The presence of the secondary infection did not appear to confuse the issue in regard to the attempt at assessment of the severity of the case from the bladder appearance.

The intensity of the cystitis together with the appearance of the ureteric orifices were pointers to the side affected by tuberculosis but could not be employed as indices of the severity of the renal lesion. In all patients under review the 'normal' ureter was successfully catheterised whereas the abnormal side was not catheterised in nine cases. In three, catheterisation could only be partially carried out. In the remaining thirteen patients ureteric catheterisation/

catheterisation was successful.

Cystoscopy is accordingly a useful method of assessing the local condition in the bladder and of confirming the side of the renal lesion. It is of limited value in assessing the severity of the lesion.

Retrograde Pyelography.

Details of many of the patients have been mentioned in chapter V together with the interpretation of the X-ray findings.

There appeared to be three groupings possible in this investigation which was dependent upon the success of ureteric catheterisation.

(1) Complete success. The ureteric catheter was successfully passed and regrograde pyelogram obtained of both kidneys.

(2) Partial success. The normal kidney was successfully catheterised but the abnormal kidney was only partially catheterised.

(3) Failure. The diseased kidney could not be catheterised and accordingly no retrograde pyelogram was obtained.

Complete success. In A.Bk. figs 28,29 the retrograde pyelogram of the left kidney showed gross dilatation of the calyces throughout the kidney. The additional information that the ureter was also involved in the disease process was found because of the irregularity seen at its upper end. A lateral view of this pyelogram, fig.29, demonstrated the severity and widespread nature of the lesion. These findings were confirmed by removal of the left kidney, figs 60,61.

A.Bt. In fig. 30 retrograde pyelogram of the right kidney showed gross dilatation of all the renal calyces whereas in fig. 31 the normal left kidney has been successfully catheterised and pyelogram obtained of it. The appearances are essentially normal apart from a slight distortion of the calyces of the lower pole, which however, did not appear to be the seat of tuberculosis. The kidney obtained at operation is seen in fig. 62 and the evidence of gross dilatation of all the renal calyces confirmed.

R.S. In fig. 41 retrograde pyelogram showed some irregularity of the calyces of the right kidney, the left kidney and ureter are grossly calcified. Unfortunately no photograph of this kidney was obtained.

Partial success.

Partial success. D.O'R. In fig. 31 the right kidney was only partially catheterised but the lower part of the ureter showed considerable dilatation. The left kidney also showed some dilatation of the pelvis with irregularity of the calyces. The right kidney was removed and is seen as fig.78. There is some narrowing of the ureter shortly after it leaves the pelvis. It is at this juncture that the ureteric catheter was obstructed.

Failure. J.McA. In fig. 37 the left ureter could not be catheterised although the faint soft tissue outline of the left kidney could be seen. The right kidney was normal in outline. The specimen obtained at operation, the left kidney, is seen in fogs 76 and 77 and also as a large section, specimen 1.

The clinico surgical investigations of renal tuberculosis together are a guide but not an accurate measurement of the extent of the pathological process taking place in the kidney. From them information is obtained indicating which side is concerned in the tuberculous process and also some idea of the extent of the lesion can be gauged. As has been seen in the retrograde pyelograms there are occasional variations in the normal pattern which are within /

within normal limits. It is not possible however from the evidence obtained from these investigations to give an accurate assessment of the prognosis as the extent of the parenchymatous damage cannot be visualised by them.

BIOCHEMICAL FINDINGS.

In chapter VII a complete review has been given of the biochemical findings followed in chapter VIII by an account of the interpretation of the results. It is proposed briefly to assess the case on these biochemical findings.

The Tm_{PAH} values, as has been stated, have arbitrarily been placed in three groupings, mild, moderate and severe and some comment has already been given of the associated alterations which have taken place in the RPF and GFR values.

Tm_{PAH}. In the mild group J.P. had a satisfactory value of Tm_{PAH} pre-operatively indicating that the amount of renal damage was not severe. The clinical assessment indicated that the amount of damage believed to be present, taking into account the various symptoms and signs obtained, was that there was moderate damage. The pathological finding showed that there was an active but very localised renal tuberculosis.

This appears to indicate that the biochemical finding in this instance was accurate.

As an example of the moderate group M.B., who is the lowest value in the moderate group, clinically was assessed to have a severely damaged kidney from the nature of her symptoms and signs. On examination of her kidney, fig. 66, it can be seen that there is a moderate amount of renal tuberculosis present although the histological appearances indicate that it was fairly early. The importance of the biochemical finding in this case is once again an accurate assessment of the quantitative amount of renal tissue damaged.

As an example of the severe group H.McL, from the Tm_{PAH} figure pre-operatively had a severe lesion. The clinical history had been indicative that the tuberculous process present in his kidneys should be severe but in actual fact pathological findings, fig. 75 showed the appearances were those of a widespread severe tuberculosis. This again would confirm that the biochemical assessment of the case had been accurate.

The pre-operative assessment of 'severe' damage may have two distinct causes, (1) extensive damage confined to one kidney, (2) less extensive disease of one kidney combined/

combined with mild disease of the other. A third possibility, - severe damage of both kidneys - would produce obvious bilateral involvement which would exclude the case from this series.

RPF and GFR. In assessing the severity of the case, according to RPF and GFR values, though some indication can be obtained from these figures, the precise character which is present in the Tm_{PAH} values has not been achieved although the general tendency of the pattern of the disease can be obtained. As an example, in J.P. the pre-operative values of RPF and GFR were high. In the mild group the pre-operative value for M.B. was also high, suggesting that the blood flow and glomerular filtration were in both instances satisfactory, whereas as has been noticed in the Tm_{PAH} results, there is considerable difference in the amount of functional renal tissue present in these two examples. In the seve e group H.McL. had a lowered RPF and GFR value which was more in keeping with the Tm_{PAH} values although the amount of renal tissue damaged could not be estimated from these figures.

The derived values are commented on more fully in Chapter VIII and are not suitable in the assessment of the case from the viewpoint of treatment and prognosis. They are more concerned with renal haemo-dynamics.

Urea Clearance Test. The urea clearance test was carried out in all cases where sufficient material was available. The values found are very much in parallel with the GFR. figures, as can be seen from the correlation coefficient +0.80, fig. 56 and the scatter diagram, fig 58. As is to be expected, the test is of little value as a means of assessing the severity of the lesion.

SUMMARY.

Thomson-Walker (1927) was adamant that catheterisation of the ureters was the most important part of the investigation of a case of renal tuberculosis. This has been reiterated by Jacobs (1934) who added that this was necessary in order to obtain specimens of urine from each kidney for examination.

From all the data produced and discussed it is suggested that the most beneficial source of information in regard to the assessment of the case, from the viewpoint of severity and prognosis, is obtained from the Tm_{PAH} results. It is also noteworthy that the clinical appraisal of the severity of the lesion cannot be estimated with accuracy without the assistance of the surgical techniques of intravenous pyelography, cystoscopy and retrograde pyelography.

CHAPTER XI

UNILATERAL RENAL DISEASE WITH HYPERTENSION

Blood pressure readings were obtained routinely on several occasions from patients suffering from renal tuberculosis who were undergoing hospital treatment. On finalising records which had been obtained in each case it was noticed that a small group appeared to have hypertension before nephrectomy. On examination of the figures one week and six months after operation, it was seen that there had been some improvement in the blood pressure findings.

This aspect has been made the subject of a separate paper (Craik and Macdonald - in preparation.) It is not proposed to deal in detail with this collateral finding as it raises a separate issue which is not the main concern of this investigation.

Seven patients were found to have hypertension, fig.101, and they all had recovery to a normo-tensive pattern six months after operation. It is interesting furthermore to note that in only two patients had there been return of hypertension, M.P and M.M., who later unfortunately succumbed to cerebral haemorrhage.

In the case of M.M. permission was obtained for removal of the remaining right kidney and this is demonstrated as figs. 102 and 103. The right kidney was long and narrow and there was a large cyst in the upper pole. The pelvic fat was considerably increased. On cut surface the upper pole is reduced to a narrow rind. Multiple retention cysts of varying size are present.

Histological examination of a representative section, fig.104 confirms the presence of hypertensive nephrosclerosis. There is also interstitial glomerulo-sclerosis and considerable atrophy of the tubules. There is no evidence of tuberculosis. On comparing this section with fig. 93, that of the left kidney obtained at operation, it can be seen that the degree of nephro-sclerosis has advanced. In fig. 105 thickening of the intima is seen with fibrosis of the media and splitting and fragmentation of the internal elastic lamina. In fig.106 a section of the renal artery is seen in which there is gross medial fibrosis with considerable intimal thickening, some splitting of the internal elastic lamina being evident in this section also.

All the other patients who had hypertension have been fully examined recently and are very well, with no symptoms/

symptoms referable to their cardio-vascular system.

Ophthalmological examination does not show any evidence of hypertensive retinopathy.

In M.P. the recurrence of hypertension is associated with the vasomotor disturbance of the menopause.

It is noteworthy that the patients who had hypertension appeared to be in the older age group.

The return to the normo-tensive pattern has been studied in considerable detail and is being commented on fully in the paper mentioned above which is in course of preparation.

CHAPTER XII

TREATMENT.

Mack (1938) in an interesting account of renal tuberculosis stated that the treatment of the disease was a race between the surgeon and the tuberculosis with the other side of the trigone as its goal.

Such was the prognosis in these pre anti-biotic days that a high mortality resulted from the operation of nephrectomy for renal tuberculosis.

Thomson-Walker (1927), commenting on the mortality occurring in the patients under review in his series, found a figure varying from 7.3 per cent to 2.5 per cent. Furthermore, many palliative operations, including transplantation of the ureters, were carried out to relieve the distressing bladder symptoms.

It is an interesting fact that since this investigation commenced in 1953 no patient has undergone transplantation of the ureters for renal tuberculosis at Stonehouse Hospital. In the previous five years there had been six patients in whom this operation had been required.

A further complication noted in the pre anti-biotic era/

era was the formation of post operative sinuses in the operation scar, a feature again noted by Thomson-Walker (1927) in his own series. Indeed Legueu (1909) demonstrated that tuberculous deposits were occasionally found in the perinephric fat.

As all the patients in this series had anti-biotic chemotherapy a brief account is now given of the routine medical treatment employed.

MODERN TREATMENT.

Twenty of the patients in this series had a course of 90 gms. streptomycin given in daily injections of 1 gm. Isoniazid commenced two to three days after the initiation of streptomycin and was given in 100 mgm. doses thrice daily, the two drugs being given concurrently.

The other two patients in the series, who were treated at Hairmyres Hospital, were also given streptomycin and isoniazid but in each case the dosage of streptomycin given prior to operation was, in one instance, 20 gms. and in the other, 25 gms. The post operative dosage was continued until a total of 90 gms. was given in all.

The treatment was arranged in such a way that nephrectomy was carried out when the patients had had 45 gms./

45 gms. streptomycin. All the patients were kept strictly in bed prior to nephrectomy.

Cystoscopic examination was carried out on several occasions and when the side affected and the extent of the lesion were determined, by utilising the evidence obtained from intravenous and retrograde pyelograms, removal of the diseased kidney was arranged to coincide with the mid point in the streptomycin therapy.

SURGICAL TREATMENT.

As all the patients in this series underwent nephrectomy, the operation carried out was by the usual technique: the kidney was mobilised through a loin incision and after ligation of the renal vessels, as much ureter as possible was freed and removed with the kidney. In no case in this series was partial nephrectomy carried out though Jacobs (1953) has recommended that this is possible if the disease is localised to one or perhaps two adjacent areas of the kidney.

Results of nephrectomy.

As has already been stated in chapter V, twelve patients pre-operatively were known to have cystitis with attendant urgency and frequency of micturition. An

An immediate effect of nephrectomy seen in all these patients was the lessening of these clamant symptoms.

Their temperament, which had previously been somewhat irritable, became more placid due to the fact that they could now have a more prolonged restful sleep at night.
In three patients however, increased frequency remained and on cultural examination of the urine they were found to have a coliform infection. This was treated by sulpha-triad and alkaline diuretic. These measures were successful in every case. One patient, R.S., had a severely contracted bladder and has required repeated courses of chemotherapy, usually PAS and isoniazid. PAS was given in a dosage of 15 gms. per day and isoniazid 300 mgms. daily, the duration of the course lasting twenty eight days in each instance. R.S. has been a very complex case to deal with since the outset of his illness because of the multiplicity of the tuberculous lesions.

Complication of nephrectomy. (a) Sinus formation.

In two patients, W.S. and J.M., there was leakage from the operation wound but this rapidly cleared up with local penicillin treatment.

(b) Bladder contracture.

In all the patients, post-operative intravenous pyelography was carried out and particular note made of the cystogram appearance. This however was inconclusive: cystoscopic examination was more exact in determining the state of the bladder mucosa. The choice of chemotherapy is important and, as has been reported by Borthwick and Dick (1957), the main problem is the choice of which combination is to be most effective in the case under surveillance. Streptomycin has been noted to produce some bladder contracture after severe cystitis due to the fibrosis which is a result of its therapeutic action: in such cases it has been found that this has been lessened by combining streptomycin with PAS or giving PAS with isoniazid.

In patients who have contracted bladder, operations have been devised to overcome this complication: these include cutaneous ureterosotomy, uretero-colic anastomosis, and ileo - cystoplasty. The last two procedures have been reported to be the most beneficial. Ileo-cystoplasty should only be employed when there is no active tuberculous disease present in the contracted bladder (Jacobs, 1957).

DISCUSSION.

Lattimer et al (1948) used 1.8 gms. streptomycin daily for 120 days and found this efficacious in the early cases of renal tuberculosis. Lloyd et al (1948) however, stated that the application of streptomycin alone was rather limited in the treatment of the condition and was certainly not of itself curative. Wimsett (1952) gave a detailed regime to be followed in the different types of patient. In his paper he agreed that little or no effect was gained by streptomycin on an destructive type of lesion which had been well established. He also stated that streptomycin had a beneficial effect on tuberculous cystitis but this was dependent on the extent of the disease present in the upper urinary system. Indeed, the drug appeared to hasten the contraction of the bladder.

PAS was given to a further twenty patients, together with 1 gm. streptomycin and Wimsett comcluded that the two drugs produced a slightly improved effect, though the established destructive type of lesion showed no response

In this series all the patients have been followed up and particular attention paid to their general condition. It is pleasing to be able to report that they are all doing very well. Increased frequency of micturition remains only/

only in one patient, R.S. who has recently been an in-patient in Stonehouse Hospital for a further course of chemotherapy.

It is noteworthy that, after the initial 15/20 doses of streptomycin, there is a general improvement in the patients' condition with lessening of the general toxic signs. In no case was there an alteration or upset to the planned routine prior to nephrectomy.

The patients' weight, as can be seen in fig.107 has improved in the majority of patients and is a significant pointer to the clinical recovery which has been made following extirpation of the organ diseased by tuberculosis.

There has been no recurrence of renal tuberculosis noted in the remaining kidney in any of the patients who comprised this series four to five years after their initial presentation of symptoms andsigns of the disease.

Future Treatment.

It is recommended that in patients who have a mild degree of renal tuberculosis, as estimated by the Inulin/PAH excretion test, they should be successfully treated by chemotherapy, i.e. a combination of two drugs such as streptomycin and isoniazid, without nephrectomy being required.

In cases judged to be in the moderate or severe groups, there is still a place for nephrectomy, either partial or total, depending on the situation and quantitative amount of tuberculosis present.

Streptomycin and isoniazid will be required in a dosage of 1 gm. streptomycin daily and 300/450 mgms. isoniazid daily. Operation should be planned to take place when the patient has had 45 gms. streptomycin.

CHAPTER XIII

SUMMARY OF THESIS

The clinical study, which is the subject of this investigation was commenced in 1953. It includes complete records of twenty two patients suffering from renal tuberculosis who have been investigated clinically, surgically and biochemically.

The patients were selected only in so far as they had nephrectomy carried out. The specimens obtained were examined bacteriologically and histologically.

It has been shown that the Tm_{PAH} results can be used as an accurate index of the quantitative severity of the lesion present and also as a measurement of the prognosis to be expected.

The derived fractions have provided information which suggests that the pathological process of renal tuberculosis produced damage of the smaller arteries, thus worsening the general effect of the infection which had occurred in the kidney. This has been confirmed by examination of the histological specimens available.

Hypertension as a complication of unilateral renal tuberculosis has been discovered as a collateral finding and an introductory comment has been made on this feature.

Finally, a brief review is given of the modern method of treatment of the condition, with a suggestion that mild cases of renal tuberculosis can now be confidently dealt with by anti-tuberculous chemotherapy alone.

CHAPTER XIV

ACKNOWLEDGMENTS

It is a privilege to acknowledge the considerable assistance which I have had from all the patients who took part in this investigation. I should also like to mention the assistance given by nursing staff and resident staff both at Stonehouse and Hairmyres Hospitals. Dr. J. Salisbury Craig has been a continual source of encouragement, as has been Dr. A. Smith, surgeon superintendent at Stonehouse Hospital.

My thanks are also due to Mr. W.S. Mack and Mr. T.L. Chapman who allowed me to use their patients for the tests. Dr. J.E.Craik has been a mainstay throughout the investigation and it is through his kind co-operation that I have been able to use figs. 1 - 4 and fig 100, volume II. I am also indebted to him for much helpful advice in the preparation of this paper.

Dr. I. Anderson and Dr. A. Kenny have been most helpful in allowing me to carry out biochemical estimations in their laboratory. Mr. Gray, clinical photographer at the Victoria Infirmary has carried out the photography and assisted in thir mounting. I am also grateful to Mr. Archibald of the /

the Pathology department of the Victoria Infirmary for the preparation of the large kidney transparencies.

I should like to state that the initiation and continuation of this work was stimulated by the late Dr. Andrew Deuchars, my colleague at Stonehouse Hospital.

I am indebted to very many other colleagues for encouragement and assistance given.

For secretarial work in this paper I am indebted to Miss McKendrick, Mrs. Torrance and in particular to Mrs. Falconer for considerable efforts afforded.

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TUBERCULOSIS OF THE KIDNEY

A Clinical Study with Special Reference to Renal Function Before and After Nephrectomy

VOLUME II

HECTOR R.F. MACDONALD

TUBERCULOSIS OF THE KIDNEY

VOLUME II

CONTENTS

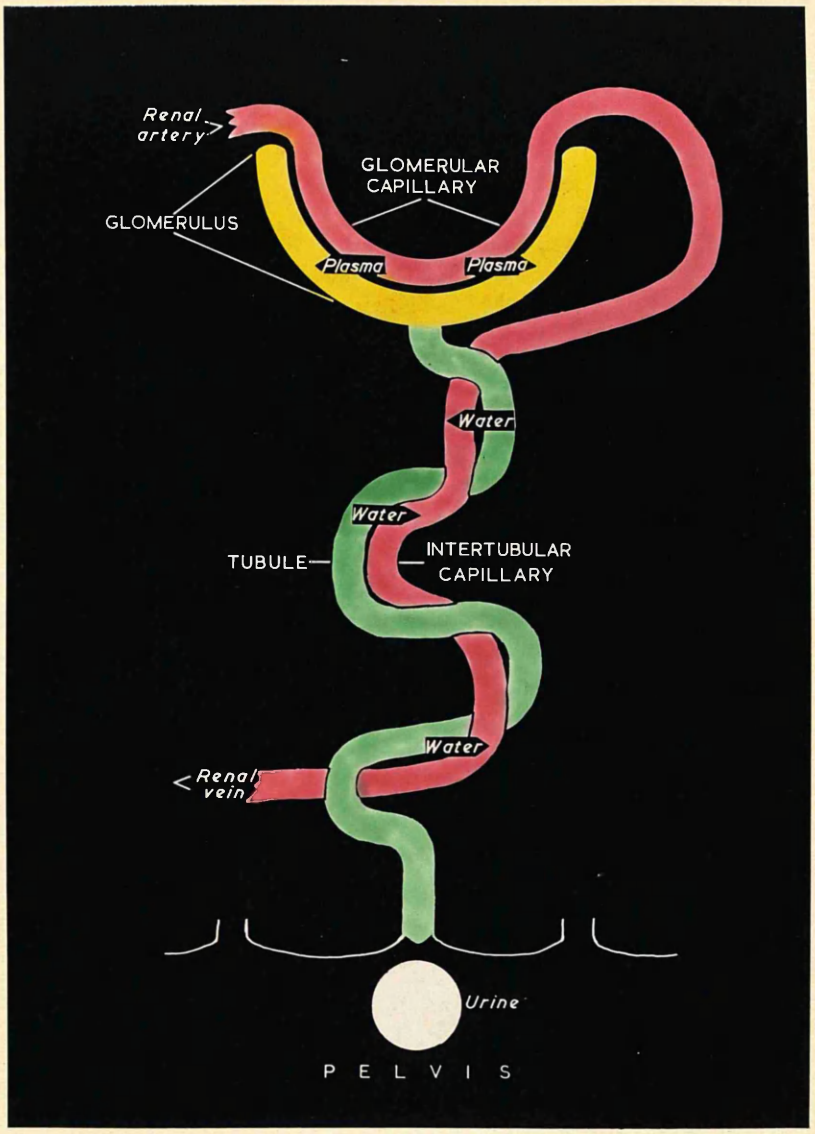


Fig.1. NEPHRON DIAGRAM

The colour scheme is uniform in all diagrams.

Yellow: Glomerular capsule and Glomerular Filtration Rate (GFR)

Red: Blood vessels and effective Renal Blood Flow (RBF)

Green: Tubules and maximal tubular excretory capacity (Tm)

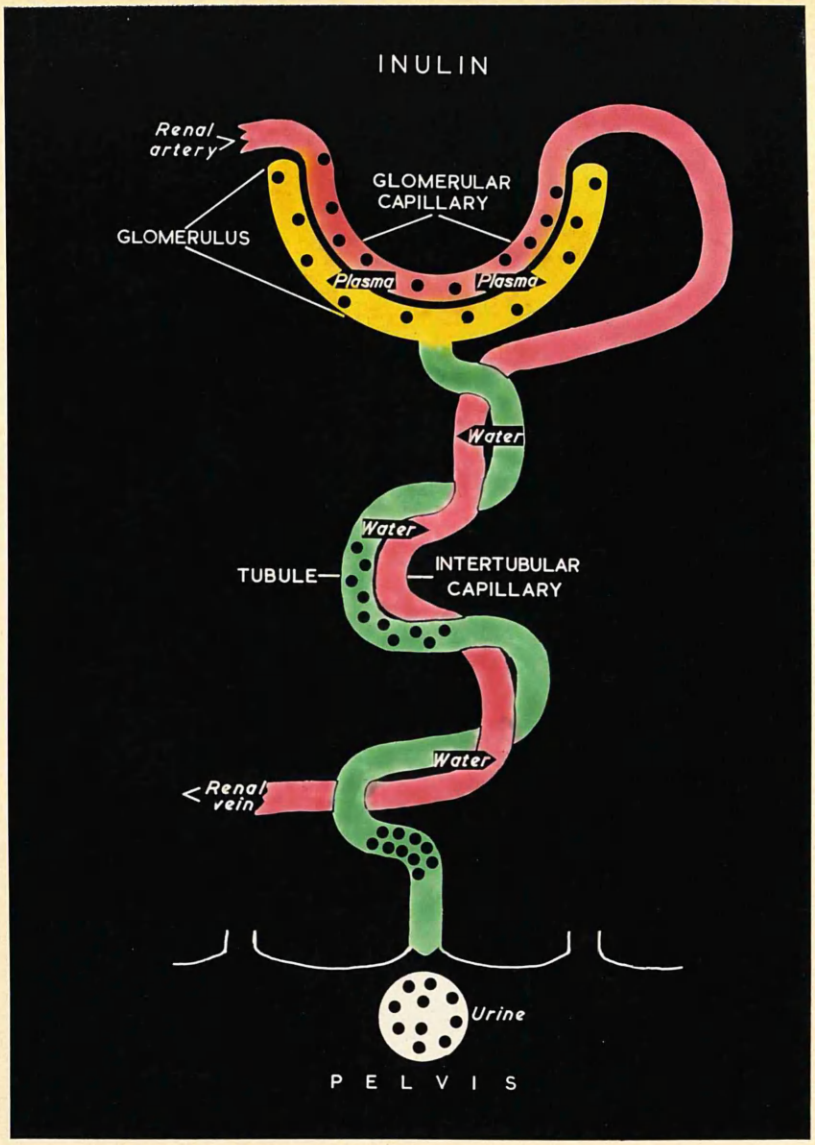


Fig.2. INULIN CLEARANCE or GLOMERULAR FILTRATION RATE

a) The glomerulus acts as a simple ultra-filter retaining only proteins, so the concentration of all solutes is the same in the glomerular filtrate as in the plasma. This is represented as 10 black dots in the capsule and 10 dots in the capillary.

b) In the tubule, water is absorbed, but the inulin, as it is neither absorbed nor excreted, is progressively concentrated. The original 10 units are contained in less and less fluid until -

c) In the pelvis the 10 units are dissolved in a single drop of urine and no extra inulin has been added.

d) Thus the Inulin Clearance gives the volume of filtrate in which the inulin was originally contained - i.e. the Glomerular Filtration Rate.

