# UPPER URINARY TRACT STONE:

# CLINICAL, EXPERIMENTAL and BIOCHEMICAL STUDIES.

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# INDEX of CONTENTS

# INDEX of CONTENTS

(Continued)



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# I N T R O D U C T I O N

1. Object and Scope of the Present Investigation.

2. Historical Background.

3. Modern Research.

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# INTRODUCTION

## 1. Object and Scope of the Present Investigation.

Stone is the commonest upper urinary tract disorder for which surgical treatment is indicated and patients suffering from it constitute a substantial proportion of all urological practice. According to Burkland and Rosenberg (1955) the average urologist in the United States sees sixty new cases each year. Less common than prostatic obstruction less lethal than tumour-formation, stone is still a potent source of ill-health; and it has great social and economic importance since it occurs at an earlier age. Furthermore, there is evidence that the incidence is increasing (Hellström, 1949). Its study, therefore, has many practical applications, and it was with this thought in mind that the present investigation was commenced in 1949.

The initial object was an accurate assessment of the incidence of post-operative recurrence and the factors related to it, in the hope that this information might be applied to the prevention of recurrence. To this end the late results of operation were studied in over 500 patients, 80 per cent. by interview and re-examination.

Impressed by the high recurrence rate revealed, experimental work was then carried out in man and animals with the aim of controlling or dispersing stones already present, or of prevent recurrence in conditions, natural and artificial, highly favourable to the development of further stone.

Whenever possible, biochemical studies of calcium metabolic disorders have been performed. Opportunity has been taken during the convalescence period after operation, of appraising the blood chemistry and urinary calcium output under controlled conditions. Modified investigations of this type have been carried out in the Out Patient Department in patients known to be suffering from post-operative recurrence and in others, conservatively treated, who frequently pass stones or have bilateral calculi. Quantitative and qualitative chemical examination of a large number of kidney and ureteric stones was done. The relationship of these results to aetiology was studied.

Thus far the emphasis had been entirely on the late results of operation, and it was felt that this gave a rather unbalanced impression of the whole subject of stone. Over 500 cases treated conservatively were therefore followed to gain some insight into the natural history of the disease. This aspect has been sadly neglected in the past; yet, without it, prognosis is difficult to assess and there is no standard or "control series" by which the results of operation may be measured.

Bilateral calculi were found in 149 patients. Since they represented a more serious form of the disease, and one in which surgical judgement was often exceedingly difficult, they were studied as a group, and a tentative scheme of management devised.

The clinical part of the investigation is therefore based on a study of over 1,000 stone patients most of whom have been interviewed and re-examined. The number is large enough to allow reasonably accurate general conclusions to be made of results with, and without, operation.

The facts relating to the entire series, i.e., the findings at the initial visit, were analysed and constituted a study of the general incidence and aetiology.

The results are considered under six headings.

i. The general incidence and aetiology - facts relating to the complete series of 1,114 patients.

ii. The natural history - the results of conservative management in 568 patients.

iii. Post-operative recurrence and the late results of operation in 546 patients.

iv. The prevention and treatment of recurrence - experimental studies in man and animals.

v. The management of bilateral calculi in 149 patients.

vi. Biochemical studies.

It is regrettable, but inevitable, that investigation of a series as large as this should produce some fairly complicated statistical information. Whenever possible, the fuller tables have been relegated to the Appendix, simplified versions being incorporated in the text. With suitable precautions against bias, consideration of these large numbers enables us to reach conclusions which might, with a smaller series, be regarded as being of doubtful validity.

These clinical, experimental and biochemical studies have occupied eight years. The patients investigated have been under the care of Mr. T. L. Chapman, Consultant Urologist to the Victoria Infirmary, Glasgow, Hairmyres Hospital, Lanarkshire and Ballochmyle Hospital, Ayrshire. Without his enthusiastic encouragement to undertake this work, his generosity in affording every facility for pursuing it, and his tolerance when the necessary investigations threatened to swamp his Department, it is doubtful if this complex study could have been undertaken. Since their inception at various times during the last twenty years, the urological units mentioned have been under Mr. Chapman's care, so that uniformity in the pre-operative investigation, surgical treatment and follow-up is assured.