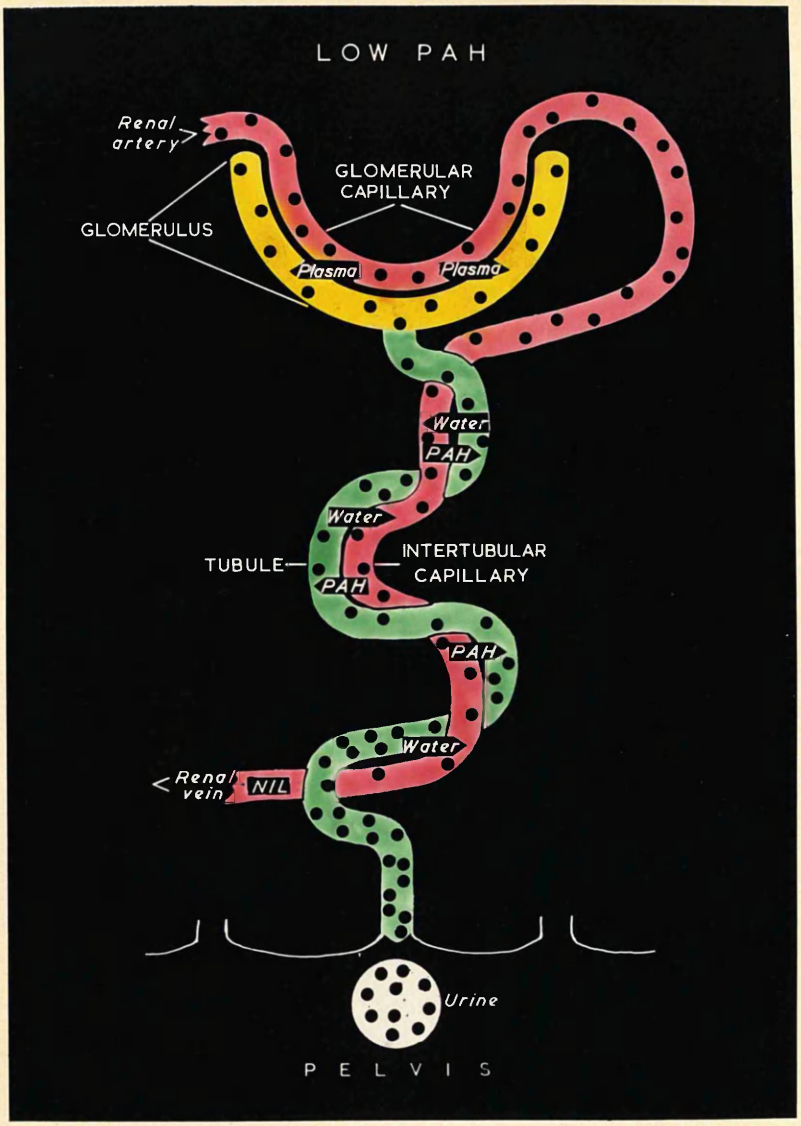


Fig.3. LOW PAH CLEARANCE OR RENAL BLOOD FLOW

a) Glomerular filtration is the same as for Inulin.

b) In the tubule PAH is actively excreted by the tubule cells.

c) Provided the blood concentration is low all the PAH has been removed from the blood by the time it reaches the venous end of the intertubular capillaries.

d) Thus all the PAH brought by the blood stream to the kidney is excreted in the urine. The PAH clearance, therefore, gives the volume of blood passing through the kidney - i.e. the Renal Blood Flow.

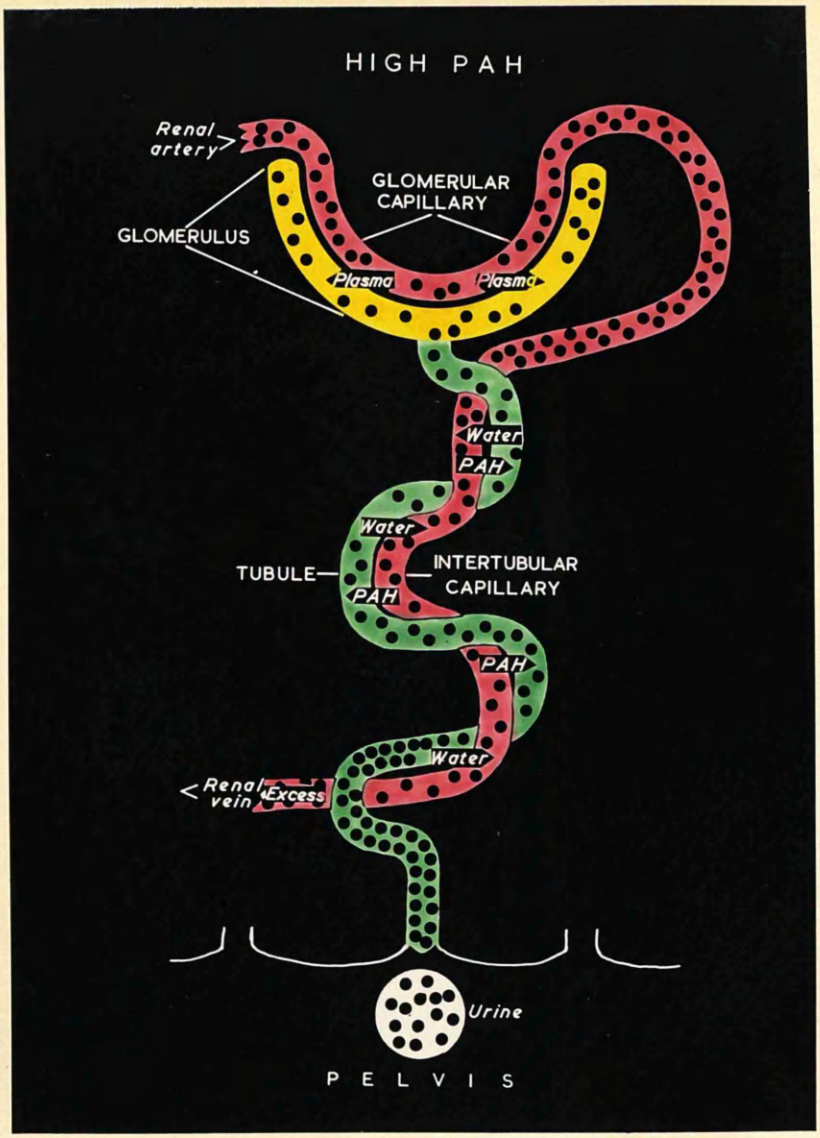


Fig. 4. HIGH PAH EXCRETION or MAXIMAL TUBULAR EXCRETORY CAPACITY

a) Glomerular filtration and tubular excretion are the same as with the low PAH clearance.

b) When the blood concentration of PAH is high, the tubules are saturated and cannot remove all the PAH from the blood, excess passing to the renal vein.

c) Raising the blood concentration does not alter the amount of PAH excreted by the tubules as these are already working to full capacity.

d) The total amount of PAH excreted per minute (note: this is not the "clearance" rate) is an index of the amount of active tubular tissue in the kidneys - i.e. the maximal tubular excretory capacity.

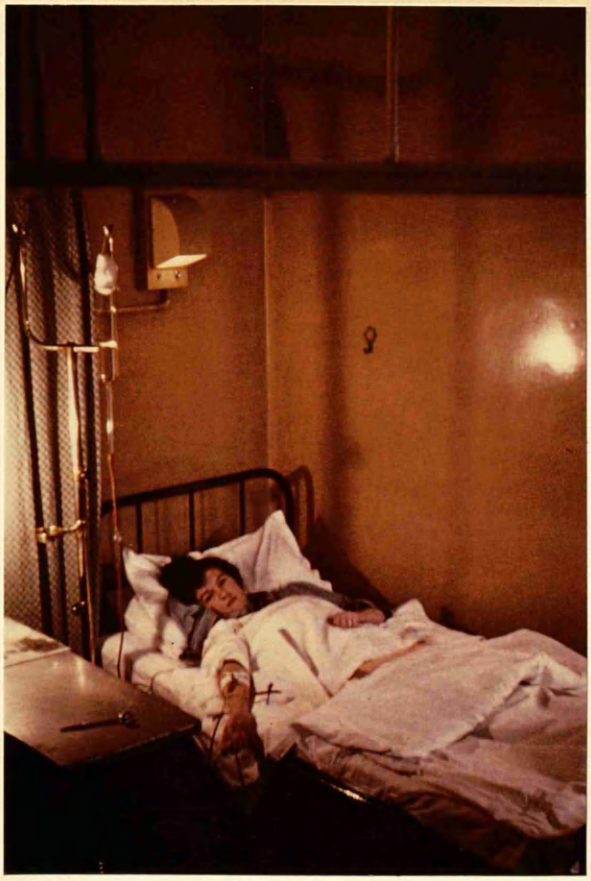


Fig. 5.

Colour photograph showing patient with intravenous saline drip established. Catheter has also been passed.

Fig. 6.

Filtration flask containing sustaining doses of PAH and Inulin in the first period.

8 ml. PAH
55 ml. Inulin
450 ml. Normal Saline.

Fig. 7.

Apparatus required to complete a test, the first period having been established.

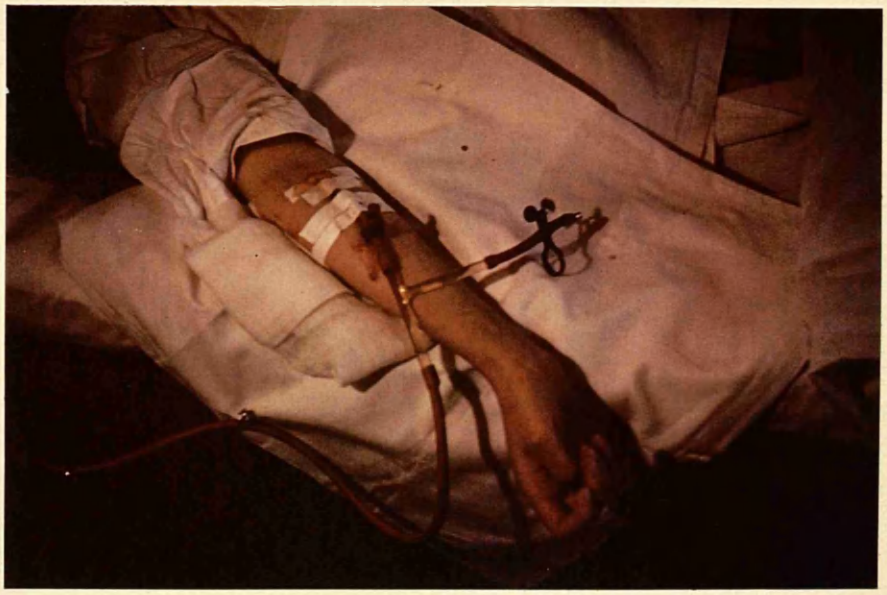


Fig. 8.

Photograph showing T-tube and intravenous needle in position.

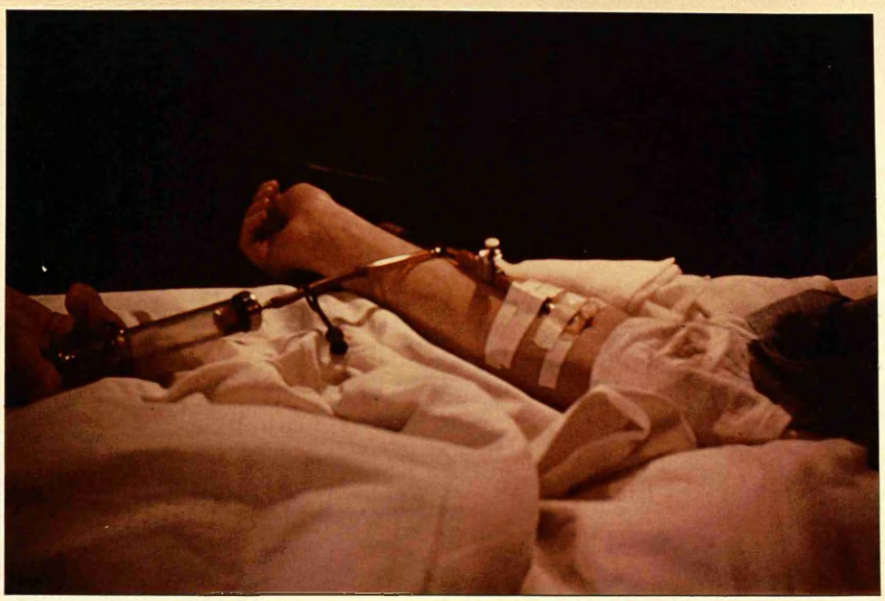


Fig. 9.

Injection of 20 ml. of PAH passing along T-tube.

Fig. 10.

Filtration flask after addition of 80 ml. of PAH.

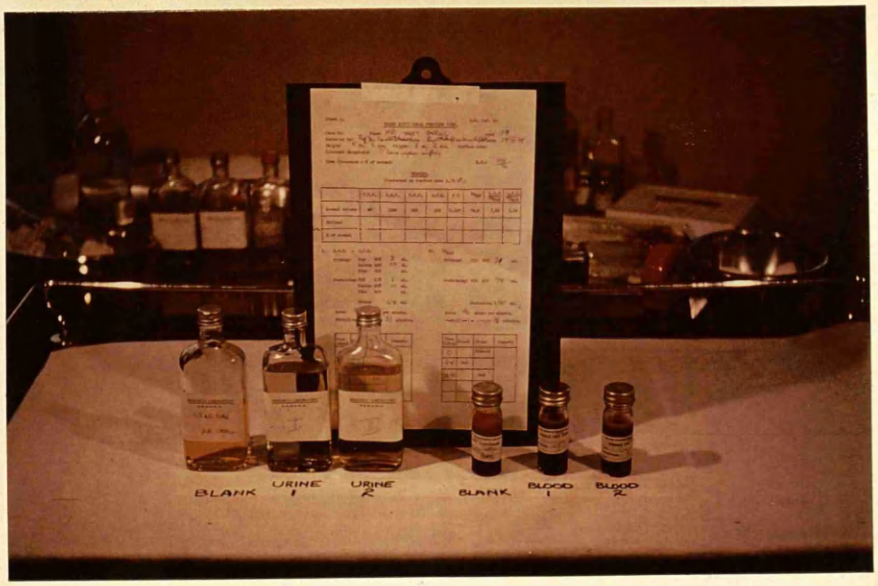


Fig. 11.

Photograph showing three urine specimens, three blood specimens and information sheet.

Sheet 1. Lab. Ref. No.

HOMER SMITH RENAL FUNCTION TEST.

Case No: Name: J.P. (1) Age: 23

Referred By: Dr. Macdonald. Stonehouse Hospital. Date: 11/10/55

Height: 5 ft. 0 ins. Weight: 8 st. 2 lbs. Surface Area: 1.47 (F = 1.18)

Clinical Diagnosis: Renal Tuberculosis.

Urea Clearance - % of normal: B.P.: 124/86

(1) 121 (corrected)

(2) 119 (corrected)

RESULTS.

(Corrected to Surface Area 1.73 M^2.)

	P.C.V.	R.B.F.	R.P.F.	G.F.R.	F.F.	Tm_{PAH}	$\frac{R.P.F.}{Tm_{PAH}}$	$\frac{G.F.R.}{Tm_{PAH}}$
Normal values	45	1136	625	123	0.197	78.9	7.92	1.56
Patient	40	1089	654	103	0.157	61.2	10.68	1.69
% of normal	-	96	104	84	80	77.5	134	108

I. R.P.F. + G.F.R.

Priming: PAH 20% 2 ml.
Inulin 10% 20 ml.

Sustaining: PAH 20% 8 ml.
Inulin 10% 55 ml.

Saline 430 ml.

Rate: 96 drops per minute.

Stabilisation period: 24 minutes.

II. Tm_{PAH}

Priming: PAH 20% 20 ml.

Sustaining: PAH 20% 80 ml.

Sustaining I 210 ml.

Rate: 96 drops per minute.

Stabilisation period: 23 minutes.

Time (mins)	Blood	Urine	Remarks
0		Discard	
17.50	1st		
30.30		1st	

Time (mins)	Blood	Urine	Remarks
0		Discard	
17.00	2nd		
29.25		2nd	

Fig. 12.

Photograph showing completed information sheet.

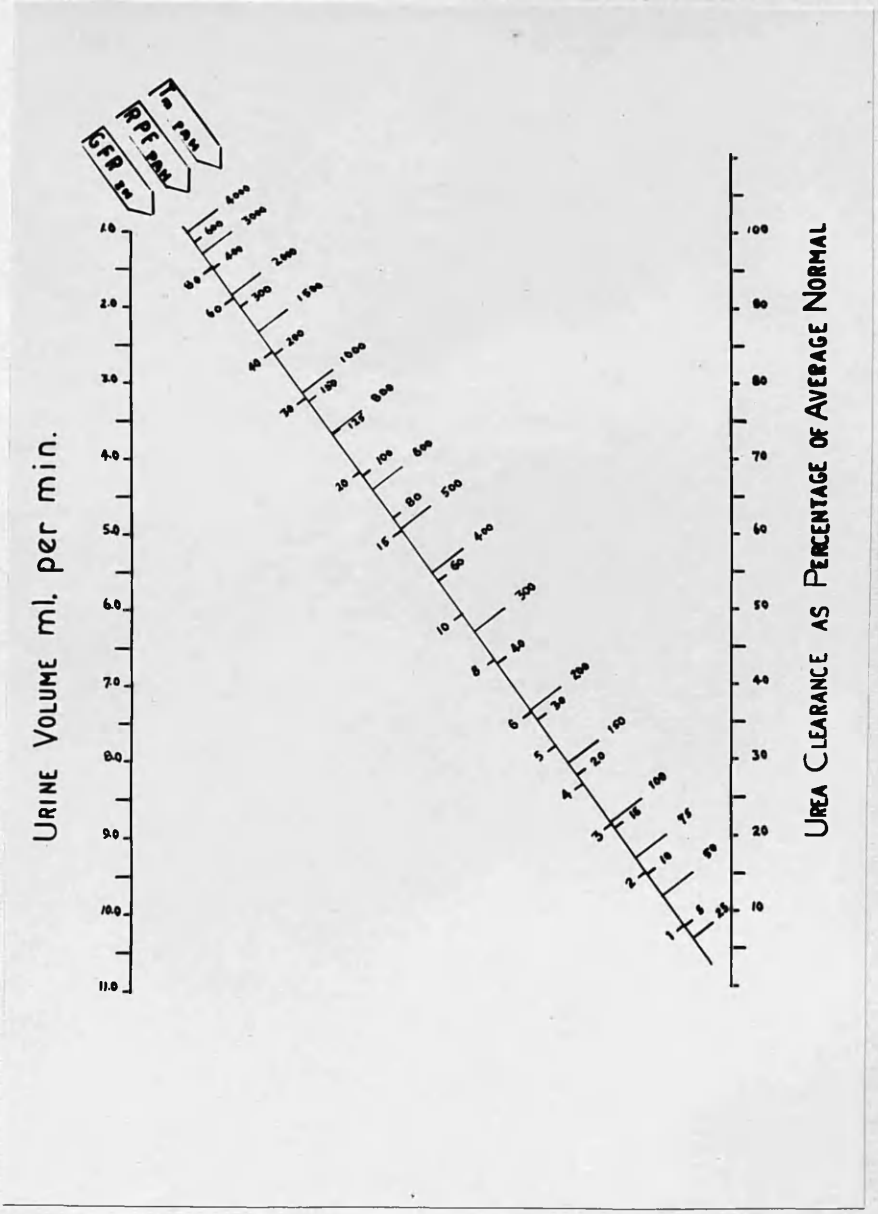


Fig. 13. Nomogram for calculating urine dilutions.

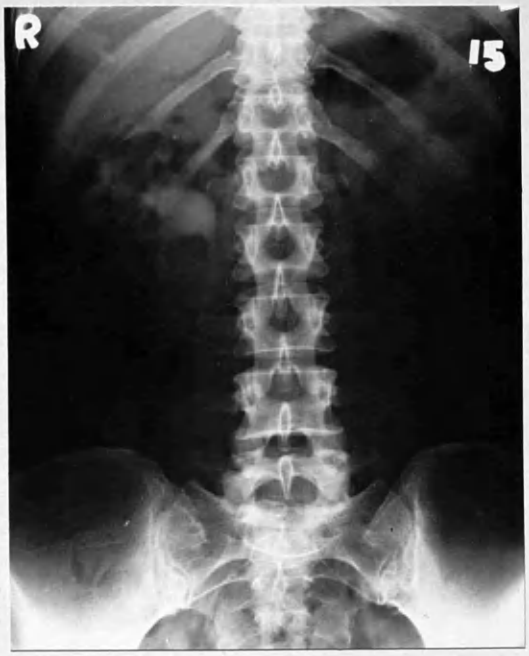


Fig. 14. ABk.

IVP at 15 minutes.
No excretion from
left kidney.

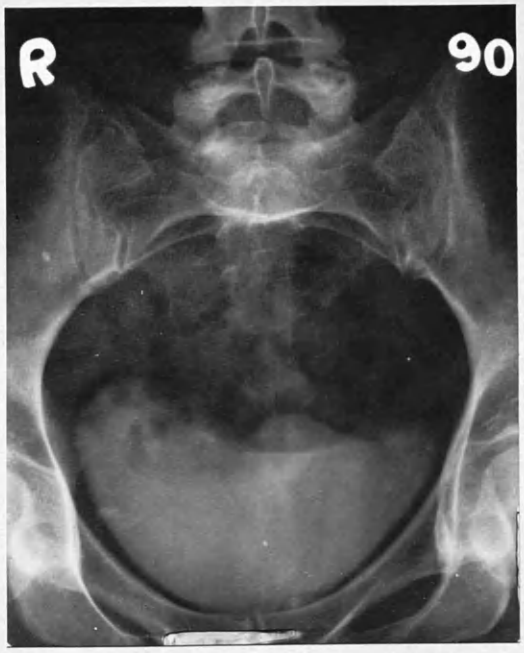


Fig. 15. ABk.

IVP at 90 minutes.
Bladder appearance.

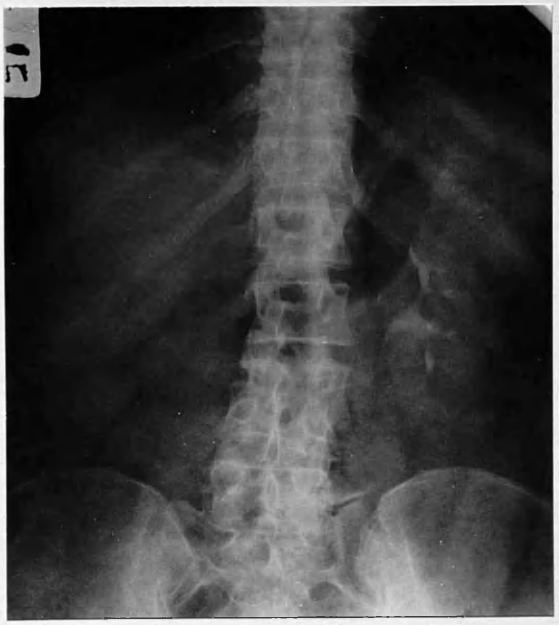


Fig. 16. EC.

IVP. No excretion from right kidney. Note old tuberculous lesion of spine L3.L4.

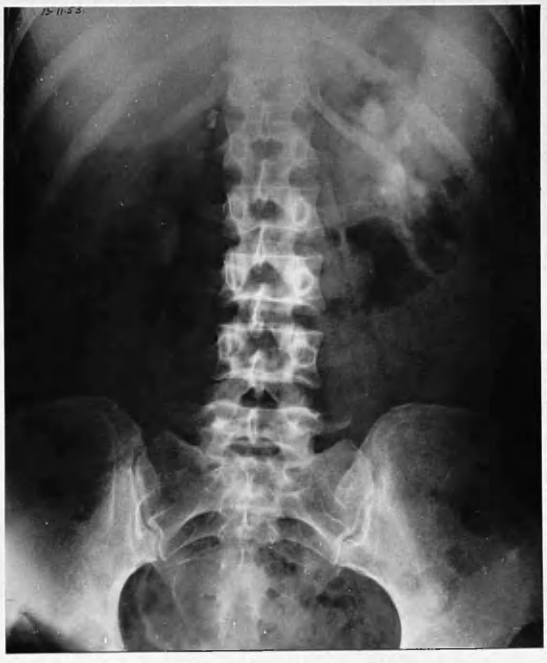


Fig. 17. MM.

IVP. Poor excretion from right kidney. Some dilatation of calyces left kidney.

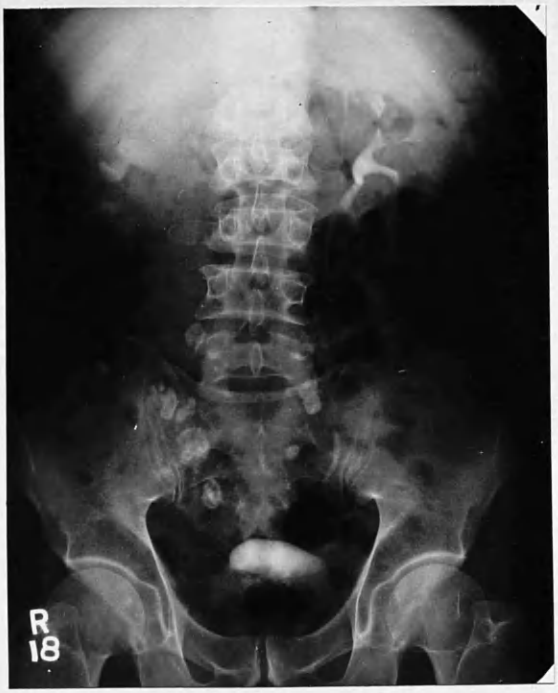


Fig. 18. JMcA.

IVP. Considerable distortion of right kidney shadow. Left kidney fairly normal. Small bladder shadow. Multiple calcified glands in abdomen.

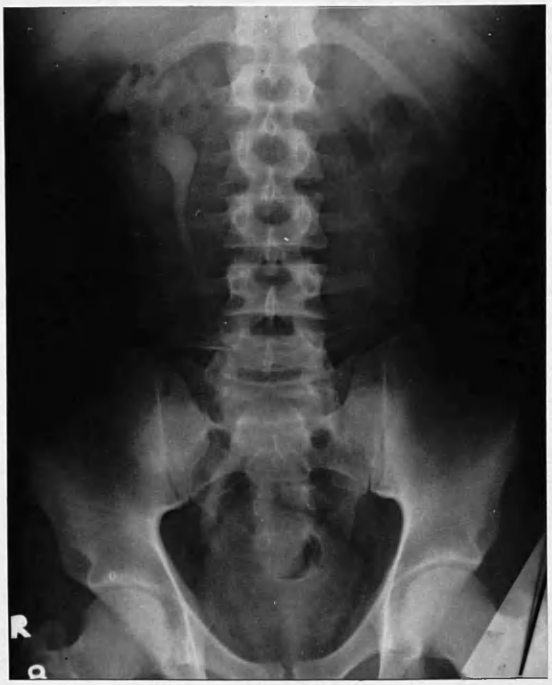


Fig. 19. HMcL.

IVP. No excretion visible from left kidney. Some dilatation of right kidney pelvis.

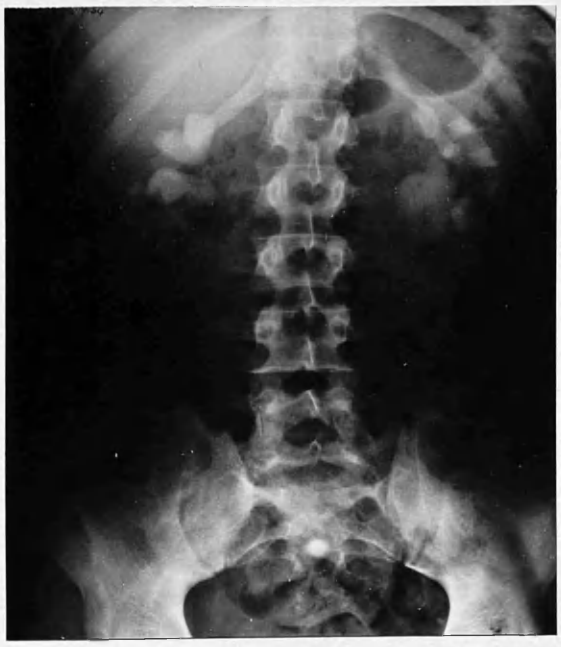


Fig. 20. DO'R.