## 2. Historical Background.

Much of the colourful and romantic history which invests urinary stone refers to the condition as it affects the bladder. The fascinating activities of the mediaeval itinerant lithotritists, who flourished on the shores of the Mediterranean, are well known and have become part of the fabric of medical history. Their skilful manipulations are to be admired even by modern standards; and in ancient times they must, to the onlooker, have bordered on magic itself. There is little doubt that these ancestors of the modern urologist kept alight the flame of major surgery when the forces of ignorance and superstition threatened to extinguish it.

In striking contrast, much less detail is available of the history of kidney stone; yet the disease has been known from the very earliest times. The most obvious reason for this lies in the fact that major surgical intervention was considered impracticable unless pus was present in the kidney. Treatment, therefore, consisted of diuretics and sedatives, and what could not be cured had to be borne. Generally speaking, the condition was regarded as non-surgical, and interest in it lapsed for several centuries.

The earliest example of kidney stone was discovered by the Egyptological Expedition of the University of California (Shattock, 1905) and was assigned to the Second Dynasty (4,400 B.C.). Four stones composed of an admixture of calcium carbonate, calcium phosphate, and calcium oxalate were found lying beside the lumbar vertebrae and were considered to be of renal origin.

The first of the four diseases of the kidney described by Hippocrates was almost certainly stone (the others perhaps being tuberculosis, tumour and pyonephrosis). The only indication for operation was the presence of pus, for which, incision, without removal of the stone was recommended. His disciples took the oath "neither will I cut them that have stone, but will leave this operation to those who are accustomed to perform it".

In the first century of the Christian Era, Rufus of Ephesus described a form of nephritis, probably calculous in origin. At that time stone was considered to be the principal cause of renal inflammation.

The ignorance of the Middle Ages is characterised by the well known and traditional figure of the uroscopist holding up to the light a beaker of urine and diagnosing by sight and smell the nature of the renal pathology.

The first recorded account of surgical removal of a kidney stone is given by Ambroise Paré in 1474, although Joly (1929) doubted its authenticity. An archer of Meudon had been condemned to death for robbing a church. He was known to be suffering from stone in the kidney and was offered a remission of sentence providing he would undergo operation. In fairy-tale fashion two stones were removed, he was cured in fifteen days, and was set free with a gift of money; "thus have kindly kings protected the arts and sciences". (Paré).

The first authentic stone operation was performed in 1633. The surgeon was Dominique Marchettis, and the patient was an Englishman, aptly named Hobson. Owing to severe bleeding when the renal substance was incised, the operation was performed in two stages. Three stones were removed. Shortly afterwards he passed a stone which had obviously been overlooked at operation. Ten years later, urine still escaped through a loin fistula.

Few stones have achieved the publicity enjoyed by those of Samuel Pepys. In 1657 Charles Bernard skilfully removed a two ounce uric acid stone from Pepys' bladder. For more than 30 years thereafter Pepys enjoyed good health. A few years before his death the suprapubic wound broke down and was healed only with some difficulty. In the interval he had passed two small stones. Autopsy showed advanced calculous pyonephrosis, the kidney having been completely destroyed. In the centre of this bag of pus lay a nest of seven uric acid stones linked together and weighing 4½ ounces. This condition may well have existed for 30 years or more - an interesting contribution to the study of the natural history of the disease. In spite of it, Pepys lived to the age of 71, with remarkably few symptoms referable to his upper urinary tract.

Two other fragments of history refer to post-mortem examinations. Ambroise Paré tells of the man who suffered a severe penetrating thoracic wound, followed by the passage of urine by mouth two days before his death. He was found to have a tightly impacted ureteric stone with great dilatation of the ureter above it. In 1707, Pope Innocent XI was shown to have bilateral branched calculi, functioning renal tissue being reduced to a mere shell.

To Lafitte in the 18th-century goes the credit for performing the first successful and orthodox nephrolithotomy. Once again, on account of the haemorrhage encountered on incising the kidney, the operation was performed in two stages; the first was the incision, and 22 days later two stones were removed, with complete recovery and healing.

With the advent of anaesthesia and antiseptic surgery, technical progress advanced rapidly. The first nephrectomy was performed by Gustav Simon in 1869, the first nephrolithotomy (as we know it today) by Morris in 1880, the first pyelolithotomy by Beck in 1881, and the first x-ray diagnosis of stone by McIntyre in 1896.

Apart from intravenous pyelography, most of the techniques for the diagnosis, localisation and removal of calculi were approaching perfection by 1917.

A rough assessment of the chemical nature of stone had been made and the fact noted that infection was often present. Work on the crystalloids (Ebstein & Nicolaier, 1891) and the colloids (Lichtwitz, 1919) was under way, but few scientific theories regarding causation or the stone-forming mechanism were propounded or vigorously upheld.

At this stage our reasoning as to the nature of stone was largely hypothetical and was based on such concepts as the hardness of water, the so-called "stone diathesis" or stone-forming "catarrh", and the theories of crystalloid hyperexcretion. The gap between the haphazard approach of the past and the modern intensive mood of enquiry was bridged by Swift Joly whose book on "Stone & Calculous Disease of the Urinary Organs" remains the great authority on the subject.

## 3. Modern Research.

The quest for the aetiology of stone has enjoyed the attention of a host of research workers since the time of Joly. It is fitting, therefore, that his statement in Ramon Guiteras lecture in 1934 should be recorded here: "Calculous disease has not changed in its salient features throughout the history of medicine. It presents the same train of symptoms, the same pathological changes and the same complications now that it did in the earliest times. It is, therefore, legitimate to assume that its aetiology has remained unchanged".

The research work performed in the 25 years between 1917 and 1942 has been summarised by Keyser (1943) who concludes; "we are much confused and bewildered. In the ultimate it seems that no two workers, chemist, pathologist or clinician are in even approximate agreement". It seems only fair to echo this sentiment today in spite of the volume of work performed since 1943.

In general it appears that two factors are essential for stone-formation. The first, and probably the more important, is some form of trauma (toxic, infective or vascular) to the epithelium overlying the renal papilla. The second factor, the precipitation of stone-forming crystals in a colloidal matrix, then comes into operation.

The Papillary Lesion. Randall's conception of the sub-epithelial calcium plaque in 1932, shone a new and powerful light on the pathogenesis of calculous disease. The work of Rosenow & Meisser (1922) and Hellström (1938) on the experimental production of infective stone, and McCarrison's observations in India (1931) on vitamin A lack, fell into line very naturally with Randall's theories. The only perplexing point that remained was: what, in the absence of vitamin A lack or of inflammatory disease, caused the plaque? This, as yet, remains unanswered.

Precipitation of Stone-forming Crystals : Calcium Metabolism.

Meyer (1927) made a great contribution by determining the conditions which govern the precipitation of stone-forming substances in the urine and these physicochemical principles have recently been emphasised by Prien (1955).

Once it was realised that 95 per cent. of urinary calculi were calcium-containing and that phosphate, oxalate and uric acid metabolism were of secondary importance, the closest study was made of calcium metabolism. Hammarsten (1937) demonstrated the importance of magnesium and vitamins A & D in keeping calcium salts in solution. The work of Albright and his co-workers in Boston (1948) on hyperparathyroidism is well known and further contributions have come from Stockholm (Hellstrom, 1955) and Leeds (Pyrah, 1955). Excessive urinary excretion of calcium has been studied by Flocks (1939). It is natural that the layman's interest should be in the direction of "dissolving stones" and Suby (1944) produced a solution containing citric acid (based on Shorr's work, 1945), and magnesium (based on Hammarsten) for this purpose. Higgins (1932) has in fact managed to produce and dissolve (by dietary means alone) calcium phosphate stones formed after a low vitamin diet in rats.