IVP. Both kidneys excreting dye. Considerable distortion and dilatation of right kidney. Some distortion and dilatation of left kidney pelvis.

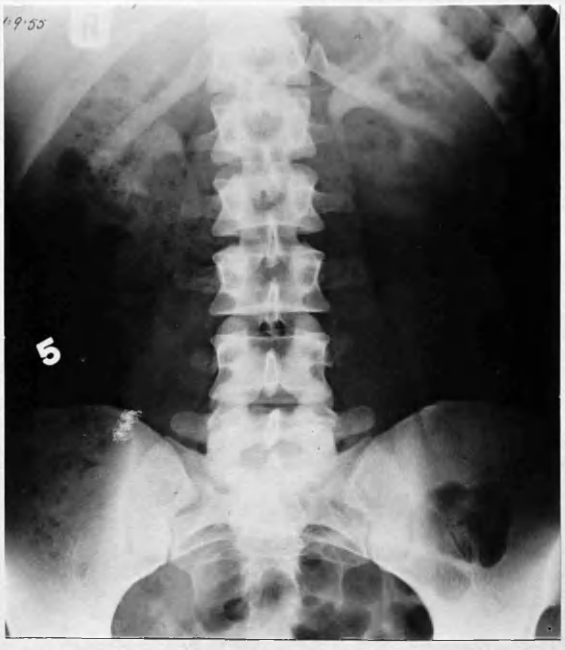


Fig. 21. JP.

IVP. Both kidneys excreting the dye. Some irregularity of lower calyx right kidney.

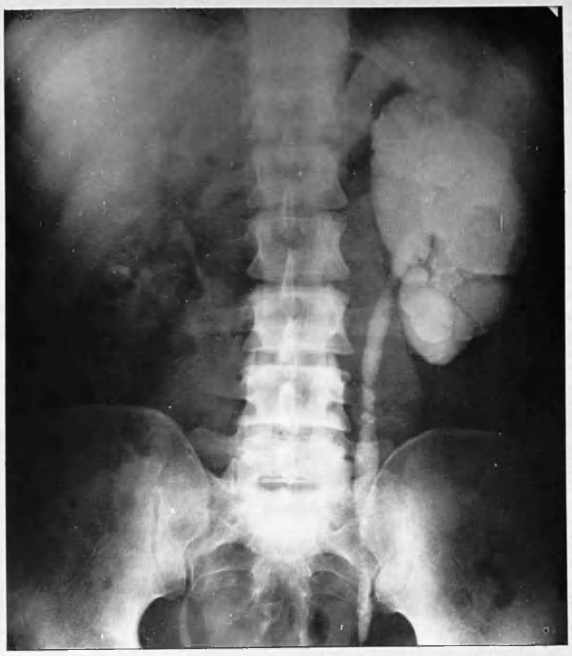


Fig. 22. RS.

Straight X-ray.
Calcified left kidney
and left ureter visible.

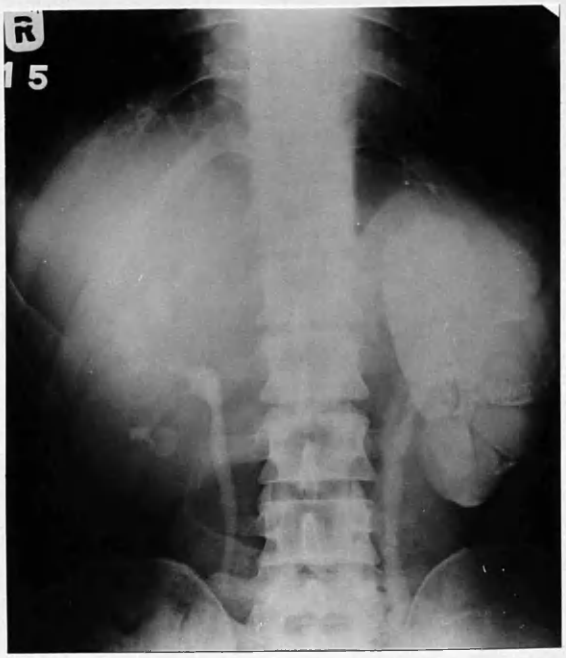


Fig. 23. RS.

IVP. Dilatation of
right kidney with
irregularity of calyx
right kidney. Left
kidney calcified and
left ureter calcified.

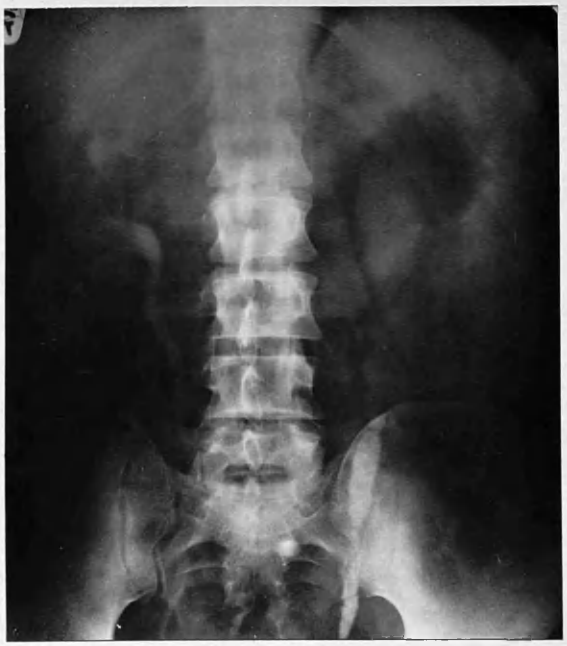


Fig. 24. RS.

IVP. Post-operatively. Remnants of calcified left ureter visible. Some irregularity of lower calyces of right kidney.

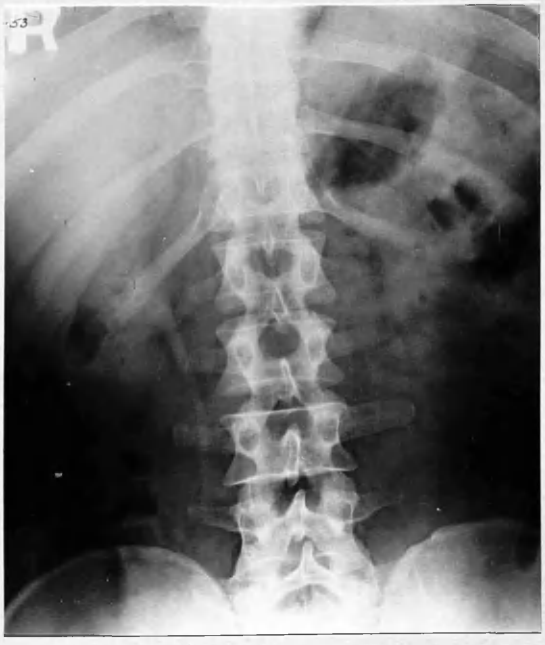


Fig. 25. AT.

IVP. No excretion seen from left kidney. Right kidney appears to be somewhat dilated.

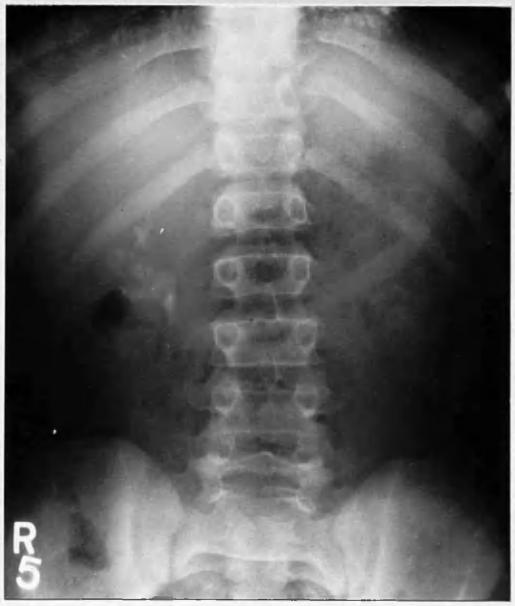


Fig. 26. RY.

IVP at 5 minutes.
No excretion seen from left kidney. Some dilatation and irregularity of outline of right kidney at 5 minutes.

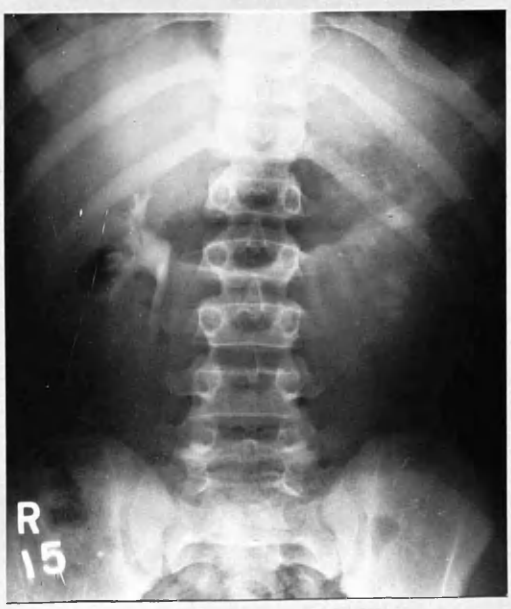


Fig. 27. RY.

IVP at 15 minutes.
Left kidney very slight shadow seen in mid pole.
Right kidney appears more normal with some dilatation of pelvis.

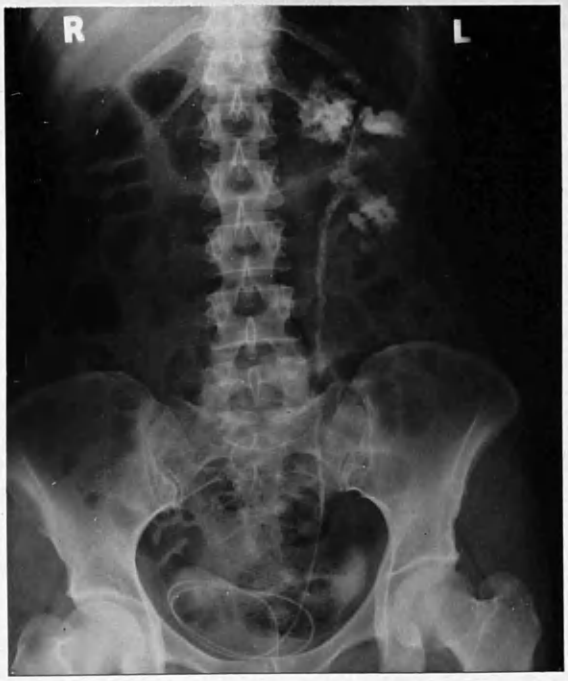


Fig. 28. A.Bk.

Retrograde Pyelogram shows gross dilatation of calyces throughout the kidney. There is also irregularity of the ureter.

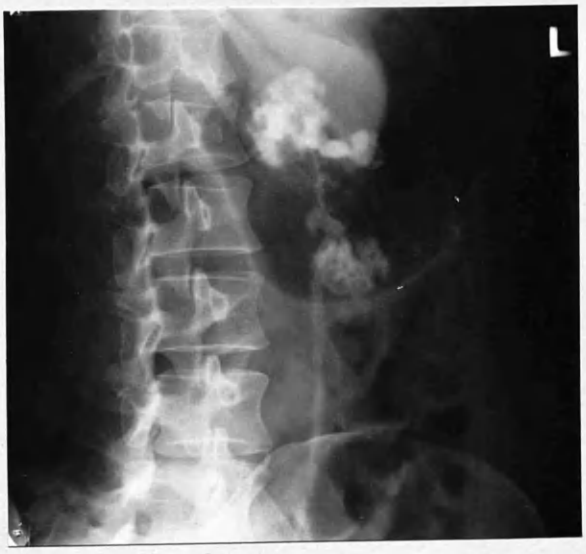


Fig. 29. A.Bk.

Lateral view shows distortion and cavitation in both upper and lower poles of the kidney. Pelvis is irregular in outline.

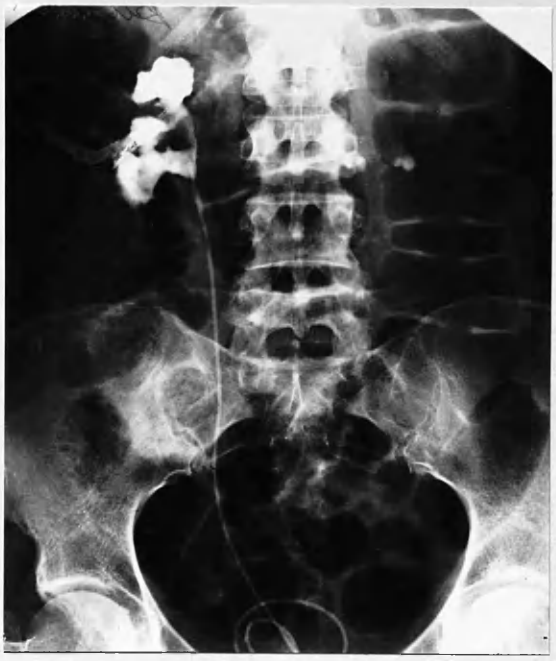


Fig. 30. A.Bt.

Retrograde pyelogram
Right kidney shows gross
dilatation of all
renal calyces.

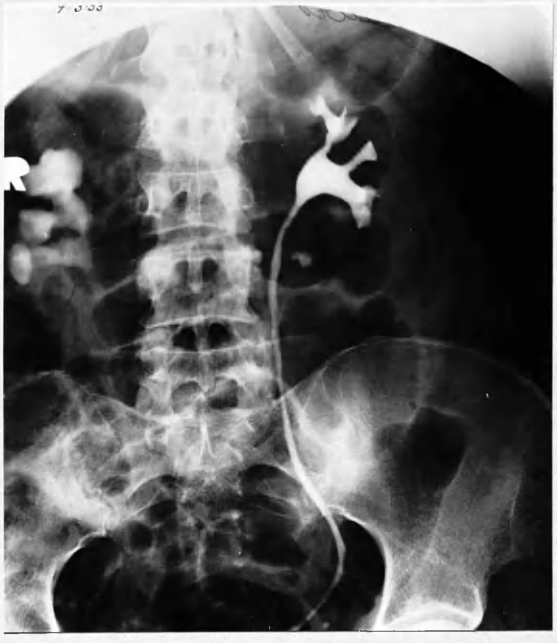


Fig. 31. A.Bt.

Retrograde pyelogram.
Right kidney grossly
abnormal. Left kidney
is normal in outline.
Slight distortion of
calyces of lower pole.
Pelvis slightly dilated.

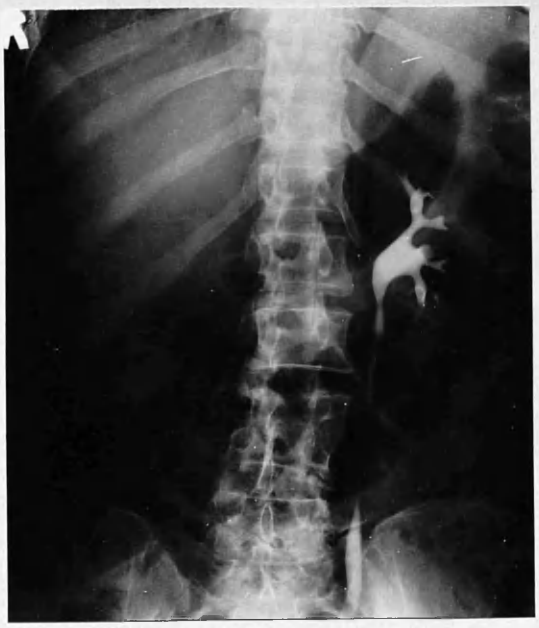


Fig. 32. E.C.

Retrograde pyelogram
Left kidney normal in
outline. Right kidney
could not be catheterised.

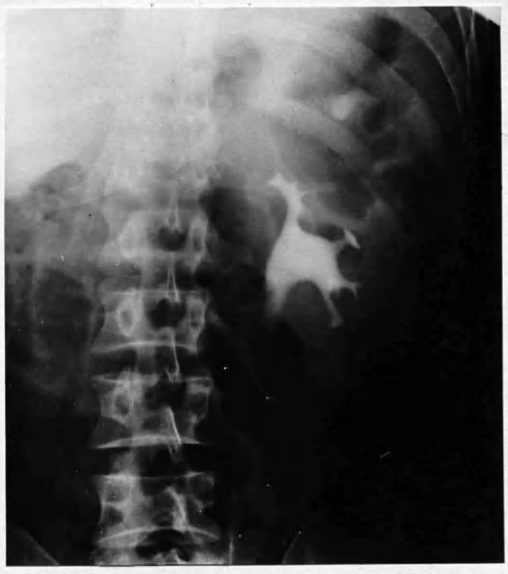


Fig. 33. A.C.

Left retrograde pyelogram.
Some dilatation of kidney
pelvis. Right ureter
could not be catheterised.

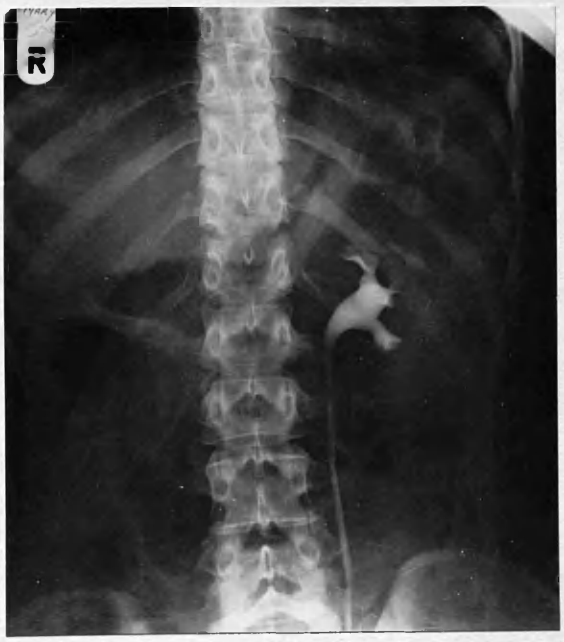


Fig. 34. M.F.

Retrograde pyelogram.
Left kidney normal in outline. Right ureter could not be catheterised.

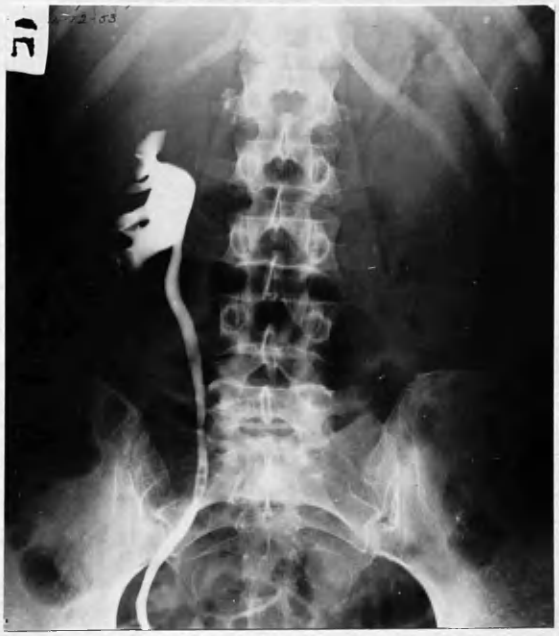


Fig. 35. M.M.

Retrograde pyelogram.
Right kidney some dilatation of kidney pelvis.
Irregularity of outline evident in upper pole.

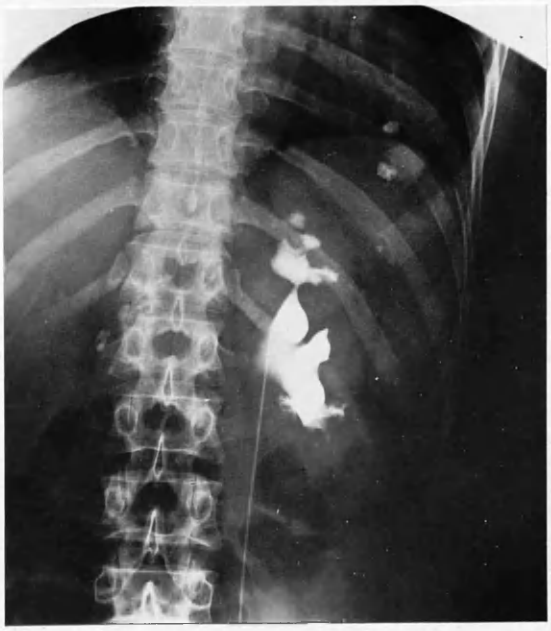


Fig. 36. M.M.

Retrograde pyelogram. Left side shows gross distortion of kidney outline with cavitation evident in upper and lower poles.

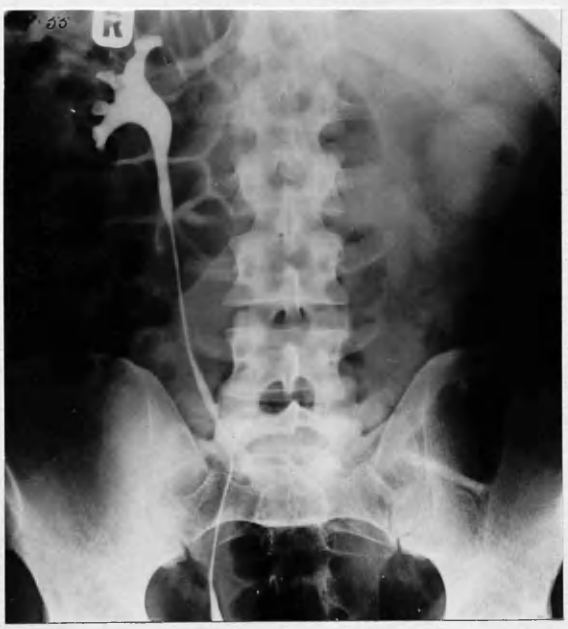


Fig. 37. J.McA.

Retrograde pyelogram. Right kidney normal in outline. Left ureter could not be catheterised. Vague outline of left kidney can be seen.

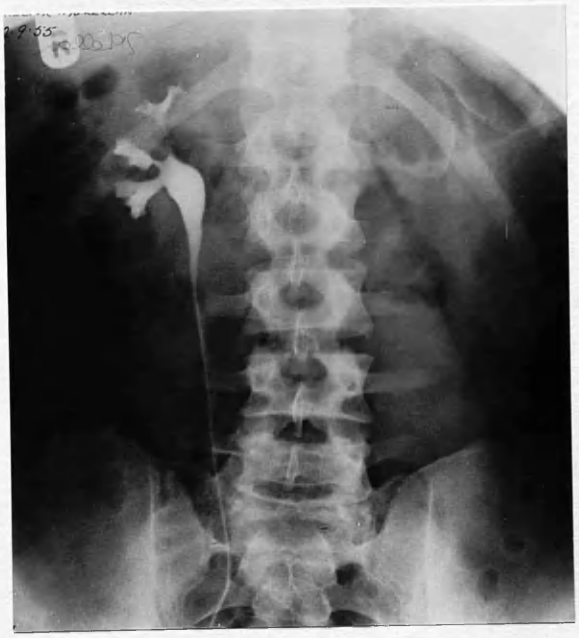


Fig. 38. H.McL.

Retrograde pyelogram. Right kidney shows normal pattern. Left ureter could not be catheterised.

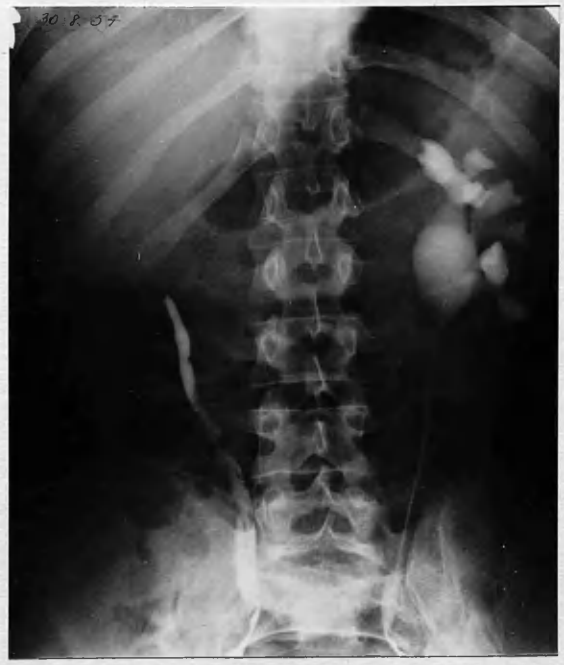


Fig. 39. D.O'R.

Retrograde pyelogram. Right ureter partially catheterised. Ureter shows considerable dilatation. No kidney shadow evident. Left kidney shows some dilatation of pelvis and slight irregularity of calyces.

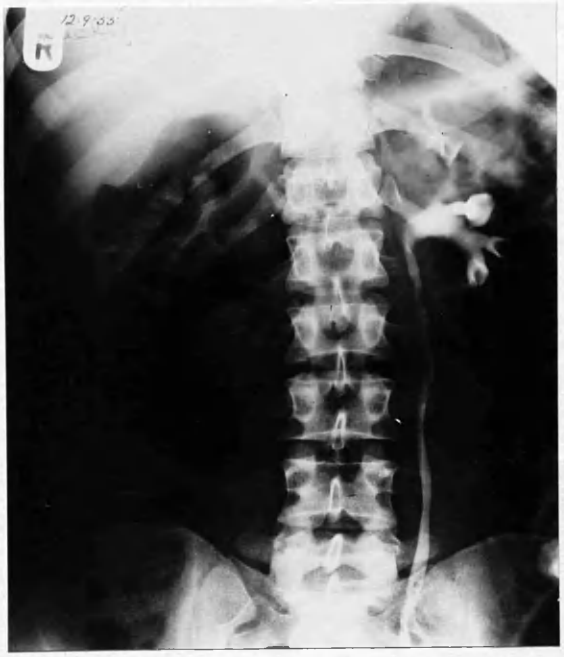


Fig. 40. J.P.

Retrograde pyelogram.
Left kidney normal.
Right ureter not catheterised.

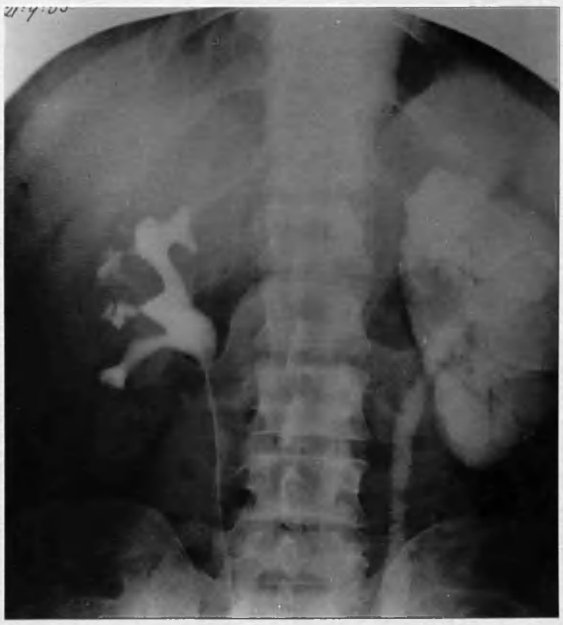


Fig. 41. R.S.

Retrograde pyelogram.
Right kidney shows some irregularity of middle calyces and dilatation of pelvis.
Left kidney and ureter grossly calcified.

RENAL TUBERCULOSIS

Blood Pressure Before and After Nephrectomy

NAME	SEX	AGE	B. P.		
			PRE-OP.	POST-OP.	
				1/52	6/12
J.M.	F.	23	116/80	120/76	130/70
M.P.	F.	46	160/100	-	128/84
A.C.	M.	32	135/80	130/76	134/80
J.P.	F.	23	128/86	120/84	130/80
R.S.	M.	35	140/100	-	120/86
T.B.	M.	45	124/70	136/84	106/84
V.B.	M.	38	130/94	130/80	118/86
J.McA.	M.	26	140/84	118/86	120/80
M.F.	F.	18	135/70	110/86	116/84
R.Y.	M.	12	112/82	106/84	110/80
W.N.	M.	29	180/100	160/100	128/96
D.O'R.	M.	18	112/80	130/84	118/86
M.B.	F.	33	130/80	124/82	132/86
A.F.	M.	29	114/90	130/90	116/86
H.P.	F.	42	130/84	118/80	120/82
W.S.	M.	62	210/110	120/74	130/96
H.McL.	M.	25	140/86	130/84	120/84
A.Bk.	F.	42	210/120	170/110	164/94
M.M.	F.	44	150/100	164/104	150/90
E.C.	F.	55	160/104	170/112	150/76

Fig. 42.

TUBERCULOSIS OF KIDNEY

Cases Arranged in Order of Descending Tm_{PAH}.

NAME	AGE	PRE-OP.	POST-OP.	
			1/52	6/12
J.M.	23	68.0	32.3	40.0
M.P.	31	65.6	44.1	40.0
A.C.	32	63.6	59.2	58.7
J.P.	23	61.2	60.4	34.0
R.S.	35	60.2	31.9	38.6
T.B.	45	53.1	62.0	50.6
V.B.	38	52.9	52.4	53.9
J.McA.	26	49.2	39.9	35.8
M.F.	18	48.9	40.6	54.4
R.Y.	12	45.7	46.8	45.0
W.N.	29	45.4	38.5	46.7
D.O'R.	18	44.6	38.6	45.4
M.B.	33	39.6	45.4	32.1
A.F.	29	38.8	15.3	56.7
H.P.	42	38.3	33.6	43.9
A.T.	32	37.9	19.1	40.1
A.Bt.	51	34.7	40.8	40.1
W.S.	62	29.7	20.2	35.0
H.McL.	25	28.1	29.1	39.1
A.Bk.	42	27.2	31.3	30.9
M.M.	44	26.8	44.0	19.6
E.C.	55	24.6	37.3	20.4

Fig. 43.

TUBERCULOSIS OF KIDNEY

Group Means of Renal Function Tests Values

GROUP		PRE-OPERATIVE			POST-OPERATIVE 1/52			POST-OPERATIVE 6/12		
		RPF	GFR	Tm_{PAH}	RPF	GFR	Tm_{PAH}	RPF	GFR	Tm_{PAH}
MILD	Mean for Group	431	82	63.7	415	69	45.6	315	72	42.3
	Mean as % Normal	69	67	80,7	66	56	57.8	50	59	53.6
MODERATE	Mean for Group	497	84	47.4	397	75	45.5	373	78	45.5
	Mean as % Normal	79	68	60.5	64	61	57.7	60	63	57.7
SEVERE	Mean for Group	240	51	31.8	284	53	30.1	223	51	36.2
	Mean as % Normal	38	41	40.4	45	43	38.1	36	41	45.9
ALL CASES	Mean	389	72	47.8	365	66	40.3	304	67	41.4
	Mean as % Normal.	62	58	60.5	58	54	51.1	49	55	52.5

Fig. 44.

TUBERCULOSIS OF KIDNEY

R.P.F. and G.F.R. Arranged According to Pre-operative Value of TmPAH Results.

NAME	R.P.F.			G.F.R.		
	PRE-OP.	POST-OP.		PRE-OP.	POST-OP.	
		1/52	6/12		1/52	6/12
J.M.	462	444	322	46	67	76
M.P.	243	235	195	57	52	58
A.C.	527	444	277	114	63	64
J.P.	654	628	449	103	85	85
R.S.	267	323	330	90	76	79
T.B.	481	376	372	97	80	78
V.B.	437	411	512	80	68	97
J.McA.	435	231	306	74	50	75
M.F.	461	440	375	92	86	80
R.Y.	450	314	422	111	63	81
W.N.	385	449	251	60	113	81
D.O'R.	672	529	435	90	84	65
M.B.	600	396	286	125	55	65
A.F.	305	468	280	56	85	70
H.P.	283	463	238	81	91	53
A.T.	416	260	215	91	32	50
A.Bt.	232	303	392	43	45	25
W.S.	170	213	184	42	47	47
H.McL.	216	384	219	42	53	44
A.Bk.	183	205	119	36	55	69
M.M.	157	141	171	22	18	41
E.C.	197	223	186	44	49	60

Fig. 45.

TUBERCULOSIS OF KIDNEY

Fractional Figures Arranged According to Pre-operative

Value of Tm_{PAH} Results.

NAME	PRE-OPERATIVE			POST-OPERATIVE					
				1/52			6/12		
	F.F.	$\frac{RPF}{Tm_{PAH}}$	$\frac{GFR}{Tm_{PAH}}$	F.F.	$\frac{RPF}{Tm_{PAH}}$	$\frac{GFR}{Tm_{PAH}}$	F.F.	$\frac{RPF}{Tm_{PAH}}$	$\frac{GFR}{Tm_{PAH}}$
Average Normal	.197	7.92	1.56						
J.M.	.100	6.79	0.68	.151	13.74	2.07	.237	8.05	1.90
M.P.	.233	3.70	0.86	.226	5.33	1.18	.296	4.88	1.44
A.C.	.216	8.29	1.79	.142	7.50	1.07	.231	4.72	1.09
J.P.	.157	10.68	1.69	.137	10.40	1.40	.198	13.20	2.50
R.S.	.144	4.44	1.50	.235	10.13	2.38	.245	8.55	2.03
T.B.	.201	9.06	1.82	.213	6.06	1.29	.209	7.35	1.54
V.B.	.182	8.26	1.50	.165	7.88	1.29	.191	9.50	1.80
J.McA.	.171	8.86	1.51	.217	5.79	1.26	.243	8.55	2.08
M.F.	.198	9.42	1.87	.195	10.84	2.12	.213	6.89	1.47
R.Y.	.247	9.84	2.42	.210	6.70	1.35	.192	9.38	1.80
W.N.	.078	8.48	1.32	.252	11.67	2.94	.323	5.38	1.73
D.O'R.	.134	15.07	2.02	.158	13.70	2.17	.152	9.59	1.21
M.B.	.209	15.15	3.15	.138	8.72	1.20	.228	8.93	2.03
A.F.	.184	7.85	1.44	.181	30.59	5.52	.250	4.93	1.23
H.P.	.285	7.38	2.11	.196	13.78	2.71	.223	5.42	1.21
A.T.	.219	11.00	2.40	.123	13.61	1.68	.232	5.36	1.25
A.Bt.	.235	5.27	1.24	.220	5.02	1.10	.210	2.97	0.62
W.S.	.247	5.72	1.41	.221	10.54	2.32	.255	5.20	1.34
H.McL.	.195	7.70	1.50	.138	13.20	1.82	.198	5.61	1.11
A.Bk.	.154	8.53	1.32	.180	9.67	1.74	.175	12.68	2.23
M.M.	.143	5.86	0.84	.130	3.20	0.42	.237	8.74	2.07
E.C.	.223	8.01	1.79	.220	5.98	1.31	.323	9.13	2.94

Fig. 46.

TUBERCULOSIS OF KIDNEY

Urea Clearance Tests Arranged According to Pre-Operative Value of Tm_{PAH}

NAME	AGE	SEX	PRE-OP. Tm_{PAH}	U.C.T.(1)			U.C.T.(2)		
				PRE-OP.	POST-OP. 1/52	POST-OP. 6/12	PRE-OP.	POST-OP. 1/52	POST-OP. 6/12
J.M.	23	F	68.0	...	46	66	...	59	58
M.P.	46	F	65.6	36	74	49	43	81	45
A.C.	32	M	63.6	68	...	...	58	...	...
J.P.	23	F	61.2	121	75	72	119	78	61
R.S.	35	M	60.2	...	88	66	...	101	67
T.B.	45	M	53.1	132	97	58	134	77	63
V.B.	38	M	52.9	98	66	67	115	63	65
J.McA.	26	M	49.2	95	49	...	71	55	...
N.F.	18	F	48.9	89	91	70	84	71	63
R.Y.	12	M	45.7	78	46	85	76	40	69
W.N.	29	M	45.4	...	...	83	...	...	62
D.O'R.	18	M	44.6	94	68	76	83	84	97
M.B.	33	F	39.6	124	37	47	83	38	37
A.F.	29	M	38.8	57	52	96	58	52	71
H.P.	42	F	38.3	102	74	63	103	90	73
A.T.	32	M	37.9	69	...	42	51	...	49
A.Bt.	51	F	34.7	36	66	33	50	57	41
W.S.	62	M	29.7	48	44	108	46	40	91
H.McL.	25	M	28.1	50	100	80	37	66	116
A.Bk.	42	F	27.2	33	55	68	41	66	63
M.M.	44	F	26.8	36	18	33	11	18	29
E.C.	55	F	24.6	53	44	42	59	50	57

Fig. 47.

Tm_{PAH} results are absolute values whereas U.C.T. results are calculated according to the Van Slyke maximum and standard clearance formulae.

TUBERCULOSIS OF KIDNEY

R.P.F. Results Arranged According to Pre-operative value.

NAME	AGE	PRE-O P.	POST-O P.	
			1/52	6/12
D.O'R.	18	672	529	435
J.P.	23	654	628	449
M.B.	33	600	396	286
A.C.	32	527	444	277
T.B.	45	481	376	372
J.M.	23	462	444	322
M.F.	18	461	440	375
R.Y.	12	450	314	422
V.B.	38	437	411	512
J.McA.	26	435	231	306
A.T.	32	416	260	215
W.N.	29	385	449	251
A.F.	29	305	468	280
H.P.	42	283	463	238
R.S.	35	267	323	330
M.P.	31	243	235	195
A.Bt.	51	232	303	392
H.McL.	25	216	384	219
E.C.	55	197	223	186
A.Bk.	42	183	205	119
W.S.	62	170	213	184
M.M.	44	157	141	171

Fig. 48.

TUBERCULOSIS OF KIDNEY

G.F.R. Results Arranged According to Pre-operative Value.

NAME	AGE	PRE-OP.	POST-OP.	
			1/52	6/12
M.B.	33	125	55	65
A.C.	32	114	63	64
R.Y.	12	111	63	81
J.P.	23	103	85	85
T.B.	45	97	80	78
M.F.	18	92	86	80
A.T.	32	91	32	50
D.O'R.	18	90	84	65
R.S.	35	90	76	79
H.P.	42	81	91	53
V.B.	38	80	68	97
J.McA.	26	74	50	75
W.N.	29	60	113	81
M.P.	31	57	52	58
A.F.	29	56	85	70
J.M.	23	46	67	76
E.C.	55	44	49	60
A.Bt.	51	43	45	25
H.McL.	25	42	53	44
W.S.	62	42	47	47
A.Bk.	42	36	55	69
M.M.	44	22	18	41

Fig. 49.

TUBERCULOSIS OF KIDNEY

G.F.R. and Tm_{PAH} Arranged According to Pre-operative Value of R.P.F. Results.

NAME	G.F.R.			Tm_{PAH}		
	PRE-OP.	POST-OP.		PRE-OP.	POST-OP.	
		1/52	6/12		1/52	6/12
D.O'R.	90	84	65	44.6	38.6	45.4
J.P.	103	85	85	61.2	60.4	34.0
M.B.	125	55	65	39.6	45.4	32.1
A.C.	114	63	64	63.6	59.2	58.7
T.B.	97	80	78	53.1	62.0	50.6
J.M.	46	67	76	68.0	32.3	40.0
M.F.	92	86	80	48.9	40.6	54.4
R.Y.	111	63	81	45.7	46.8	45.0
V.B.	80	68	97	52.9	52.4	53.9
J.McA.	74	50	75	49.2	39.9	35.8
A.T.	91	32	50	37.9	19.1	40.1
W.N.	60	113	81	45.4	38.5	46.7
A.F.	56	85	70	38.8	15.3	56.7
H.P.	81	91	53	38.3	33.6	43.9
R.S.	90	76	79	60.2	31.9	38.6
M.P.	57	52	58	65.6	44.1	40.0
A.Bt.	43	45	25	34.7	40.8	40.1
H.McL.	42	53	44	28.1	29.1	39.1
E.C.	44	49	60	24.6	37.3	20.4
A.Bk.	36	35	69	27.2	31.3	30.9
W.S.	42	47	47	29.7	20.2	35.0
M.M.	22	18	41	26.8	44.0	19.6

Fig. 50.

TUBERCULOSIS OF KIDNEY

R.P.F. and Tm_{PAH} Arranged According to Pre-operative Value of G.F.R. Results.

NAME	R.P.F.			Tm_{PAH}		
	PRE-OP.	POST-OP.		PRE-OP.	POST-OP.	
		1/52	6/12		1/52	6/12
M.B.	600	396	286	39.6	45.4	32.1
A.C.	527	444	277	63.6	59.2	58.7
R.Y.	450	314	422	45.7	46.8	45.0
J.P.	654	628	449	61.2	60.4	34.0
T.B.	481	376	372	53.1	62.0	50.6
M.F.	461	440	375	48.9	40.6	54.4
A.T.	416	260	215	37.9	19.1	40.1
D.O'R.	672	529	435	44.6	38.6	45.4
R.S.	267	323	330	60.2	31.9	38.6
H.P.	283	463	238	38.3	33.6	43.9
V.B.	437	411	512	52.9	52.4	53.9
J.McA.	435	231	306	49.2	39.9	35.8
W.N.	385	449	251	45.4	38.5	46.7
M.P.	243	235	195	65.6	44.1	40.0
A.F.	305	468	280	38.8	15.3	56.7
J.M.	462	444	322	68.0	32.3	40.0
E.C.	197	223	186	24.6	37.3	20.4
A.Bt.	232	303	392	34.7	40.8	40.1
H.McL.	216	384	219	28.1	39.1	39.1
W.S.	170	213	184	29.7	20.2	35.0
A.Bk.	183	205	119	27.2	31.3	30.9
M.M.	157	141	171	26.8	44.0	19.6

Fig. 51.

TUBERCULOSIS OF KIDNEY

Group Means of Fractional Figures

GROUP	PRE-OPERATIVE			POST OPERATIVE					
				1/52			6/12		
	FF	RPF / Tm_{PAH}	GFR / Tm_{PAH}	FF	RPF / Tm_{PAH}	GFR / Tm_{PAH}	FF	RPF / Tm_{PAH}	GFR / Tm_{PAH}
Tm > 75%	.170	6.78	1.30	.178	9.42	1.62	.241	7.88	1.79
Tm 50% - 75%	.178	10.52	1.95	.194	8.92	1.70	.219	8.20	1.71
Tm < 50%	.209	7.48	1.56	.179	11.73	2.07	.234	6.67	1.56

Fig. 52.

CORRELATION OF Tm_{PAH} with R.P.F.

1. Observation No.	2. Tm_{PAH} x	3. R.P.F. y	4. x^2	5. y^2	6. x x y
1.	68.0	462	4624.00	213444	31416.0
2.	65.6	243	4303.36	59049	15940.8
3.	63.6	527	4044.96	277729	33517.2
4.	61.2	654	3745.44	427716	40024.8
5.	60.2	267	3624.04	71289	16073.4
6.	53.1	481	2819.61	231361	25541.1
7.	52.9	437	2798.41	190969	23117.3
8.	49.2	435	2420.64	189225	21402.0
9.	48.9	461	2391.21	212521	22542.9
10.	45.7	450	2088.49	202500	20565.0
11.	45.4	385	2061.16	148225	17479.0
12.	44.6	672	1989.16	451584	29971.2
13.	39.6	600	1568.16	360000	23760.0
14.	38.8	305	1505.44	93025	11834.0
15.	38.3	283	1466.89	80089	10838.9
16.	37.9	416	1436.41	173056	15766.4
17.	34.7	232	1204.89	53824	8050.4
18.	29.7	170	882.09	28900	5049.0
19.	28.1	216	789.61	46656	6069.6
20.	27.2	183	739.84	33489	4977.6
21.	26.8	157	718.24	24649	4207.6
22.	24.6	197	605.16	38809	4846.2
Total.	984.1	8233	47826.41	3608109	392990.4
Mean Value	44.7	374	2173.93	164005	17863.2

Standard deviation of Tm_{PAH} = 13.26

Standard deviation of R.P.F. = 155

Correlation co-efficient r = + 0.56

Fig. 53.

CORRELATION OF Tm_{PAH} with G.F.R.

1. Observation No.	2. Tm_{PAH} x	3. G.F.R. y	4. x^2	5. y^2	6. x x y
1.	68.0	46	4624.00	2116	3128.0
2.	65.6	57	4303.36	3249	3739.2
3.	63.6	114	4044.96	12996	7250.4
4.	61.2	103	3745.44	10609	6303.6
5.	60.2	90	3624.04	8100	5418.0
6.	53.1	97	2819.61	9409	5150.7
7.	52.9	80	2798.41	6400	4232.0
8.	49.2	74	2420.64	5476	3640.8
9.	48.9	92	2391.21	8464	4498.8
10.	45.7	111	2088.49	12321	5072.7
11.	45.4	60	2061.16	3600	2724.0
12.	44.6	90	1989.16	8100	4014.0
13.	39.6	125	1568.16	15625	4950.0
14.	38.8	56	1505.44	3136	2172.8
15.	38.3	81	1466.89	6561	3102.3
16.	37.9	91	1436.41	8281	3448.9
17.	34.7	43	1204.09	1849	1492.1
18.	29.7	42	882.09	1764	1247.4
19.	28.1	42	789.61	1764	1180.2
20.	27.2	36	739.84	1296	979.2
21.	26.8	22	718.24	484	589.6
22.	24.6	44	605.16	1936	1082.4
Total	984.1	1596	47826.41	133536	75417.1
Mean Value	44.7	73	2173.93	6070	3428.05

Standard deviation of Tm_{PAH} = 13.26
Standard deviation of G.F.R. = 27.2
Correlation co-efficient r = + 0.46

Fig. 54.

CORRELATION OF UREA CLEARANCE TEST (low PAH) with Tm_{PAH}.

1. Observation No.	2. U.C.T.(low PAH)	3. Tm_{PAH}	4. x^2	5. y^2	6. x x y
1.	27	65.6	4503.36	729	1771.2
2.	51	63.6	4044.96	2601	3243.6
3.	91	61.2	3745.44	8281	5569.2
4.	99	53.1	2819.61	9801	5256.9
5.	73	52.9	2798.41	5329	2803.7
6.	71	49.2	2420.64	5041	3493.2
7.	67	48.9	2391.21	4489	3276.3
8.	59	45.7	2088.49	3481	2696.3
9.	71	44.6	1989.16	5041	3166.6
10.	93	39.6	1568.16	8649	3682.8
11.	43	38.8	1505.44	1849	1668.4
12.	77	38.3	1466.89	5929	2949.1
13.	52	37.9	1436.41	2704	1970.8
14.	27	34.7	1204.09	729	936.9
15.	36	29.7	882.09	1296	1069.2
16.	38	28.1	789.61	1444	1067.8
17.	25	27.2	739.84	625	680.0
18.	27	26.8	718.24	729	723.6
19.	40	24.6	605.16	1600	984.0
Total	1067	8105	37517.21	70347	47009.6
Mean value	56	42.7	1974.59	3702	2474.2

Standard deviation of U.C.T.(low PAH)= 23.8

Standard deviation of Tm_{PAH} = 12.3

Correlation coefficient r = + 0.32

Fig. 55.

CORRELATION OF UREA CLEARANCE TEST (low PAH) with G.F.R.

1. Observation No.	2. U.C.T.(low PAH) x	3. G.F.R. y	4. x^2	5. y^2	6. x x y
1.	27	57	729	3249	1539
2.	51	114	2601	12996	5814
3.	91	103	8281	10609	9373
4.	99	97	9801	9409	9603
5.	73	80	5329	6400	5840
6.	71	74	5041	5476	5254
7.	67	92	4489	8464	6164
8.	59	111	3481	12321	6549
9.	71	90	5041	8100	6390
10.	93	125	8649	15625	11625
11.	43	56	1849	3136	2408
12.	77	81	5929	6561	6273
13.	52	91	2704	8281	4732
14.	27	43	729	1849	1161
15.	36	42	1296	1764	1512
16.	38	42	1444	1764	1596
17.	25	36	625	1296	900
18.	27	22	729	484	594
19.	40	44	1600	1936	1760
Total	1067	1400	70347	119720	89087
Mean Value	56	74	3702	6301	4689

Standard deviation of U.C.T.(low PAH) = 23.8
Standard deviation of G.F.R. = 28.7
Correlation co-efficient r = + 0.80

Fig. 56.

CORRELATION OF R.P.F. with G.F.R.

1. Observation No.	2. R.P.F. x	3. G.F.R. y	4. x^2	5. y^2	6. x x y
1.	462	46	213444	2116	21252
2.	243	57	59049	3249	13851
3.	527	114	277729	12996	60078
4.	654	103	427716	10609	67362
5.	267	90	71289	8100	24030
6.	481	97	231361	9409	46657
7.	437	80	190969	6400	34960
8.	435	74	189225	5476	32190
9.	461	92	212521	8464	42412
10.	450	111	202500	12321	49950
11.	385	60	148225	3600	23100
12.	672	90	451584	8100	60480
13.	600	125	360000	15625	75000
14.	305	56	93025	3136	17080
15.	283	81	80089	6561	22923
16.	416	91	173056	8281	37856
17.	232	43	53824	1849	9976
18.	170	42	28900	1764	7140
19.	216	42	46656	1764	9072
20.	183	36	33489	1296	6588
21.	157	22	24649	484	3454
22.	197	44	38809	1936	8668
Total	8233	1596	3608109	133536	674079
Mean Value	374	73	164005	6070	30640

Standard deviation of R.P.F. = 155
Standard deviation of G.F.R. = 27.2
Correlation co-efficient r = + 0.79

Fig. 57.

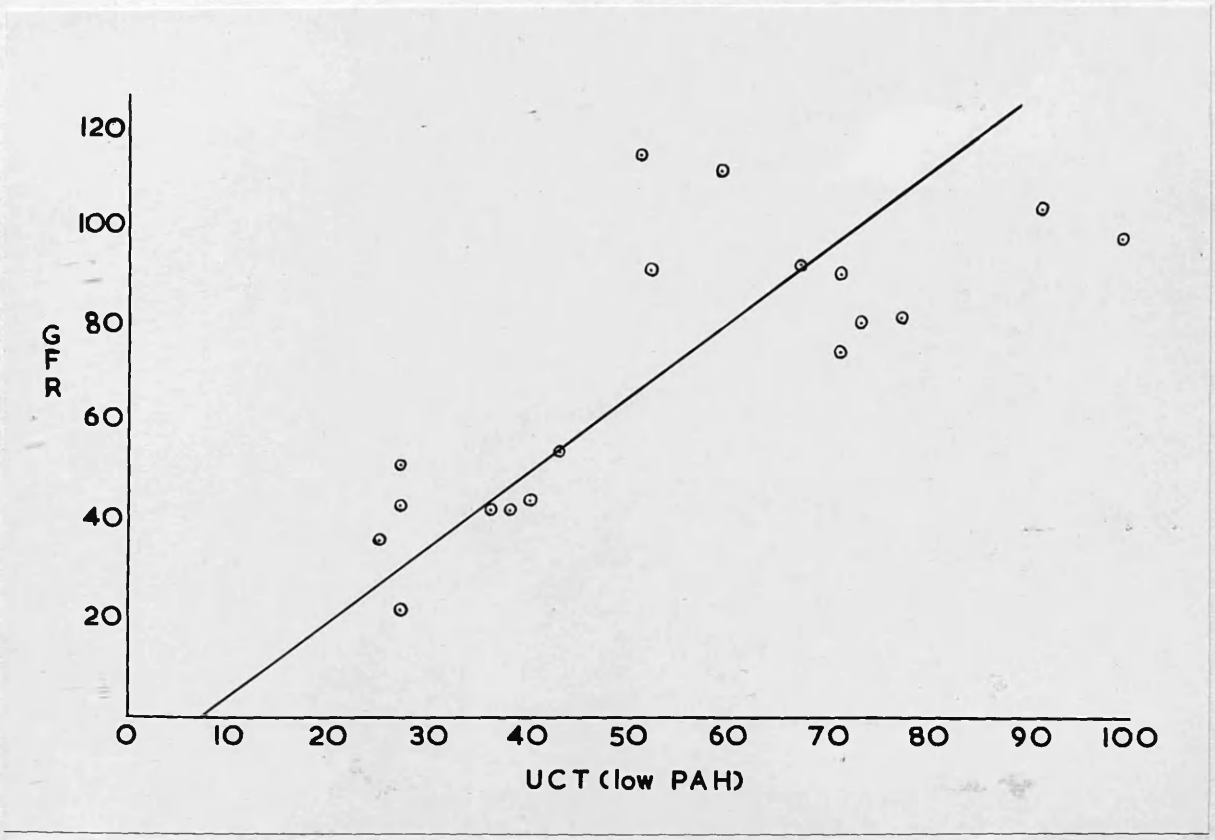


Fig. 58.