Recent Trends.

(a) Microradiographic Techniques in Stone Analysis.

Dissatisfaction with the more traditional biochemical techniques of stone analysis led to improved methods employing x-ray microdiffraction (Prien, 1949; Lagergren, 1956). From crystallography a new understanding of the nature of the crystals is growing.

(b) Carr (1954) has also employed painstaking radiographic methods in studying papillary pathology. From these he concluded that many small stones previously thought to be formed on a Randall plaque are, in fact, lodged in a dilated or blocked lymphatic which he called a "pouch".

(c) The biocolloids of urine are the latest object of exhaustive research. For long their importance has been appreciated but their precise chemical nature has eluded definition, short of the fact that they are probably acid mucopolysaccharides. The work of Butt and his associates (1952) on hyaluronidase therapy; of Boyce and his co-workers (1954) on the ion-binding properties of mucoproteins; of Baker & Sison (1954) on selective staining techniques to demonstrate altered itssue mucopolysaccharides in renal calculous disease; and of Ravich & Ravich (1954) on surface tension measurements, has rekindled interest in the subject. Herein may lie the basic cause of stone. In health the colloids are "protective"; in stone disease, having undergone some alteration, they form the cement or "skeleton" of the stone, without which it is doubtful if stone-formation can occur.

One feature of modern research which quickly becomes apparent is the need for teamwork. Intimate understanding of the problems involved in upper urinary tract stone presumes a knowledge of colloid chemistry, crystallography, calcium metabolism, renal pathology, and radiology, and this is obviously an impossible accomplishment for the individual. The team therefore has a clinician as its director and consists of biophysicist, biochemist, radiologist and pathologist.

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# FOREWORD

Sheer weight of numbers has necessitated the transfer of the Figures, Diagrams and photographed Tables to Volume II, in company with the Appendix. To minimise inconvenience they are arranged in exactly the sequence described in the text. It should therefore be possible to proceed from one Table or Figure to the next in conjunction with the reading matter in Volume I.

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## PART I.

# THE GENERAL INCIDENCE, DIAGNOSTIC FINDINGS AND POSSIBLE AETIOLOGICAL FACTORS IN 1,114 CASES OF UPPER URINARY TRACT STONE

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PART I.

## GENERAL INCIDENCE, DIAGNOSTIC FINDINGS AND POSSIBLE AETIOLOGICAL FACTORS

The results of the routine investigations performed before operation constitute the "General Incidence and Diagnostic Findings". Predisposing causes revealed by special questioning or examination are grouped under the heading of "Possible Aetiological Factors".

### Section I. Source of Material and Method of Study.

Source of Material.

The total series of 1,114 patients was derived from three sources (Table I):-

(I) The Urological Department (U.D.Series), 891 Patients.

This group is the backbone of the whole investigation. The patients in question have been under the care of one urologist, or his junior colleagues, so that uniformity has been maintained in respect of diagnostic criteria, indications for operation, and follow-up technique. The patients (891) constitute 80 per cent. of the complete series (1,114); and those undergoing operation (323) represent 60 per cent. of the operation series of 546 (Table I).

(2) The Victoria Infirmary General Surgeons (V.I.Surg.Series) 161 Patients.

The senior surgeons of the Victoria Infirmary kindly gave permission for review of their cases, all treated by operation. Some could not be traced, but valuable information has been gained from studying some results 30 or more years after operation. They represent 14.5 per cent. of the total series, or 30 per cent. of all patients treated by operation.

(3) Other Surgeons. (Others), 62 Patients.

Inevitably, with the shift of population over the years, a Urological Department collects cases treated by operation elsewhere. These patients have been referred only when symptoms were severe enough to take them to their family doctors. They therefore introduce a considerable element of bias if studied in terms of post-operative recurrence, and their main value is that they provide general information about age, sex, side, etc.

Method of Study.

(1) Extraction of Information from Case Records.

The physical task of handling and analysing the mass of information relating to over 1,000 patients was lightened by constructing for each a transcription card. On one side of this information already available in the case records was summarised under the following headings:-

(a) General: date of birth, sex, occupation, date when first seen, duration and nature of symptoms.

(b) Initial Examination: clinical, urine, x-ray and biochemistry.

(c) Operation and post-operative course.

(d) Immediate post-operative examination with special reference to a check x-ray (to exclude residual stones), urine examination, and biochemical studies.

(e) Follow-up information: the results of earlier reviews.

(f) Date and cause of deaths, if known.

(2) Follow-Up.

The ideal investigation attempts to trace, interview, and re-examine all patients still alive, and to ascertain the date and cause of death in the case of those who have died since last seen. Strenuous efforts were made to attain this ideal.

Patients were routinely sent an introductory questionnaire with a stamped addressed label enclosed. If they replied they were asked to attend for interview. If there was no reply the questionnaire was repeated; and if there was still no reply, or the envelope was returned marked "deceased" or "gone away", the family doctor was written for information regarding the date and cause of death, or their latest address and present condition. Many patients who had moved to new houses were traced after a visit by the Social Service Department to their old address.

In spite of these measures, Table II shows how far short of perfection this follow-up has fallen. For simplicity, three categories have been designated:-

(a) Interviewed. (70 per cent.) Fortunately this was possible in 95 per cent. of the Urological department series, which provides the main material for study. The 778 patients have been personally interviewed and examined.

(b) Replied by Questionnaire. (20 per cent.) All indirect methods of obtaining information have been included, viz., questionnaire reply by patients who stated that they were unwilling or unfit to attend for interview; letters from family doctors or relatives; and Social Service Department reports. Helpful though such knowledge may be, firm conclusions can rarely be drawn from it in the 213 patients concerned.

(c) Untraced. (10 per cent.) Prolonged search failed to trace 123 patients, regarding whom only the information from the case record is available for analysis.

(3) Interview.

The 778 patients personally interviewed were thoroughly questioned on the following lines:-

(a) Where there was some doubt in the matter, they were asked to confirm that the information transcribed from the case record was accurate.

(b) Their progress since they were last seen was determined in terms of work record, general health, and urological symptoms such as colic, haematuria, frequency, pyuria, or the passage of stones.

(c) A painstaking effort was made to assess any predisposing causes of stone-formation. They were therefore asked about:-

1. The nature of their occupation.

2. Any family history of stone.

3. Periods spent in hot climates.
4. Pregnancies and associated renal disease.
5. Preceding renal disease (pyelitis, nephritis, or scarlet fever with renal complications).
6. Peptic ulcers, especially when alkali therapy had been prolonged.
7. Prolonged recumbency due to bone and joint disorders.
8. Dietary habits (particularly for sources of oxalate).
9. Night vision (as a test of Vitamin A intake).
10. Medicines regularly prescribed.
11. Any personal theories of the patient regarding aetiology.

(4) Investigation.

All 778 patients interviewed had bacteriological and cytological examination of the urine, and a plain film of the urinary tract carried out. When doubtful opacities or definite stones were seen on this straight x-ray plate, selective use was made of intravenous and retrograde pyelography.

Those who had recurrence or had passed stones frequently were studied biochemically. Serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, plasma proteins and blood urea were estimated. A rough impression of urinary calcium output was obtained, using the Sulkowitch test, and after admission more detailed studies were made of urinary calcium excretion after six days on a fixed low calcium intake. They were asked to provide stones whenever possible. Many brought crumbling fragments of stone, lovingly preserved since the date of operation.

(5) Causes of Death.