Scatter diagram showing correlation between GFR (Glomerular Filtration Rate) and UCT (Urea Clearance Test)

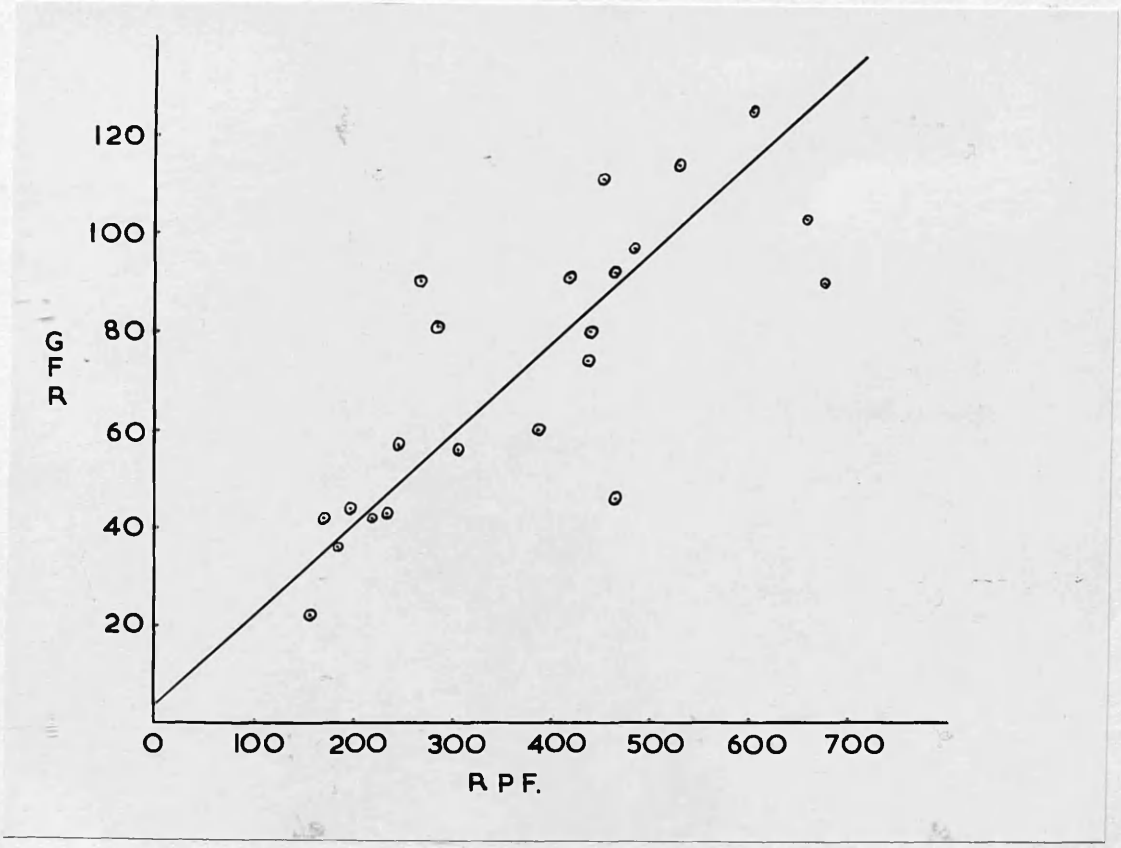


Fig. 59.

Scatter diagram showing correlation between GFR (Glomerular Filtration Rate) and RPF (Renal Plasma Flow)

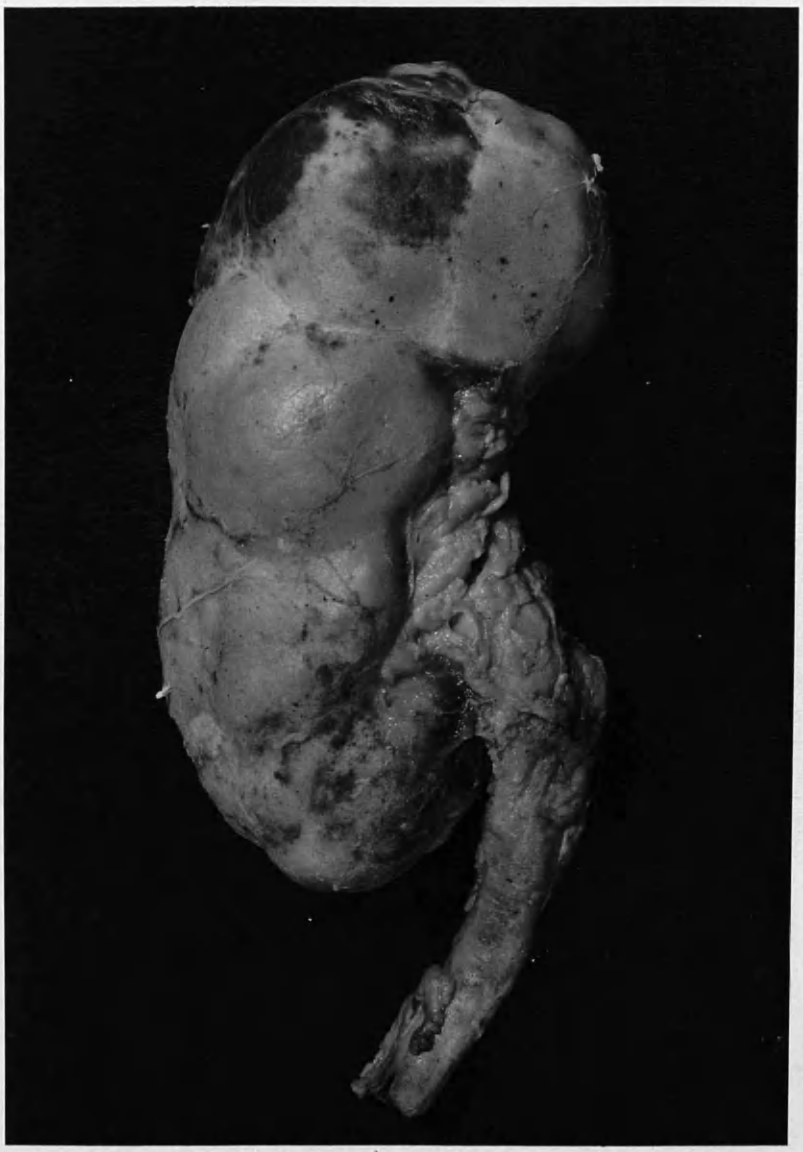


Fig. 60. Left kidney. A.Bk. Female. Age 42.

Surface is lobulated suggesting the presence of abscesses. Weight was 250 gms.

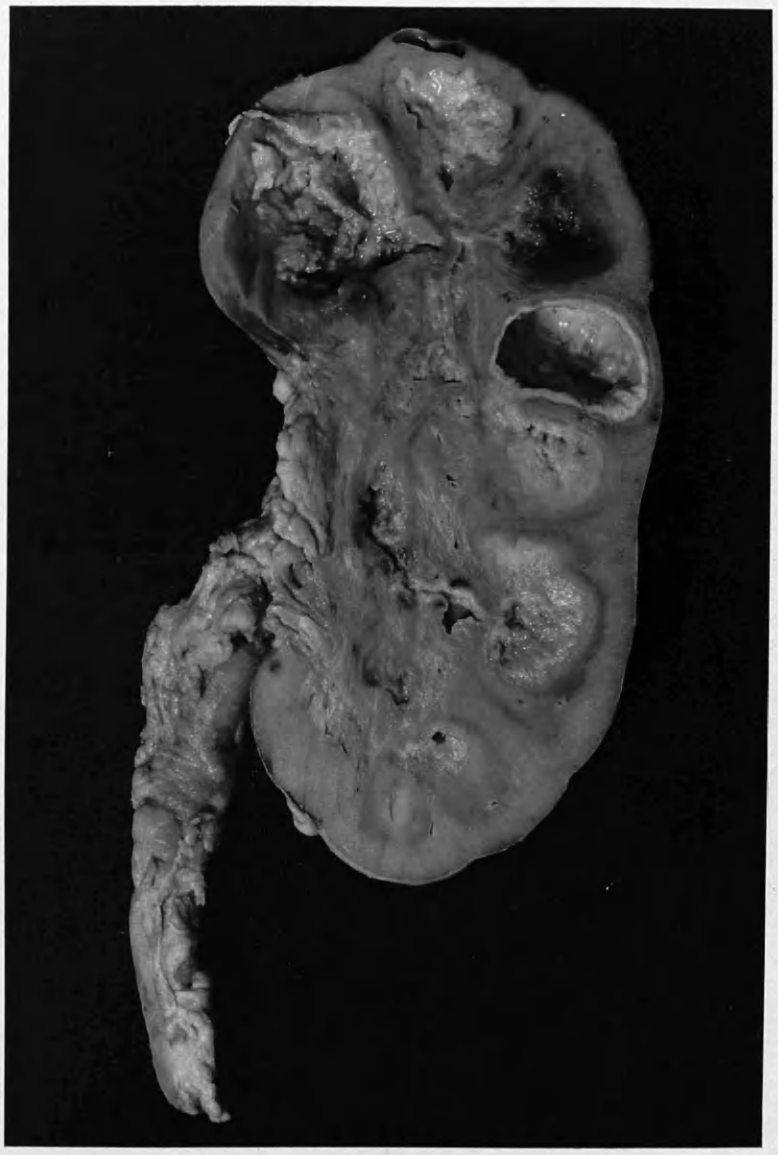


Fig. 61. Left kidney. A.Bk. Female. Age 42.

The cut surface reveals the presence of five large caseous abscesses.
Histologically an advanced renal tuberculosis.

Tubular function:-

Pre-operative 34% of average normal.

Fig. 62. Right kidney. A.Bt. Female. Age 52.

A small kidney weighing 112 gms. and showing cut surface. The pelvis is dilated and lined by tuberculous granulation tissue; multiple scattered tubercles are present in the medulla and cortex - some of which are caseous.
Histologically a widespread tuberculosis.

Tubular function:-

Pre-operative 44% of average normal.

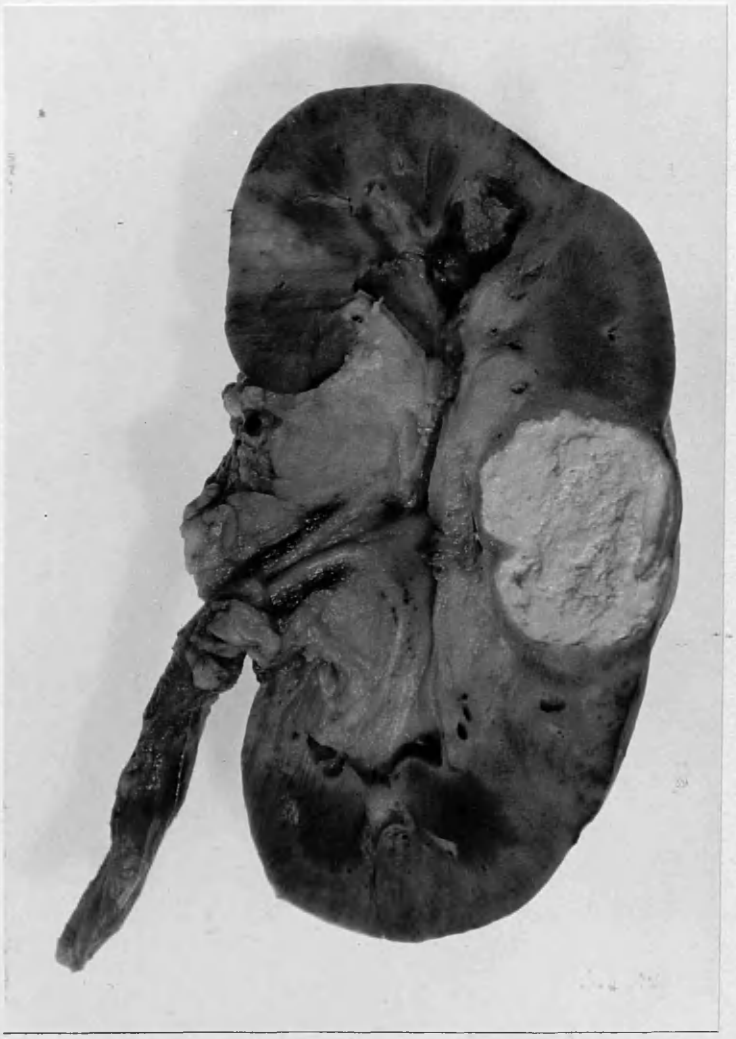


Fig. 63. Right kidney. T.B. Male. Age 45.

This kidney measured 130 x 60 x 60 mms. and weighed 245 gms. On cut surface a large lobulated abscess is present in the mid zone of the kidney. The lower calyces are dilated.

Histologically an active renal tuberculosis.

Tubular function:-

Pre-operative 67% of average normal.

Fig. 64. Right kidney. V.B. Male. Age 38.

This kidney measured 110 x 60 x 85 mms. and weighed 265 gms. There is gross foetal lobulation.

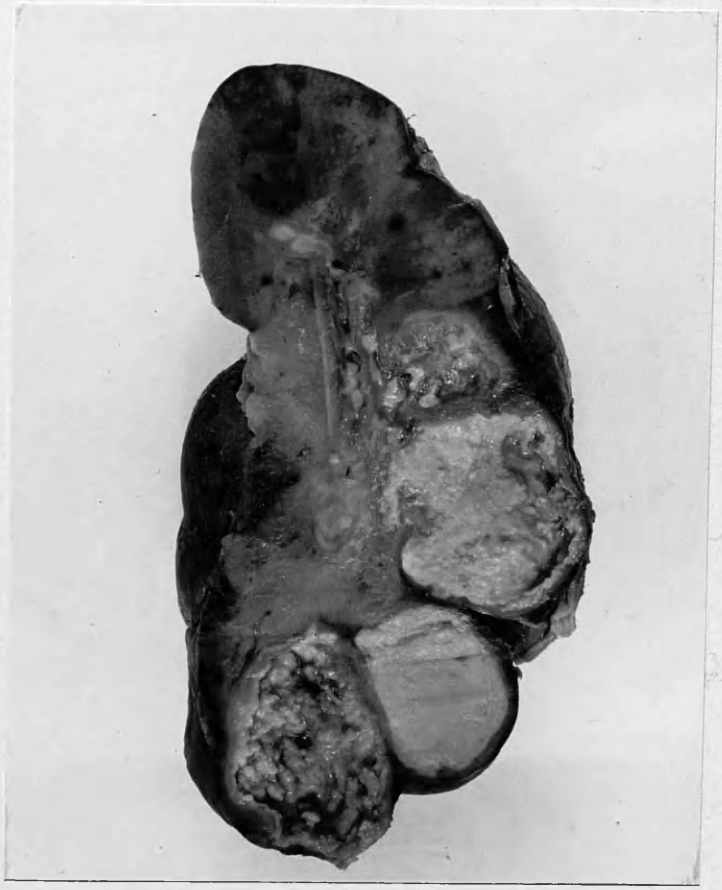


Fig. 65. Right kidney. V.B. Male. Age 38.

On cut surface the kidney is a bag of caseous pus with a small area of relatively normal tissue at the upper pole.
Histologically an active caseating tuberculosis.

Tubular function:-

Pre-operative 67% of average normal.

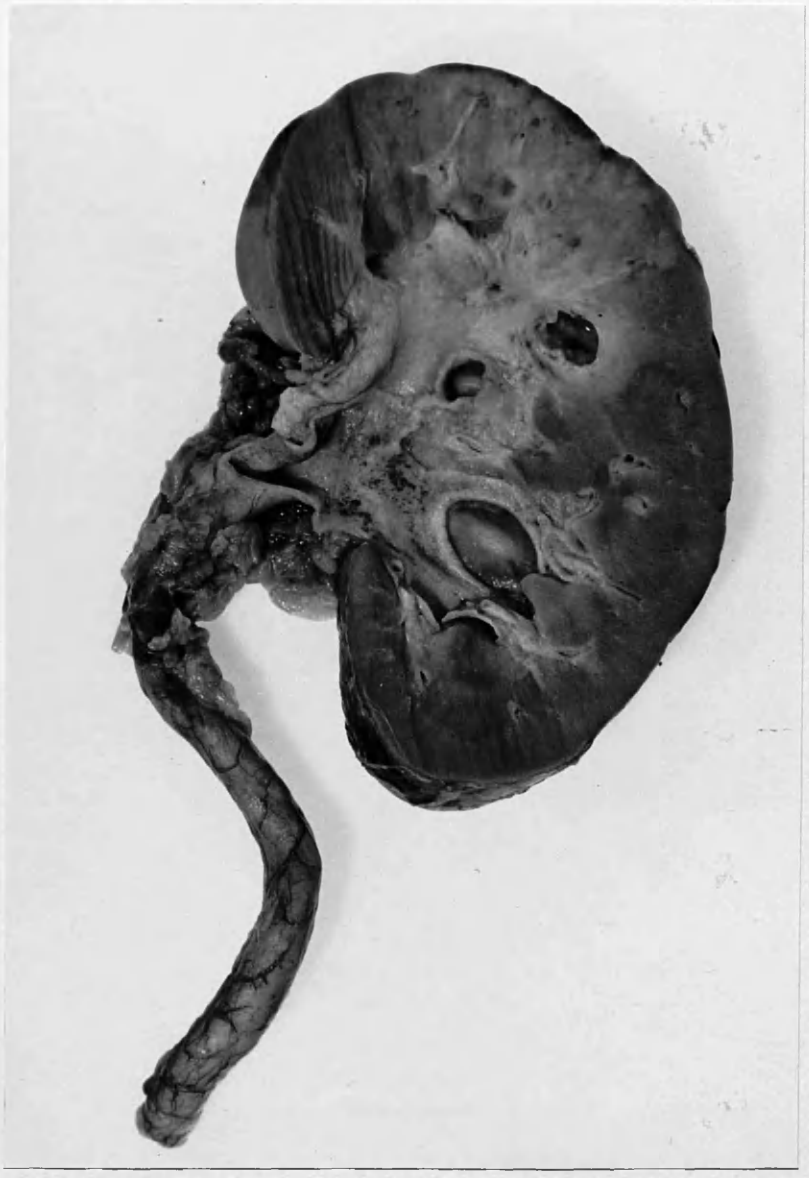


Fig. 66. Left kidney. M.B. Female. Age 33.

Kidney is of normal contour measuring 120 x 60 x 35 mms.
On section the primary calyces and pelvis are dilated.
A tuberculous cavity is seen in the mid zone. Many petechial haemorrhages in pelvic mucosa.
Histologically an early renal tuberculosis.

Tubular function:-

Pre-operative 50.2% of average normal.

Fig. 67. Right kidney. A.C. Male. Age 32.

A normally shaped kidney weighing 180 gms. with an irregularly lobulated surface, without abscess or scar.

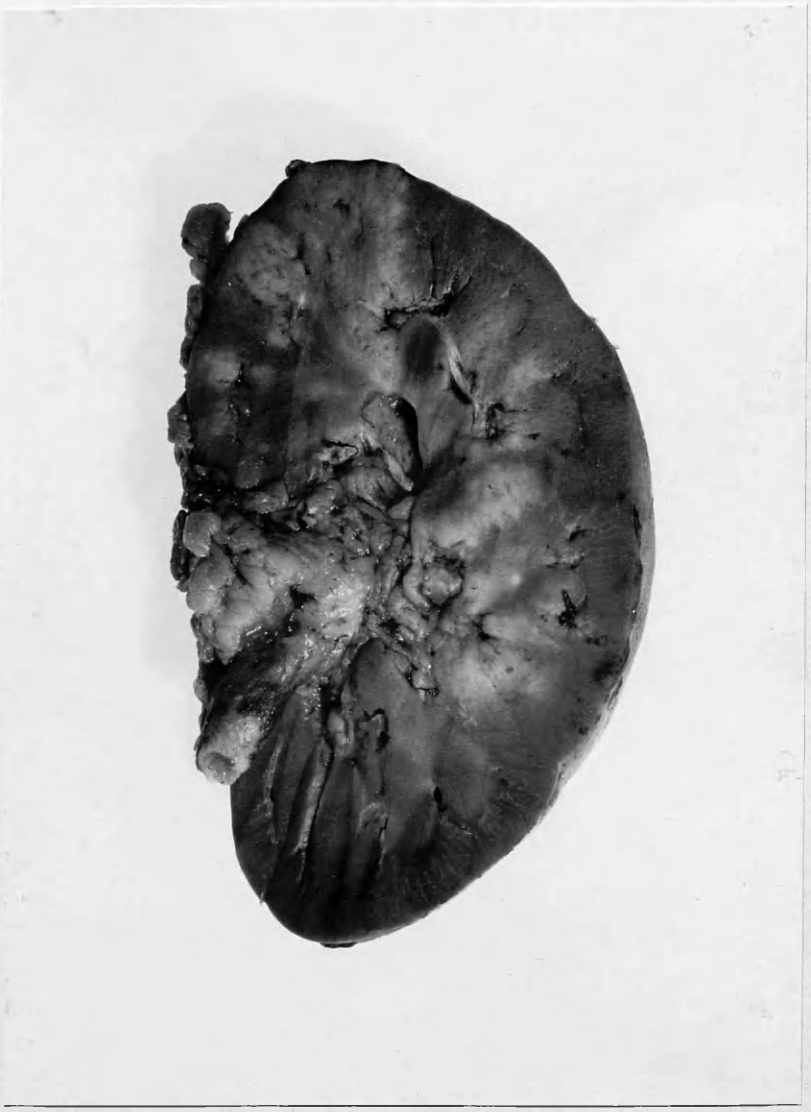


Fig. 68. Right kidney. A.C. Male. Age 32.

On cut surface there is coalescing tuberculosis confined to the medulla. There is no caseation. Histologically a proliferative tuberculosis.

Tubular function:-

Pre-operative 81% of average normal.

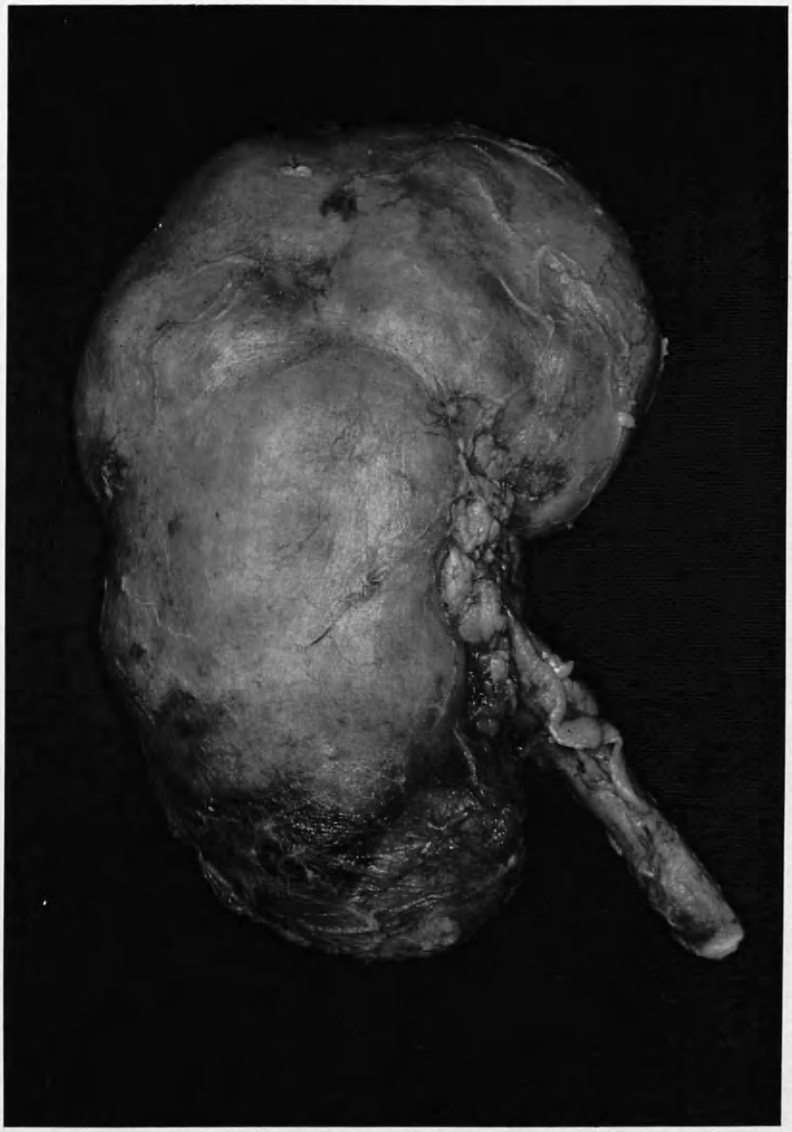


Fig. 69. Right kidney. A.F. Male. Age 29.

A very large lobulated kidney weighing 405 gms.
Upper pole is wide but the lower pole narrow and haemorrhagic.
The kidney felt cystic.

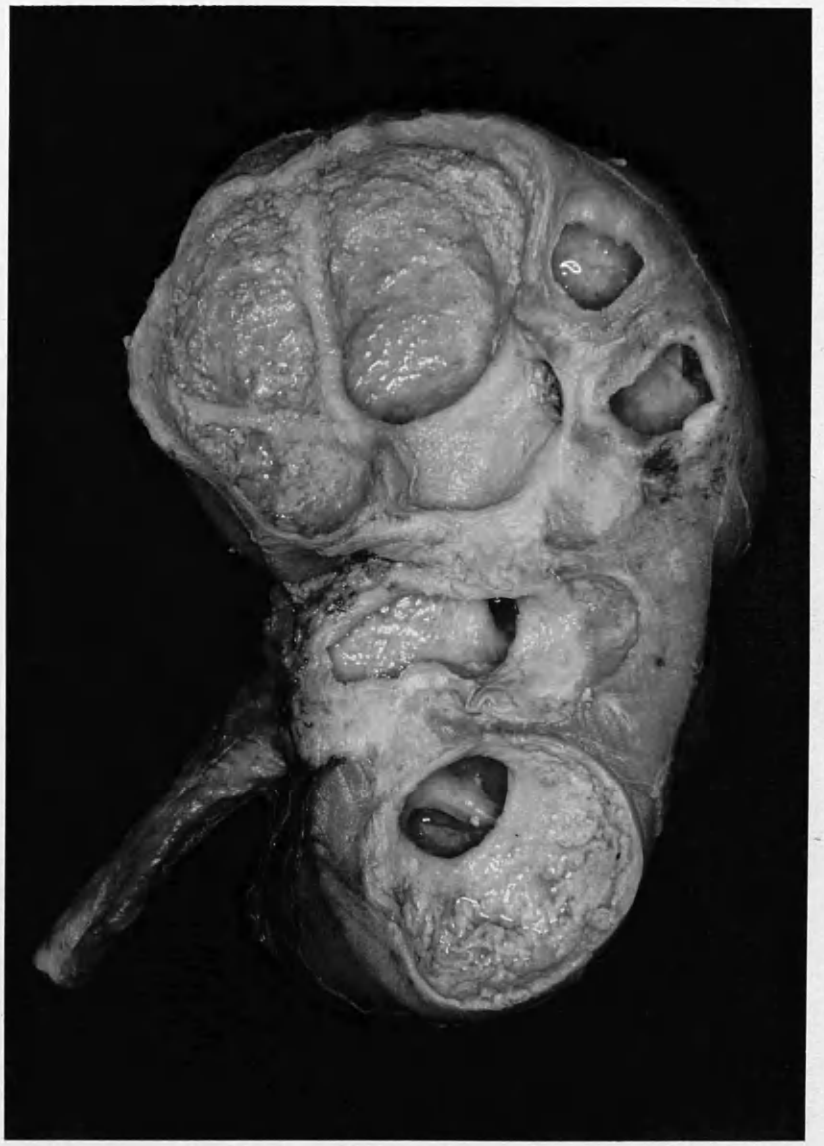


Fig. 70. Right kidney. A.F. Male. Age 29.