In Table II it will be seen that conditions associated with the urinary tract have accounted for the deaths of 39 patients, or less than 4 per cent. of the total series of 1,114. Upper urinary tract stone can therefore scarcely be regarded as one of the more lethal conditions affecting man. In all, 135 patients died at some time during the period of observation, but 96 were due to extra-urinary causes. Of the 39 urinary deaths, 23 were post-operative, and 16 were due to renal failure not immediately associated with operation.

The findings after interview and re-examination of these 778 patients were entered on the reverse of the original transcription card, which was then ready for analysis.

## Section II. General Incidence and Diagnostic Findings.

Although the results detailed in this section refer to the complete series of 1,114 cases, information was not always available for the full total. When this is so, the available total is stated.

The term "operation" indicates that an open surgical procedure has been used. Likewise, "no operation" means that no open operation has been carried out. Lower ureteric stones treated by endoscopic procedures were included in the "no operation" series since the first object at that time was the study of the late results of open operation. This terminology is awkward, but for tabulation purposes has the great merit of brevity. It so happened that the numbers were almost equal, 546 occurring in the "operation", and 568 in the "no operation" series. (Table III).

(1) Increasing Incidence of Upper Urinary Tract Stone.

It is apparent from Fig.1 that Sweden experienced a marked increase in the incidence of upper urinary tract stone in the 20 years after the end of the First World War (Hellström, 1949). (This may have been associated with vitamin A deficiency caused by the export of dairy milk produce to the combatants). A "stone wave" swept over Europe in the late twenties (Grossmann, 1938). Calcium oxalate was the principal constituent, and younger patients tended to be affected. The stones must have been small enough to pass, because it will be seen from Fig. 1 that only one patient in ten required operative treatment, in striking contrast to the present series in which operation was required in half the total number of patients. In spite of the high nutritional standards prevailing in the United States, a recent stone survey has reported a slight increase there also (Burkland and Rosenberg, 1955). The incidence in Britain is difficult to assess, but stone operations in this series for the decades 1926 to 1935; 1936 to 1945; and 1946 to 1955, numbered 105, 249 and 326 respectively.

(2) Length of Follow-Up.

Information relating to 974 patients (480 with, and 494 without operation) is detailed in the Appendix, Table 1, page i, and in diagrammatic form in Fig.2. The summary in the top right hand corner of Fig. 2 shows that 64 per cent. had been followed for more than five years, 35 per cent. for more than ten years, and 7 per cent. for more than 15 years. Satisfactory conclusions cannot be drawn from an analysis of any series of stone cases followed for less than five years. The interval between operation and detection of recurrence, for example, is ten years or more in 16.8 per cent. of recurrent stones. In the same way, the natural history of the disease can only be studied over lengthy periods. After ten years, larger numbers of the operation series (black columns) have been followed.

(3) Sex.

The male/female ratio for the total series was very nearly two to one. This supports the male predominance reported by Barney (1922) seven to two; Twinem (1937) five to three; Grossmann (1938) four to one; and Harrington (1940) two to one. The most interesting feature of Table IV is the difference between the "operation" series (M/F = 1.25 : 1) and the "no operation" series "M/F = 3 : 1). In other words, 240 of the total of 385 women (just over 60 per cent.) required operation, compared with 306 of 729 men (40 per cent.). Alternatively, the ladies may be better at passing small stones which are never identified, so that they show no opacity when they come for x-ray and the condition remains an "undiagnosed colic"; whereas the same size of stone may be arrested sufficiently long in men to appear on x-ray and only be passed thereafter.

(4) Side. (Table V).

The sides were almost equally affected, and 13.4 per cent. had bilateral calculi. Swift Joly (1929) found roughly the same incidence, but Winsbury-White (1936) and Twine, (1937) found that the left side was involved slightly more often, due to a closer lymph connection between the kidney and the lower urinary tract on that side. The data on the right half of Table V indicate that bilateral stone constituted 17.6 per cent. of the "operation" series, and only 9.0 per cent. of the "no operation", showing that two out of three came to operation, compared with one out of two for unilateral stone.