On cut surface it is grossly hydronephrotic.
The pelvis, primary and secondary calyces are
all distended.
Histologically an advanced tuberculous pyelonephritis.

Tubular function:-

Pre-operative 49% of average normal.

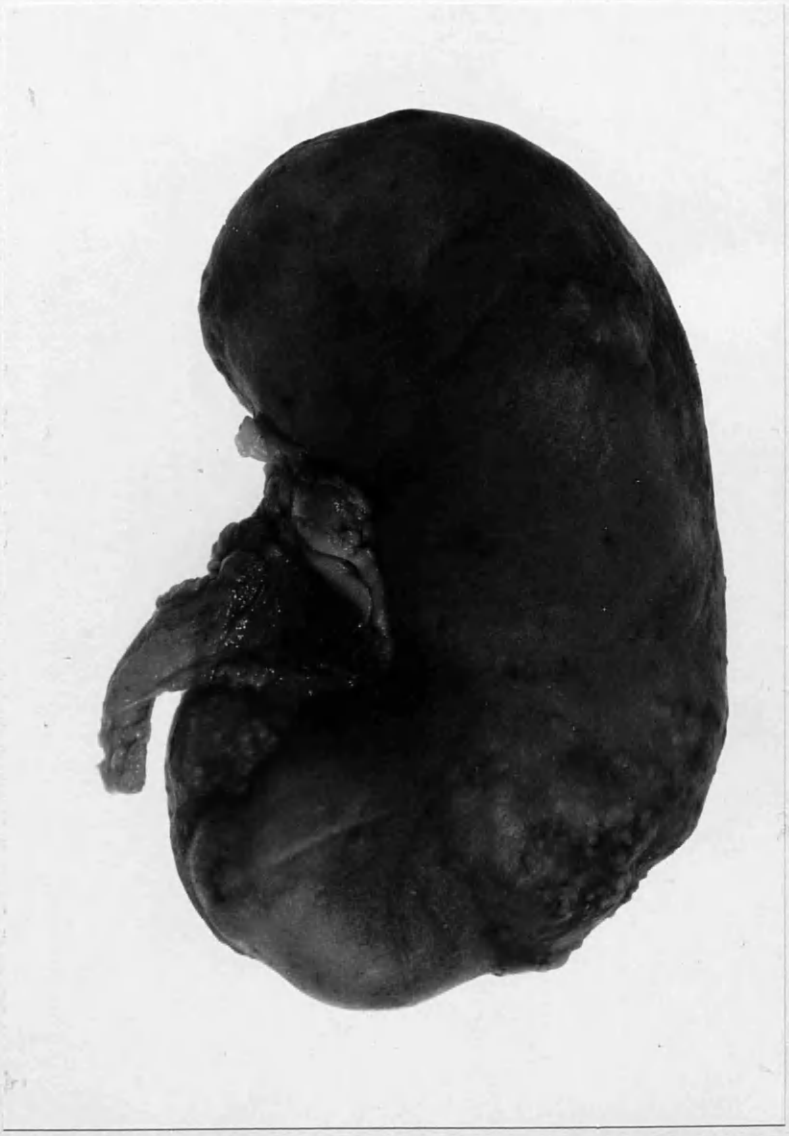


Fig. 71. Right kidney. M.F. Female. Age 18.

Kidney of normal size and contour weighing 175 gms.

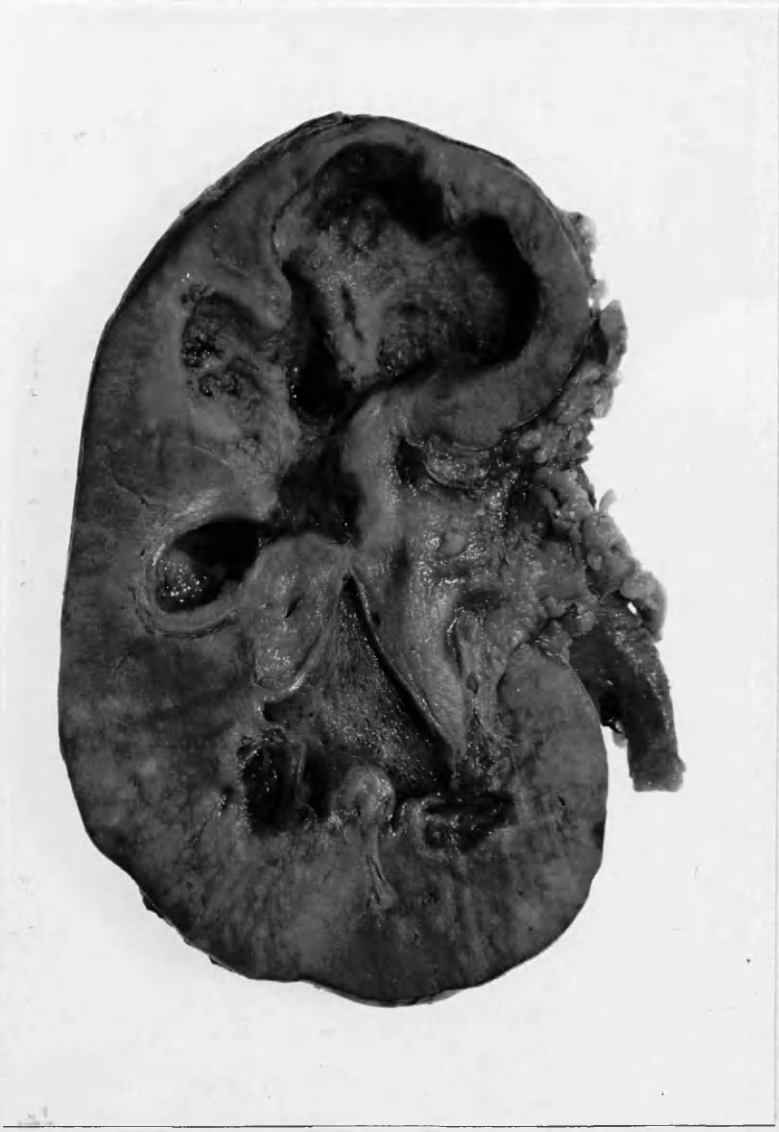


Fig. 72. Right kidney. M.F. Female. Age 18.

On cut surface the primary and secondary calyces are grossly dilated, especially in the upper half. Abscess cavities are seen in the lower pole. (The calyces contained blood stained inspissated pus.) Histologically a widespread and advanced tuberculosis.

Tubular function:-

Pre-operative 62% of average normal.

Fig. 73. Left kidney. M.M. Female. Age 44.

This kidney weighed 175 gms. Several small cysts present.

Fig. 74. Left kidney. M.M. Female. Age 44.

On cut surface the cysts are seen to be confined to the cortex. Scattered tuberculous cavities are most numerous at the poles.

Tubular function:-

Pre-operative 34% of average normal.

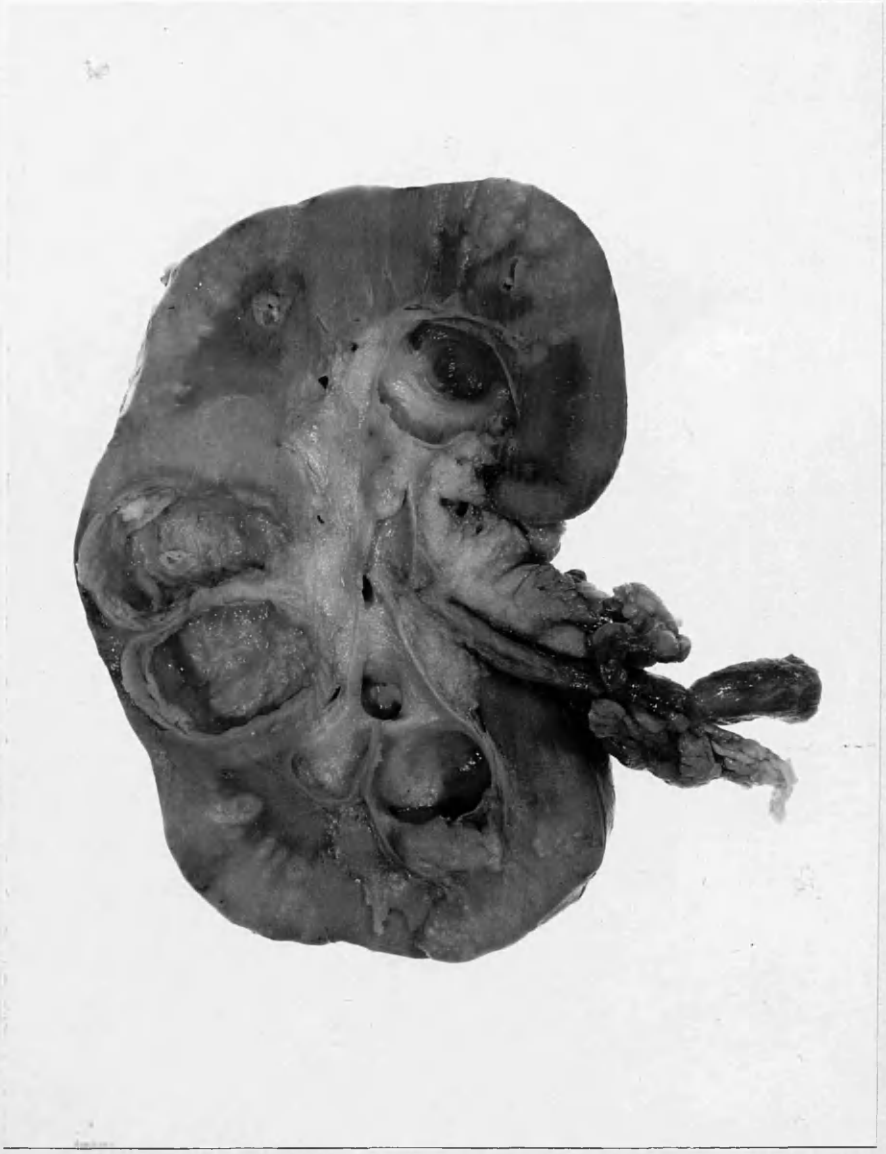


Fig. 75. Left kidney (x 4/5) H.McL. Male. Age 25.

A large lobulated kidney with a smooth surface measuring 145 x 80 x 75 mms. and weighing 425 gms.

On cut surface pelvis and all the calyces are grossly dilated and filled with caseous pus. Histologically a widespread tuberculosis.

Tubular function:-

Pre-operative 35.7% of average normal.

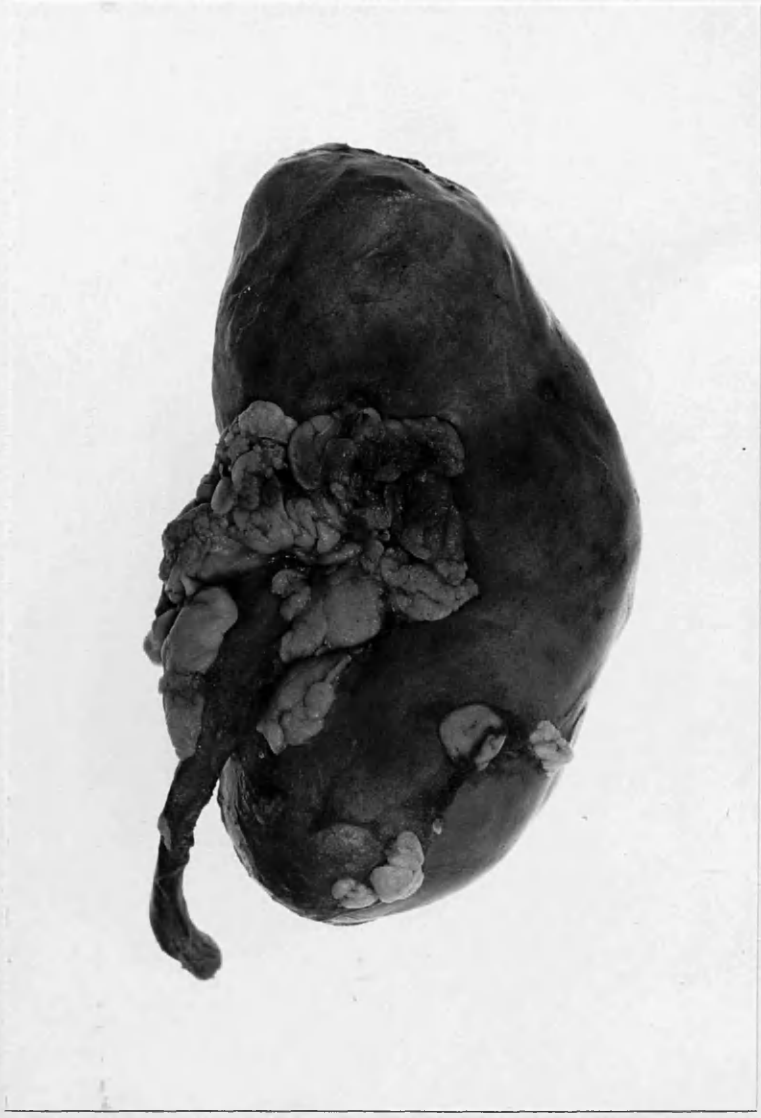


Fig. 76. Left kidney. J.McA. Male. Age 26.

Kidney of normal contour weighing 155 gms.

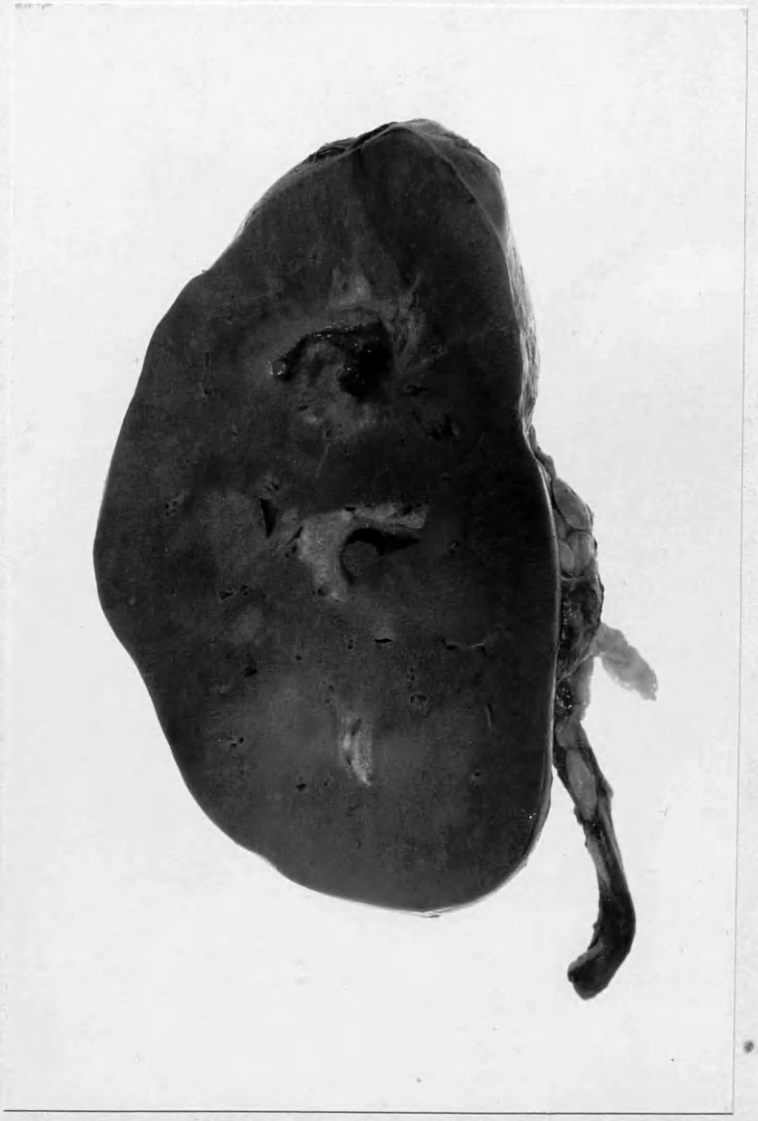


Fig. 77. Left kidney. J.McA. Male. Age 26.

On cut surface the pelvis, primary and secondary calyces are dilated and filled with caseous pus.

Histologically a widespread tuberculosis.

Tubular function:-

Pre-operative 62% of average normal.

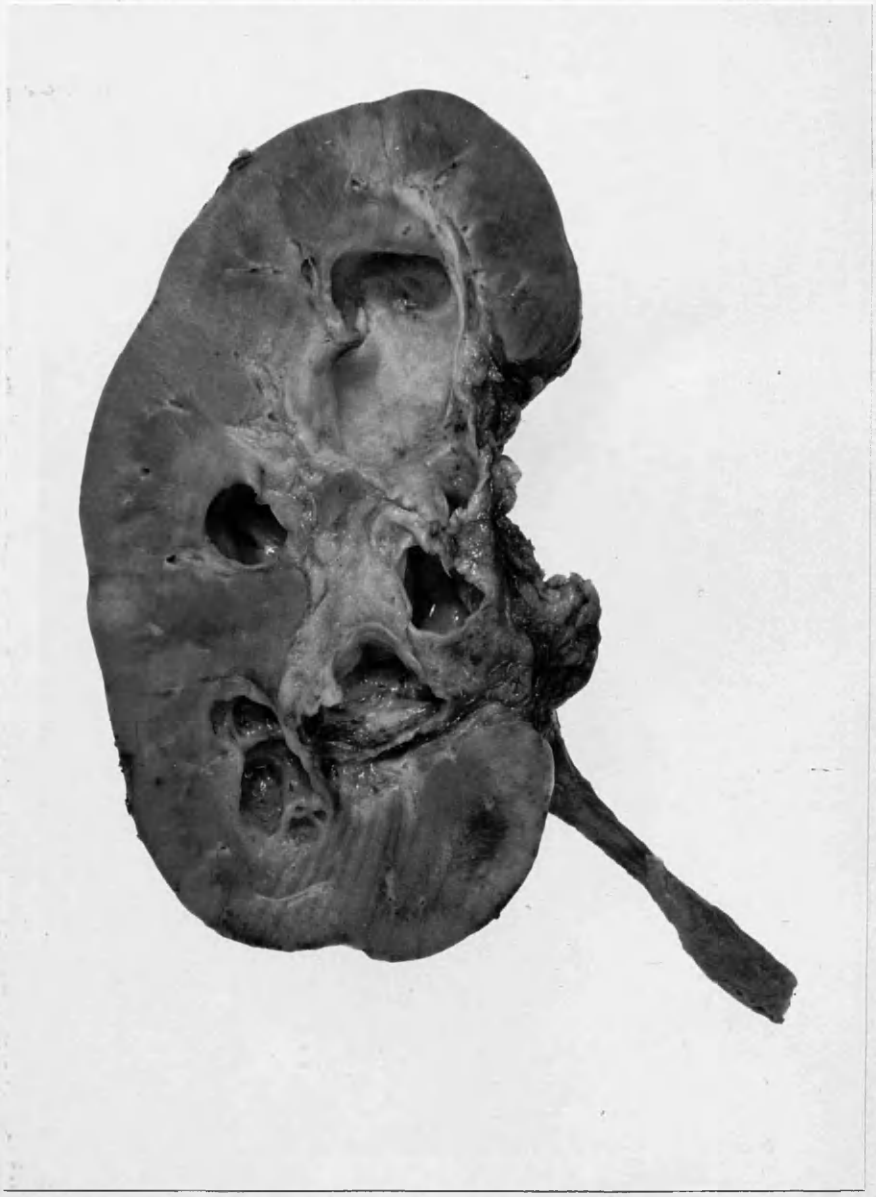


Fig. 78. Right kidney. D.O'R. Male. Age 18.

Normal shaped kidney with dilated pelvis. Weight 185 gms. On cut section the primary and secondary calyces are seen to be dilated.

Histologically an unusually widespread tuberculosis.

Tubular function:-

Pre-operative 56% of average normal.

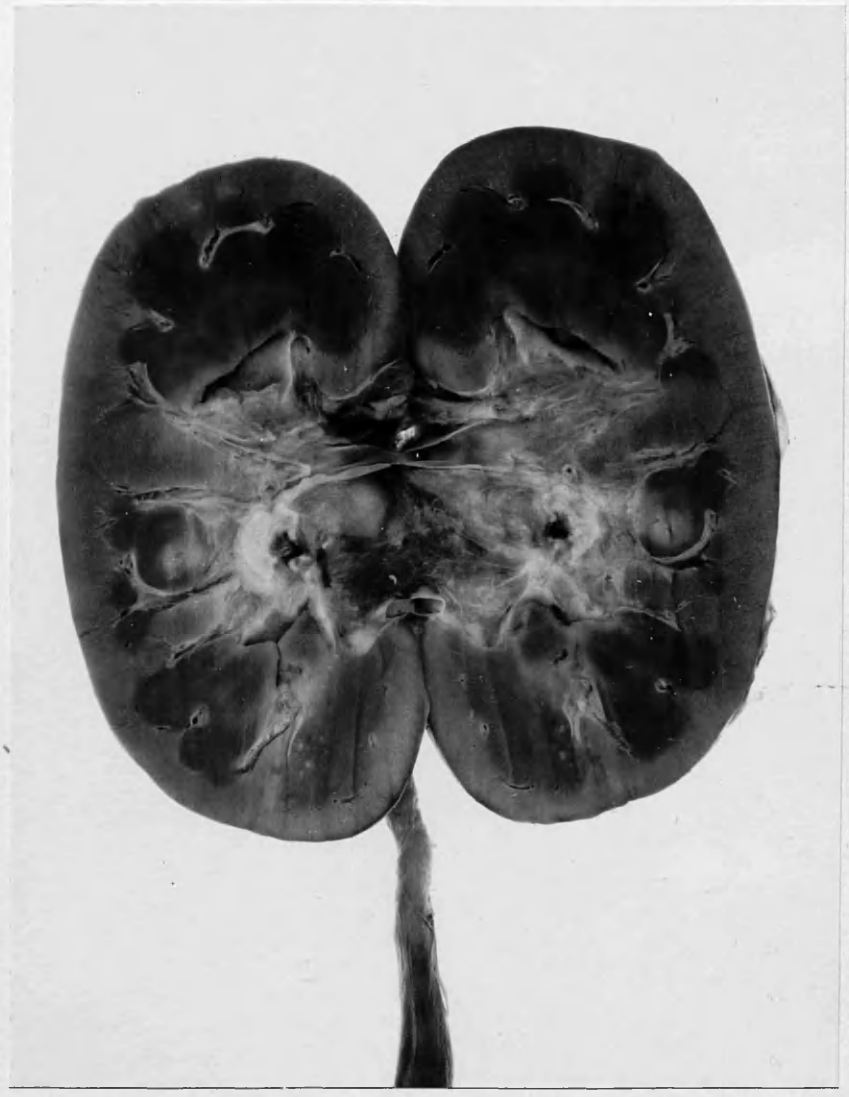


Fig. 79. Right kidney. H.P. Female. Age 42.

Kidney appeared to be normal weighing 120 gms.
On cut surface two small points of fibrosis are seen in a pyramid at the lower pole.

Histologically a healing tuberculosis.

Tubular function:-

Pre-operative 49% of average normal.

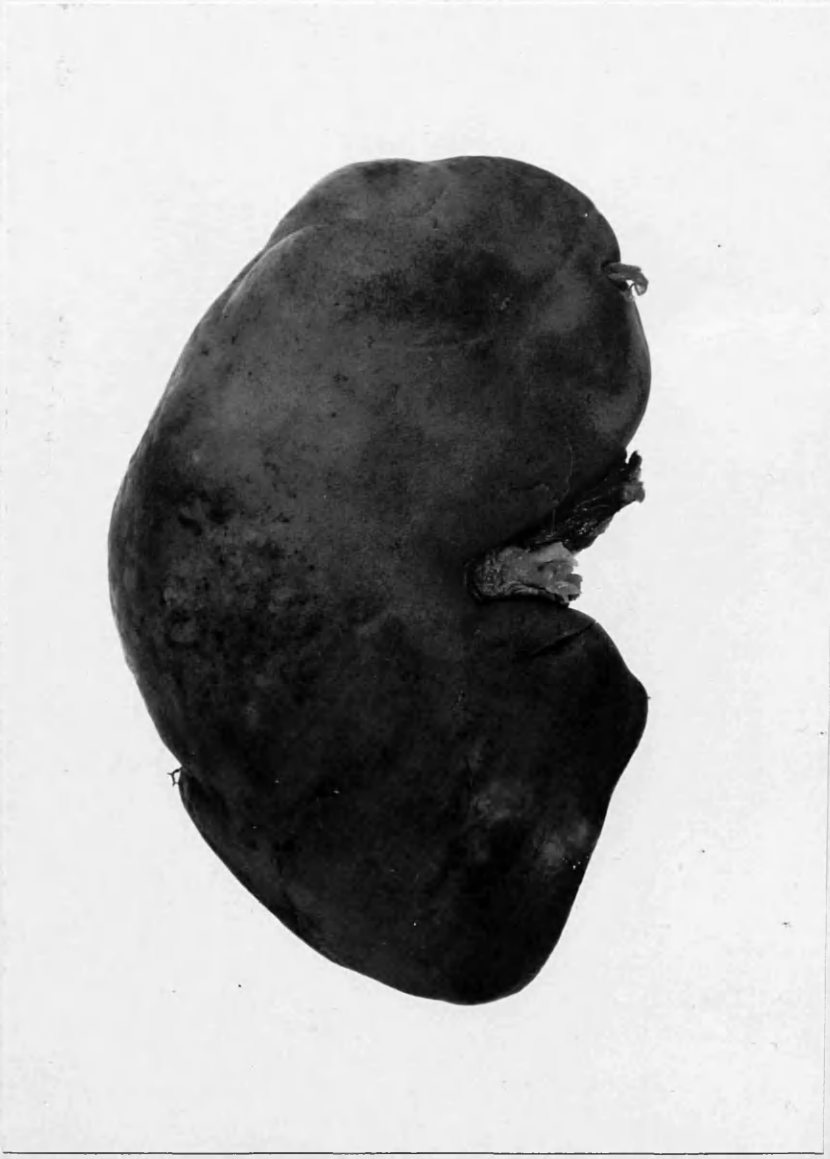


Fig. 80. Right kidney. J.P. Female. Age 23.

Normal shaped kidney measuring 120 x 70 x 40 mms. and weighing 160 gms. On the posterior aspect two groups of tubercles present at the upper pole and another larger group seen in the mid zone.

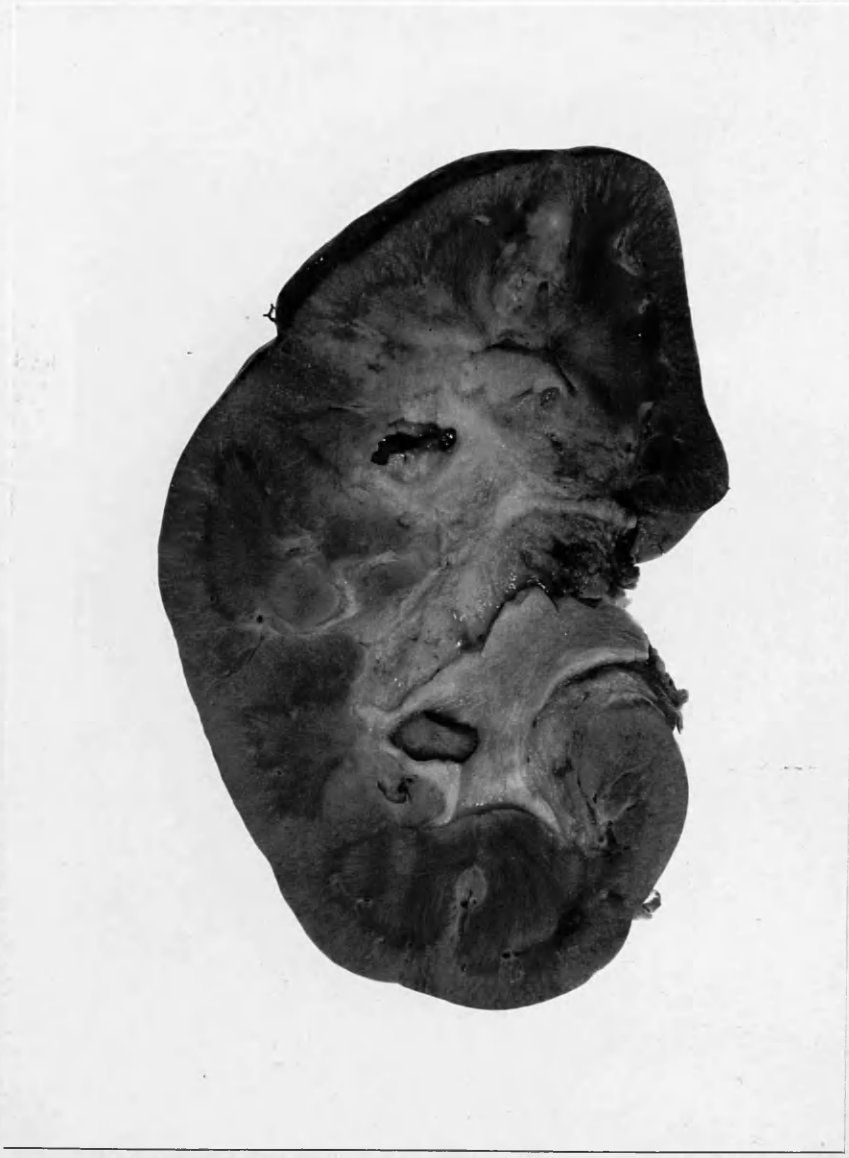


Fig. 81. Right kidney. J.P. Female. Age 23.

On the cut surface pelvis is slightly dilated and tiny coalescing tubercles are present underlying the superficial lesions.
Histologically an active but very localised renal tuberculosis.

Tubular function:-

Pre-operative 77.5% of average normal.

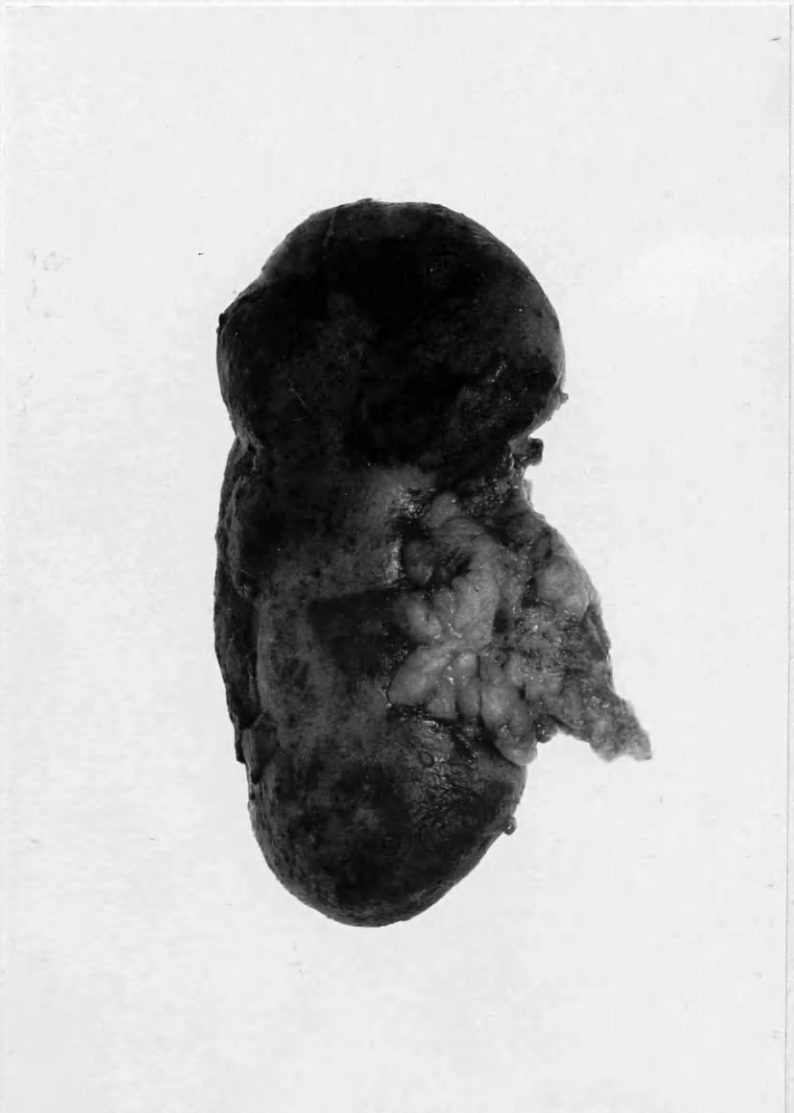


Fig. 82. Left kidney. W.S. Male. Age 62.

A small kidney of normal shape weighing 100 gms. and showing a finely granular surface with a few depressed scars.

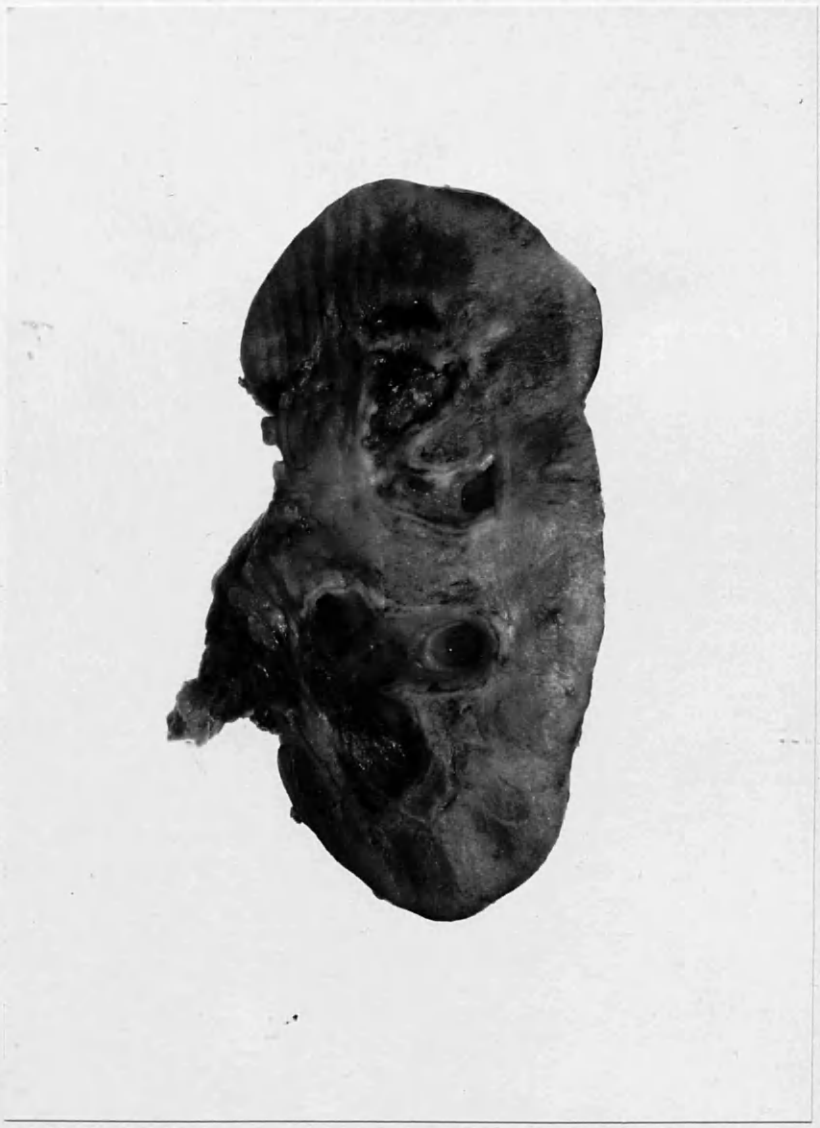


Fig. 83. Left kidney. W.S. Male. Age 62.

On cut surface the pelvis is slightly dilated and the primary and secondary calyces considerably dilated. In the upper pole large numbers of small abscesses are seen in the pyramids and the cortex.

Histologically a widespread proliferative tuberculosis.

Tubular function:-

Pre-operative 38% of average normal.

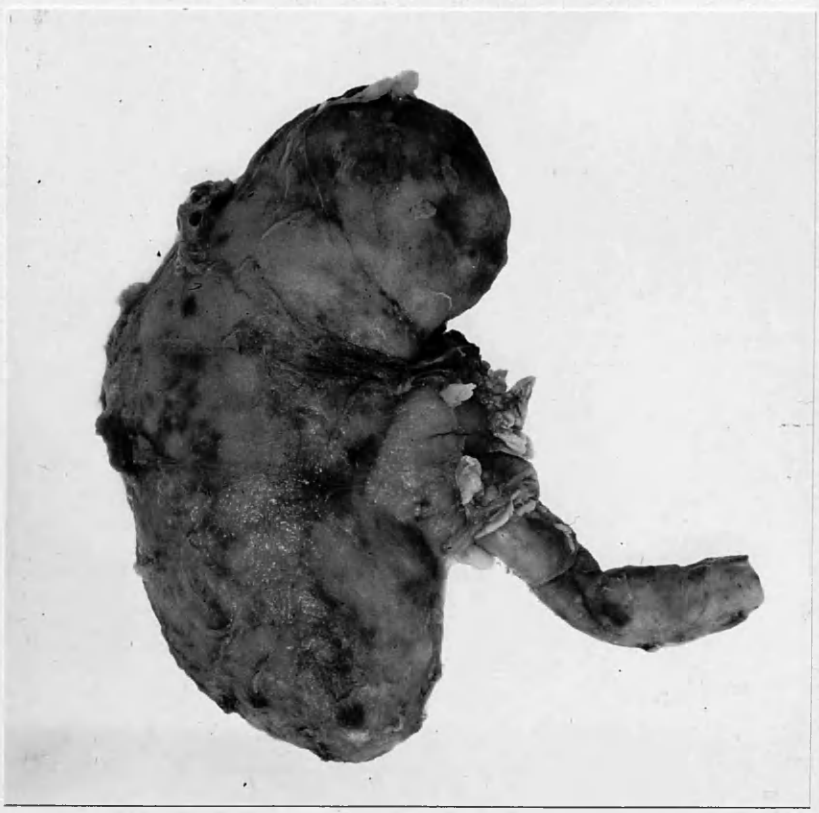


Fig. 84. Left kidney. A.T. Male. Age 32.

This is a small but unusually thick kidney weighing 170 gms. The surface shows faint foetal lobulation and contains many depressed scars but no abscesses.

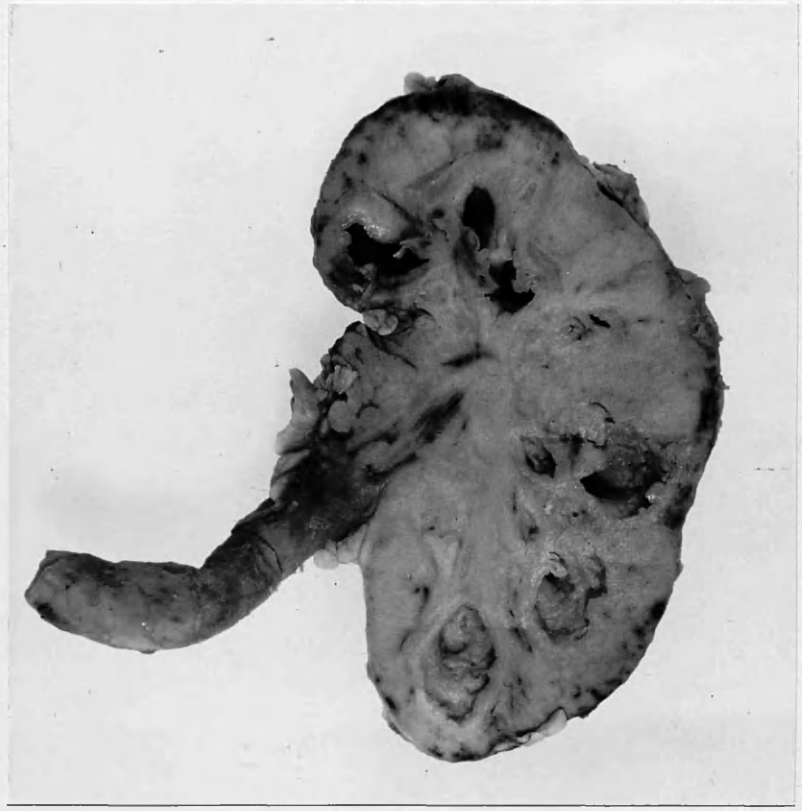


Fig. 85. Left kidney. A.T. Male. Age 32.

The cut surface reveals the primary and secondary calyces to be grossly dilated and containing caseous pus. The ureter is thickened.

Histologically an active tuberculosis.

Tubular function:-

Pre-operative 48% of average normal.

Fig. 86. Left kidney. R.Y. Male. Age 12.

A small kidney weighing 90 gms. Two isolated large abscesses are visible on the anterior surface near the lower pole and in the middle of the posterior surface. On cut surface the kidney is hydronephrotic. All the calyces and the pelvis are dilated.

Histologically a widespread caseating tuberculosis.

Tubular function:-

Pre-operative 57% of average normal.

Fig. 87. A.Bk. H. & E. x 50.

Tuberculous pyelitis with considerable round cell reaction. Caseation and fibrosis evident. Treated with Streptomycin and PAS.

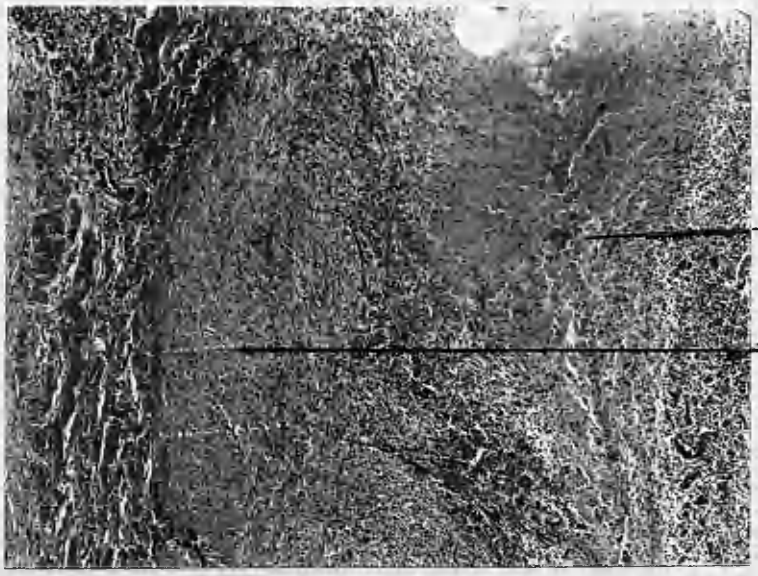


Fig. 88. A.Bk.

Ureteritis. Reactive fibrosis.
Attempt to shut off tuberculous lesion.

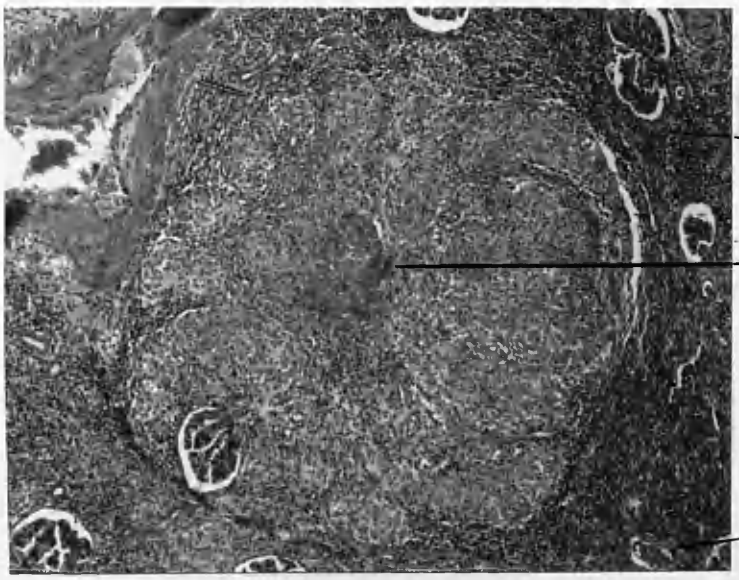


Fig. 89. V.B. H & E x 65.

Tubercles are undergoing invasion by granulation tissue.
Treated with Streptomycin and INAH.

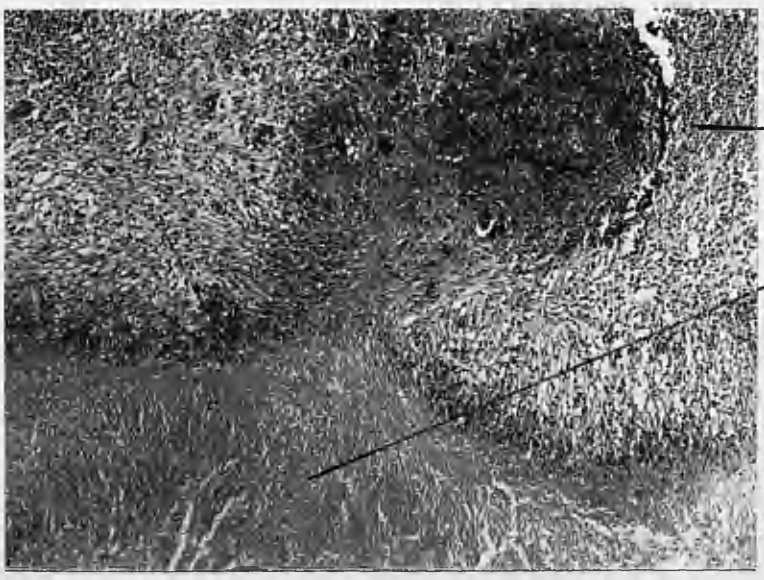


Fig. 90. M.B. H & E x 65.

Large caseous area undergoing granulation.
Treated with Streptomycin and INAH.

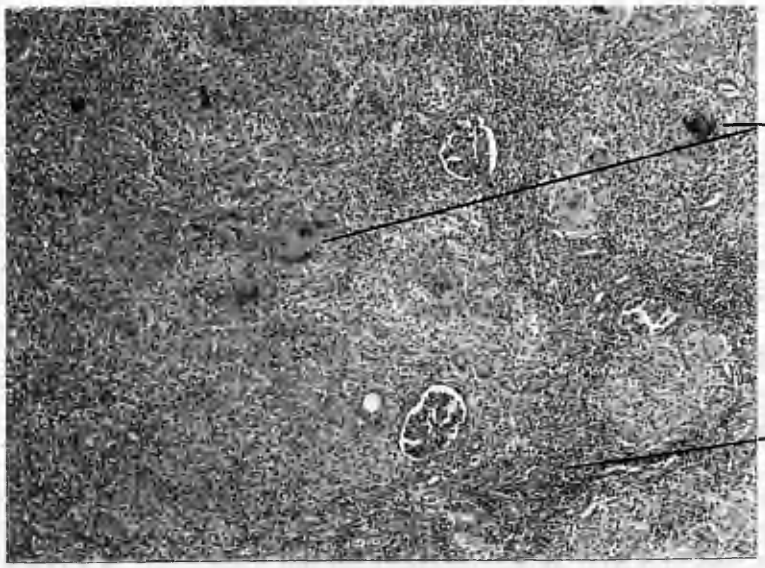


Fig. 91 . A.C. H. & E. x 65.

Several giant cell systems evident.
Considerable granulation taking place.
Treated with Streptomycin, INAH and PAS.

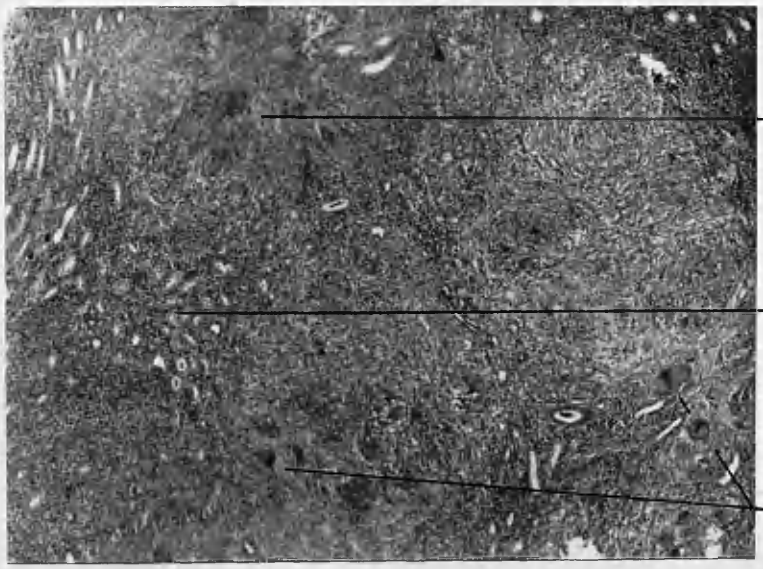


Fig. 92. M.M. M.G. x 50.

Caseating tubercles present with considerable
fibro-blastic reaction.
Nephrosclerosis evident.
Treated with Streptomycin and INAH.

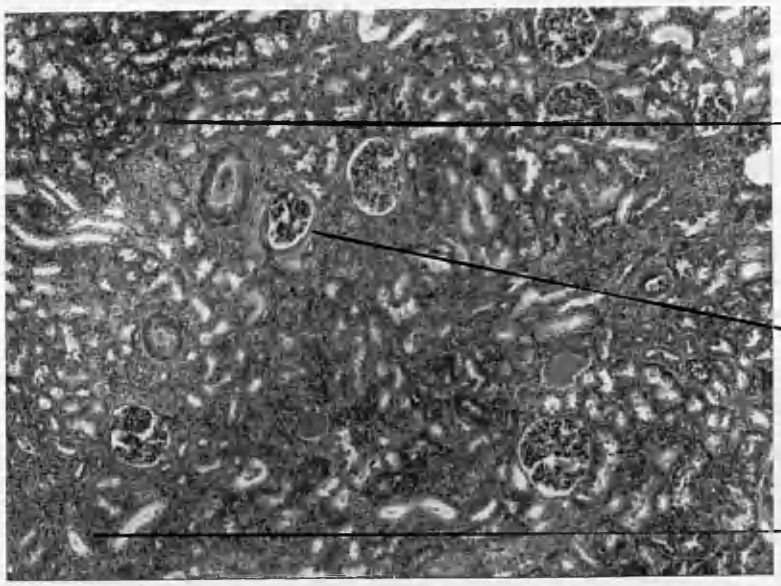


Fig. 93. M.M. M.G. x 50.

Nephrosclerosis with destruction and reactive fibrosis evident. Occasional giant cell systems.

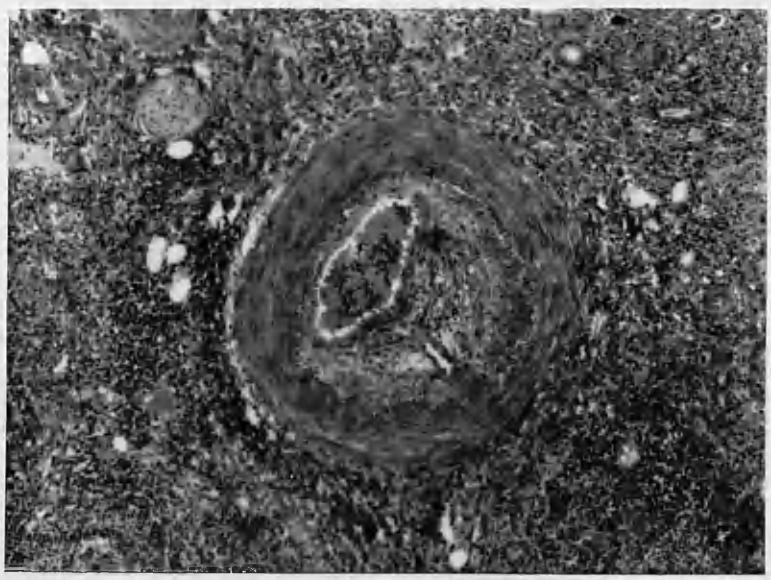


Fig. 94. M.M. M.G. x 85

Endarteritis of middle sized vessel with surrounding reactive fibrosis.