(5) Age.

Information relating to 1,007 patients is given in five year groups in the Appendix, Tables II and III on pages two and three.

(a) Age at onset of symptoms (Fig.3.).

The average age at onset of symptoms was:-

| | | |
|---|---|---|
| Without operation | - | 41.0 years. |
| With operation | - | 37.3 years. |
| Total series | - | 39.1 years. |

There was no appreciable sex difference. The inference is that operation cases represent a more severe form of the disease which declares itself two years earlier.

(b) Age at operation (or at diagnosis in "no operation" Series) (Fig.4.).

The average age at operation or diagnosis was:-

| | |
|---|---|
| Without operation | - 43.0 years |
| With operation | - 39.0 years |
| Total series | - 41.6 years |

Again there is a difference of approximately four years between those with and without operation. Men averaged 37 years at operation, and women 40.8 years.

For the total series, then, the average age at the onset of symptoms was 39.1 years, and at operation or diagnosis, 41.6 years. There is therefore an average duration of symptoms of 2.5 years.

Scrutiny of Figs. 3 and 4 reveals that the majority of patients are aged 25 to 55. Joly (1929) found this span to be 20 to 50 years, as did the majority of U.S. urologists (Burkland and Rosenberg, 1955); but Barney (1922) found that most of his patients were 20 to 30 years old, as did Hellström (1938) in his Staphylococcal stone series.

(6). Symptoms.

The incidence of symptoms in 1,061 patients is recorded in some detail in the Appendix, Table IV, page four. The presenting symptoms are summarised in Fig.5.

Pain due to distension of the renal pelvis is the main symptom. Only 89 (less than 9 per cent.) had no pain, but other symptoms led to the discovery of the underlying lesion, and 50 of the 89 eventually came to operation. The commoner symptoms may be listed thus:-

(a) Colic (617). This represented approximately 60 per cent., after those free from pain (89) were subtracted from the available total (972). The fact that 386 of the 617 patients with colic did not require operation emphasises the belief that "small dogs (or stones) bark most loudly".

(b) Lumbar Pain (355). The remaining patients had a constant dull ache in the kidney angle.

(c) Passage of Stones (232). Colic followed by the passage of a stone is considered "complete", and the incidence of this is therefore 232/617, or just under 40 per cent. A single stone was passed by 149 patients, and 83 patients passed more than one stone.

(d) Haematuria (380). Haematuria, visible to the naked eye, was present in just over one third of patients. The figures for colic, pain, passage of stones and haematuria were therefore much the same as those found by Joly (1929) and Schenck and Lane (1937).

(e) Pyuria (160), Frequency (113), Dysuria (180). These figures do not suggest that the majority were infected when first seen. The actual incidence of infection was 50 per cent.

(7) Duration of Symptoms.

The estimated duration of symptoms in 641 cases is tabulated in detail in the Appendix, Table V, page 5, and summarised as a histogram in Fig.6.

The length of time for which stone patients will tolerate their symptoms before seeking medical advice is a constant source of wonder. One elderly man was delighted to find that his backache disappeared as soon as a kidney stone had been removed. Only then did he realise that he had suffered needlessly for more than 40 years. Barney (1922) found that symptoms had been present for more than three years in 39 out of 70 cases. In this series of 641 patients, symptoms had been present for more than five years in 28 per cent. and for more than ten years in 16 per cent. It has already been calculated from the ages at onset of symptoms and at diagnosis, that the average duration of symptoms is 2½ years.

(8) Urine Examination at Diagnosis.

A detailed account of the findings on bacteriological and cytological examination of the urine at diagnosis in 665 patients is provided in the Appendix, Tables VI and VII, pages six and seven. The subject is studied under four headings:-

(a) Urine reaction. The reaction was acid in 270 out of 481 patients studied (approx. 60 per cent.). In the case of operation patients it was acid in 101 out of a total of 170. This is interesting when it is recalled that stone-formation occurs more readily in an alkaline infected urine.