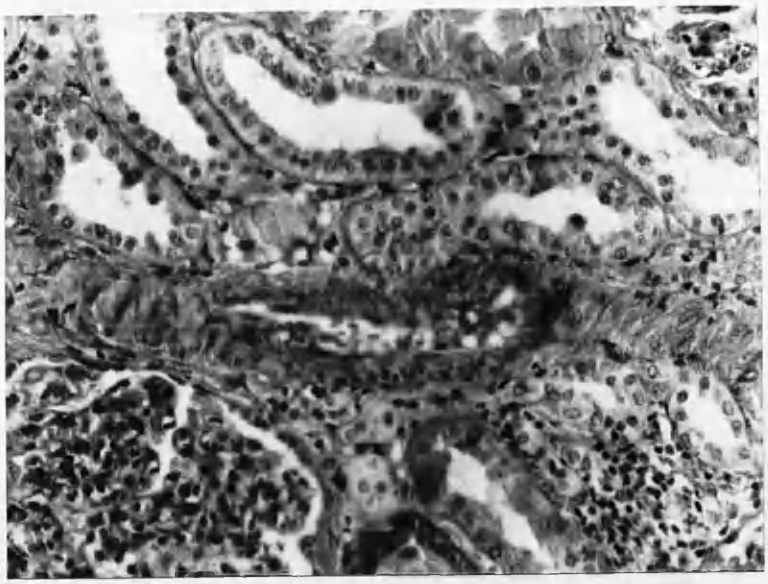


Fig. 95. M.M. M.G. x 250.

Arteriolar endarteritis.

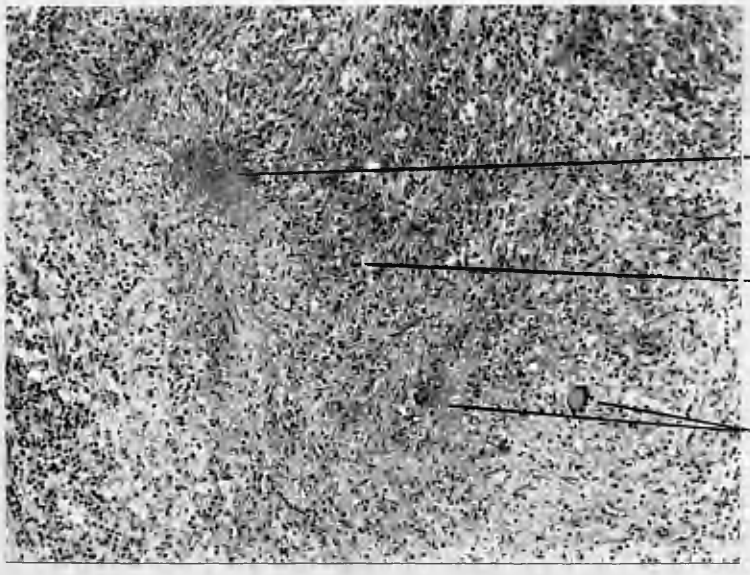


Fig. 96. H.McL. H. & E. x 110.

Granulation invading caseating tubercles.
Treated with Streptomycin and INAH.

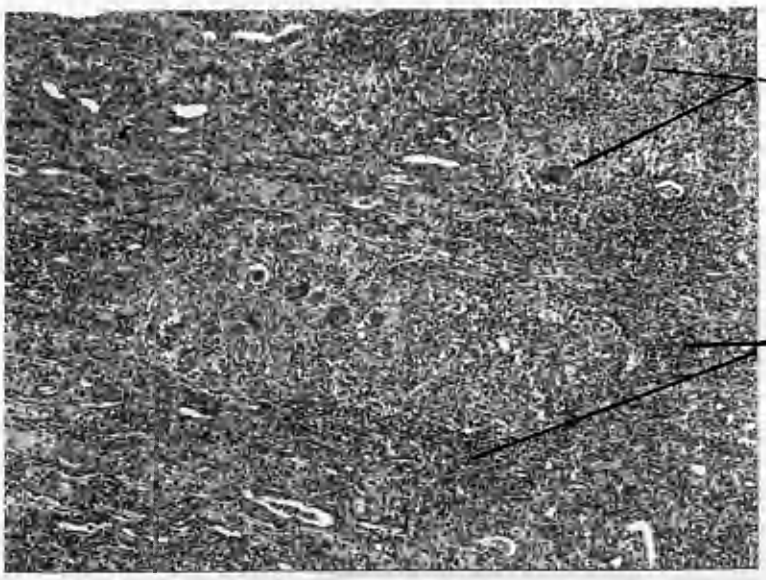


Fig. 97. M.P. H. & E. x 65.

Considerable fibrosis evident.
Multiple giant cell systems.

Treated with INAH only.

RENAL TUBERCULOSIS
UNTREATED

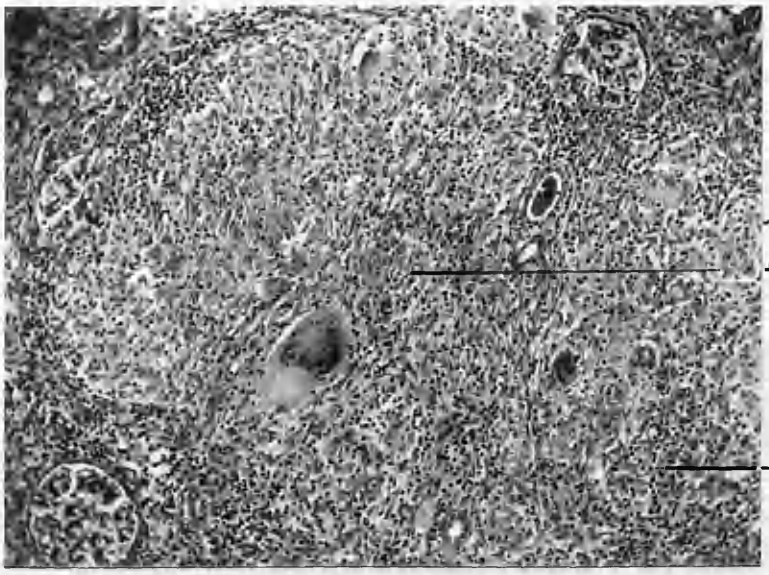


Fig. 98. S.W. H. & E. x 110.

Widespread renal tuberculosis.
There is no evidence of any healing reaction.

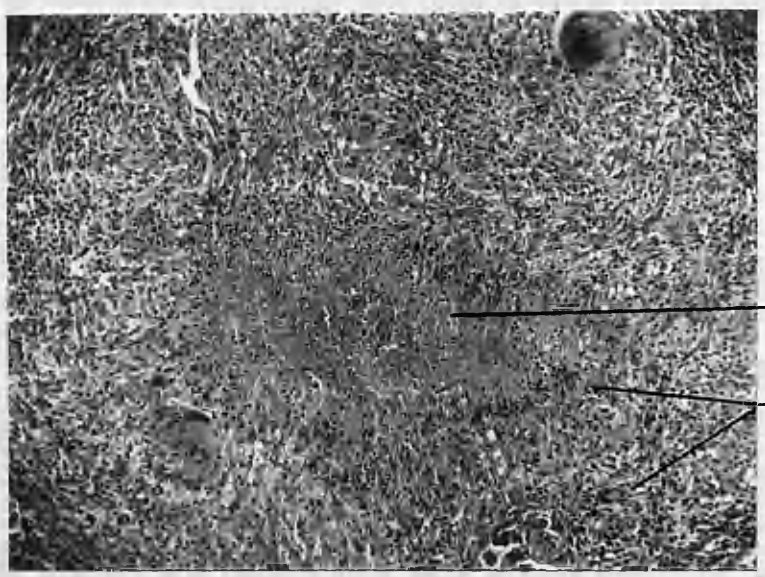


Fig. 99. S.W. H.& E. x 110.

Area of caseation evident with mild reactive fibrosis taking place.

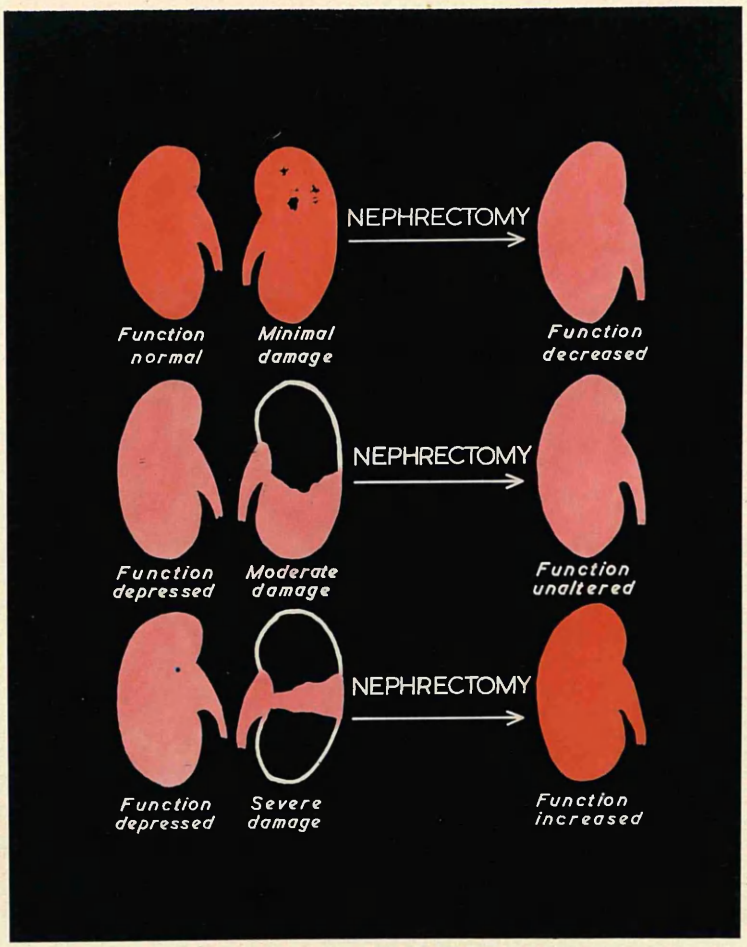


Fig. 100.

(1) When a kidney with minimal damage is removed a large amount of normally functioning renal tissue is lost. In spite of hypertrophy of the remaining kidney the loss is not entirely made good.

(2) When a tuberculous lesion of moderate severity is present in one kidney the function of the remaining kidney is depressed. Nephrectomy removes comparatively little functional tissue so that hypertrophy of the remaining kidney makes up the loss.

(3) A severely damaged kidney contains little or no functional tissue and also depresses the function of the contralateral kidney. When the diseased organ is removed the remaining one hypertrophies with the result that there is an overall gain in renal function.

TUBERCULOSIS OF KIDNEY

Effect of Nephrectomy on Hypertension

NAME	AGE	SEX	PRE-OP	POST-OP 6/12	POST-OP 4 years
M.P.	46	F.	160/100	128/84	170/106
R.S.	35	M.	140/100	120/86	130/88
W.N.	29	M.	180/100	128/96	136/84
W.S.	62	M.	210/110	130/96	160/98
A.Hc.	42	F.	210/120	164/94	158/96
M.M.	44	F.	150/100	150/90	260/140 +
E.C.	55	F.	160/104	150/76	150/84

+ Patient now deceased.

Fig. 101.

Fig. 102. M.M. Right kidney. Autopsy specimen.

Long narrow kidney measuring 130 x 60 x 35 mms. and weighing 145 gms. Upper pole replaced by large cyst 40 mms. in longest diameter. Great increase in pelvic fat.

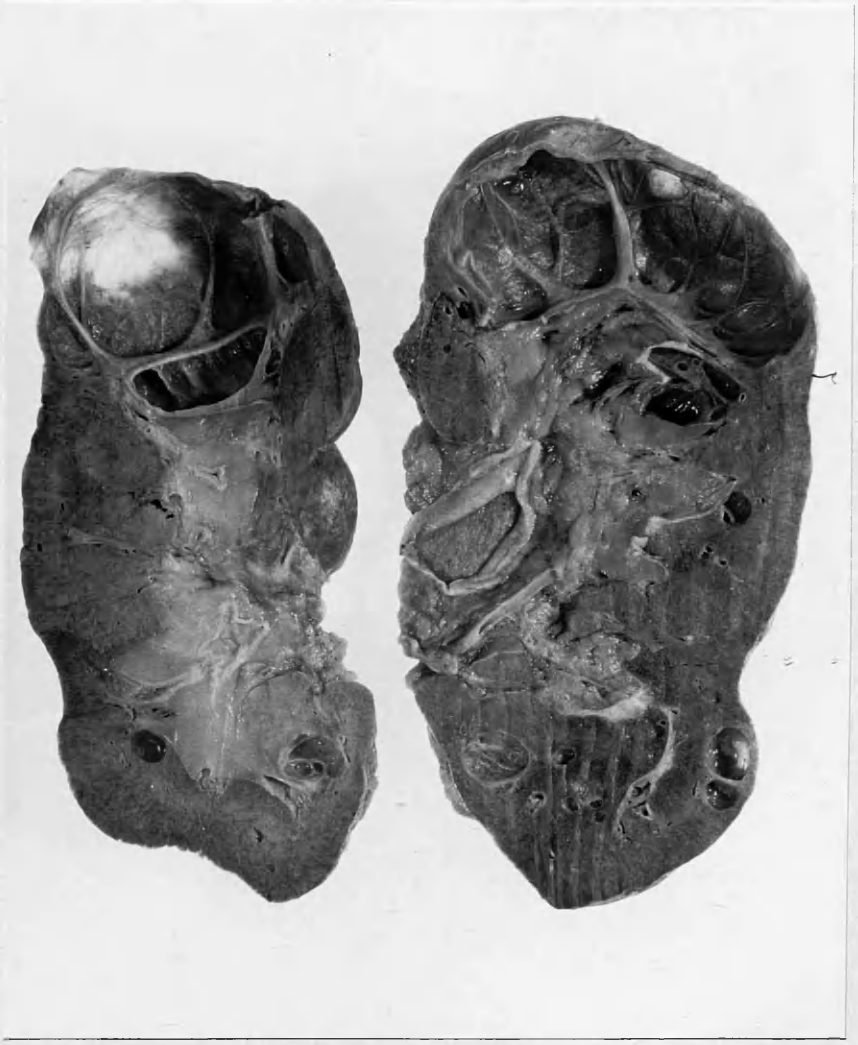


Fig. 103. Right kidney. Autopsy specimen. M.M. Female. Age 44.

On cut surface the upper pole is reduced to a narrow rind. There are multiple large and small retention cysts evident. Pelvic fat was increased.

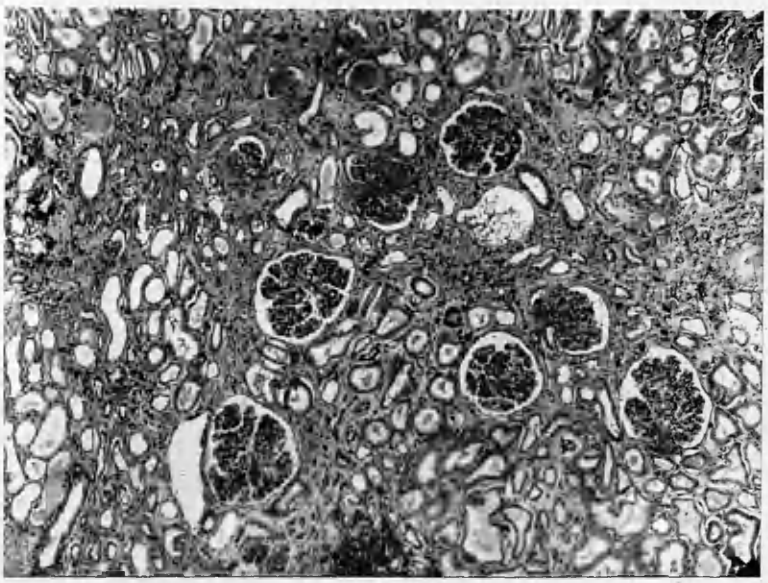


Fig. 104. M.M. M.G. x 50.

Severe hypertensive nephro-sclerosis.
There is interstitial fibrosis, glomerulo-sclerosis and considerable tubular atrophy.
In comparison with Fig. 93 the degree of nephro-sclerosis is increased.

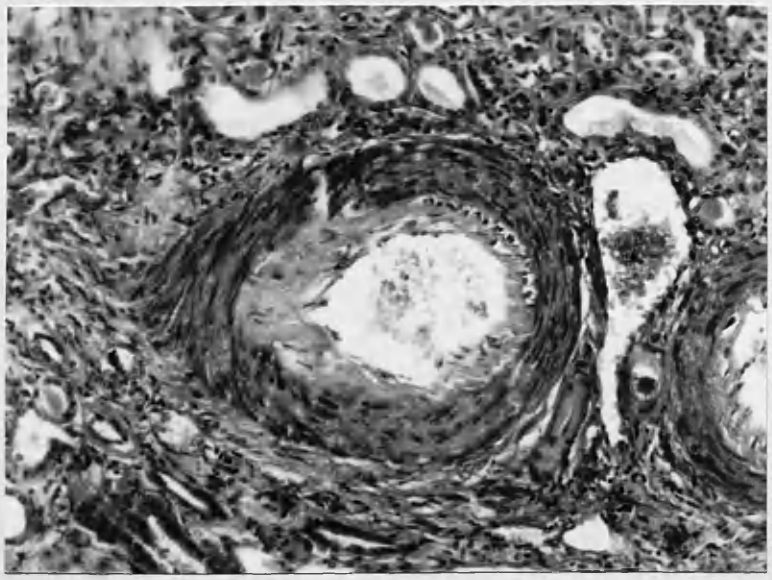


Fig. 105. M.M. M.G. x 170.

Intra-lobular artery.
There is thickening of the intima, fibrosis of the media and splitting and fragmentation of the internal elastic lamina.
No evidence of tuberculosis.

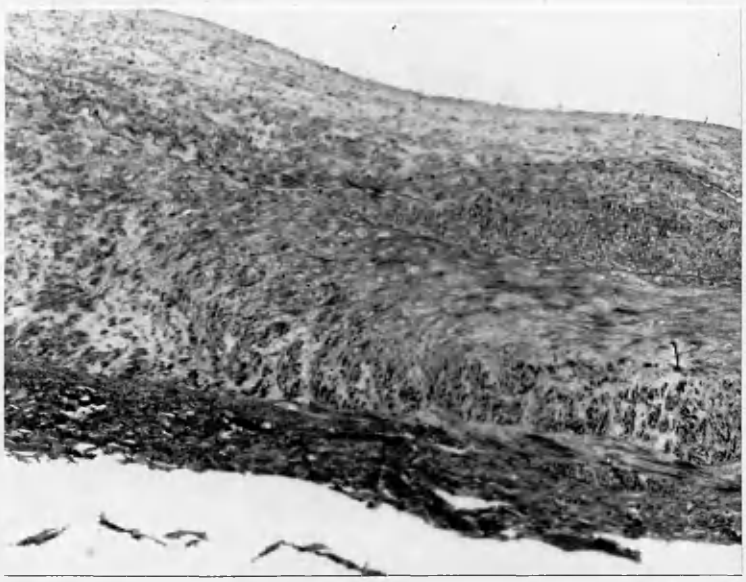


Fig. 106. M.M. M.G. x 65.

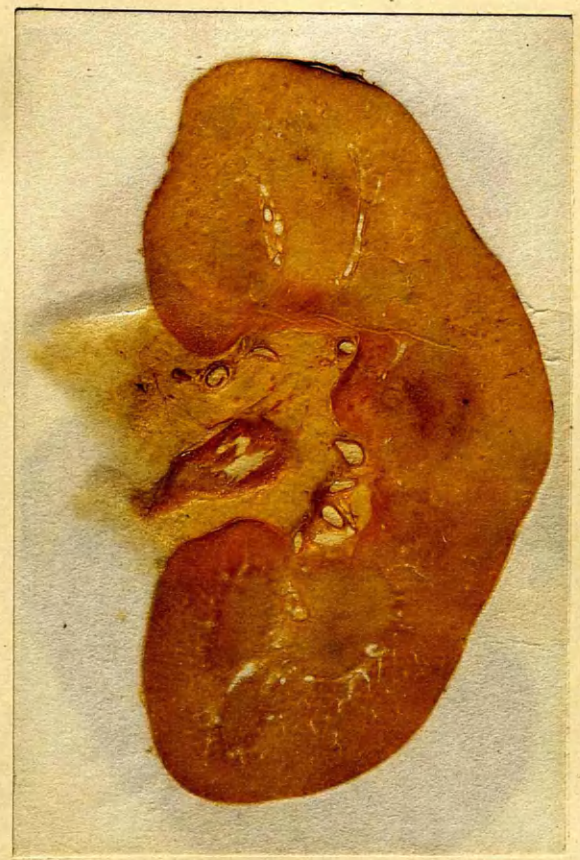
Renal artery.
Gross medial fibrosis and considerable intimal thickening. Some splitting of the internal elastic lamina.

TUBERCULOSIS OF KIDNEY

Weight before and six months after nephrectomy

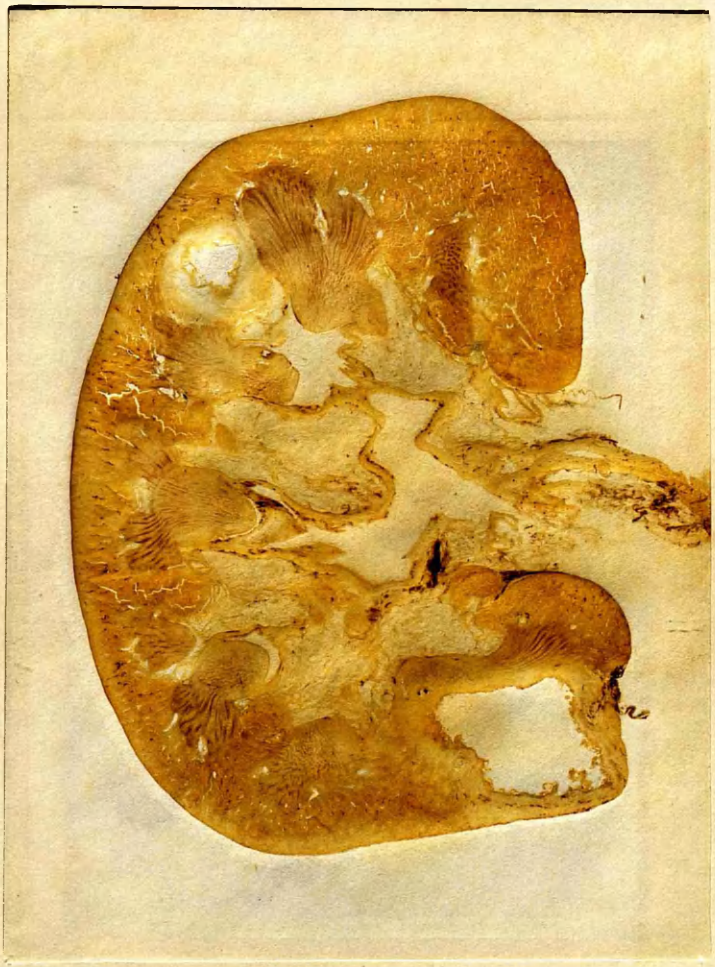
NAME.	1st Weight. St.	lbs.	2nd Weight. St.	lbs.
W.N.	10	0	11	8
J.M.	8	11	9	5
M.P.	9	0	9	0
A.C.	9	10	10	12
J.P.	8	2	9	7
R.S.	9	10	11	4
T.B.	9	11	11	3
V.B.	15	0	14	6
J.McA.	12	12	12	10
M.F.	7	0	7	6
A.F.	9	7	10	0
H.P.	8	12	9	2
A.T.	10	3	12	5
A.Bt.	9	12	10	12
W.S.	10	12	12	4
H.McL.	11	4	12	0
A.Bk.	8	2	7	6
M.M.	8	0	9	0
E.C.	9	5	10	10
R.Y.	7	0	7	5
D.O'R.	9	0	9	0
M.B.	8	4	9	2

Fig. 107.

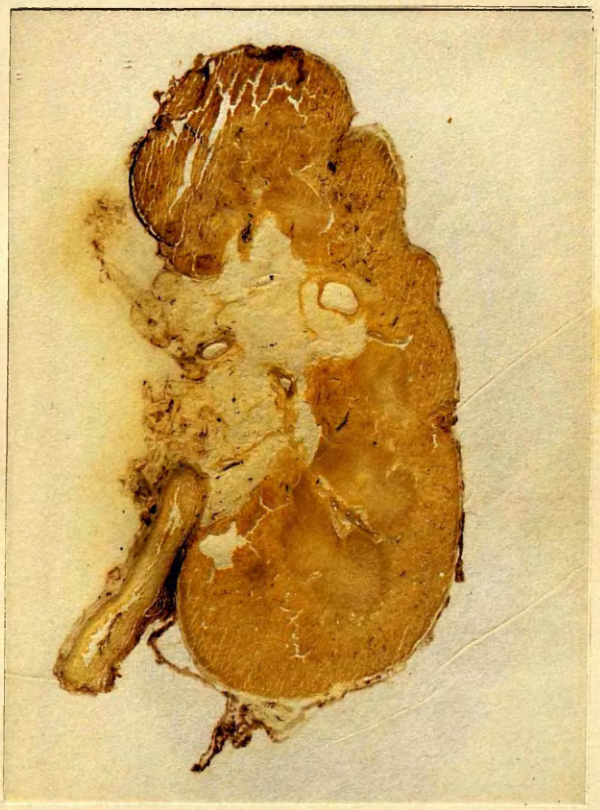


Specimen 1.

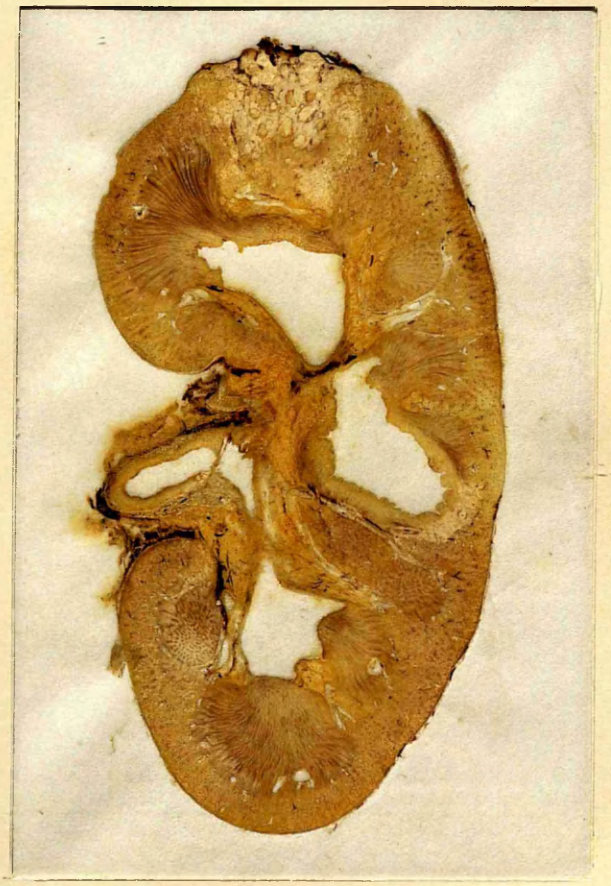
Specimen 2.



Specimen 3.



Specimen 4.



Specimen 5.