(b) Incidence of Infection (Table VI). Almost one half (331 of 665) were infected when the diagnosis was established. As might be expected, 60 per cent. of operation cases were infected, compared with 40 per cent. of those not treated by operation. Other investigations disagree with these figures. Higgins (1952) found infection in 87 per cent. of 800 stone patients; Lett (1936) in 82 per cent. of 419; and Harrington (1940) in 74 per cent. of 480.

(c) The Infecting Organism. (Table VI). Sterile pyuria was the only indication of infection in 173 patients. Organisms were present in the remaining 158, and B.Coli, alone or in mixed infection, occurred in 112 (over 66 per cent.). The notorious urea-splitters, Proteus and Staph. Aureus, were present singly or in mixed infection in 29 patients (20 per cent.). Their importance in stone-formation is universally acknowledged, but the role of B. Coli is less easy to determine. Illyes (1934) maintained that B.Coli could assist in the production of coral calculi, but Rovsing (1924), Joly (1929) and Winsbury-White (1936) considered that B.Coli played no part in stone-formation. In the same way, Hellström (1938) thought that B.Coli were mainly secondary invaders, but that occasionally they might be able to split urea. In Hellström's opinion the Staphylococci found in the nucleus of the stone were the principal culprits.

(d) The Role of Infection in Primary and Recurrent Stone Formation.

The part played by infection in primary stone-formation is undetermined and will be discussed under "Possible Aetiological Factors". There is, however, little doubt that pre-operative urinary infection is closely related to post-operative recurrence of stone. (Table VII). The first point of interest in this table is that 39.2 per cent. of the "no operation" series were infected when first seen, compared with 61.3 per cent. of those treated by operation. The lower table shows that stone recurred in 20.3 per cent. of patients whose urine was sterile before operation, and in 45.1 per cent. of those whose urine was infected. Conversely, of those patients who later developed recurrence, 78 per cent. had pre-operative urinary infection. These results are in agreement with the findings of Brongersma (1924), Rovsing (1924), Illyes (1934), Oppenheimer (1937), Twinem (1937), Keyser (1943), Hellström (1949), and Smith (1939).

(9) <u>Initial Radiological Findings.</u>

Detailed information regarding the site, size and number of the stones in 1,027 patients, and the state of the kidney function in 932, is presented in the Appendix, Table VIII, page eight. For further analysis these are divided into 481 "no operation" and 546 "operation" cases in Appendix, Tables IX and X, pages nine and ten.

A diagrammatic attempt has been made to summarise this complex subject in Fig.7. (Composite diagram).

(a) <u>Site of Stones. (Table VIII).</u> Renal and ureteric calculi were equally represented and at this stage only 7.6 per cent. were bilateral. Insufficient information was available to determine with accuracy the site of 108 renal and 39 ureteric stones.

Lett (1936) found that the ratio of renal to ureteric stone was 2 to 1; Winsbury-White (1936) 2 to 1; and Joly (1929) 5 to 1. These authors were, however, considering only calculi requiring operation. The stones would therefore be larger and more easily trapped in the kidney. In this series the kidney/ureteric ratio in operation cases was 360/129, or 3 to 1. Where operation was not performed, the kidney/ureteric ratio was 109/337, or 1 to 3. In a nutshell, the majority of ureteric stones were small and 75 per cent. were expected to pass naturally, whereas 75 per cent. of kidney stones were sufficiently large that operative treatment was required. The favourite sites were the renal pelvis, the lower calyx and the lower third of ureter (Fig.7).

(b) Number of Stones. (Table IX and Fig.7). Approximately 80 per cent. of renal and 95 per cent. of ureteric stones were single. Multiple stones (more than three), on the other hand, occurred much more commonly in the kidney (10.8 per cent.) than in the ureter (0.3 per cent.). In the operation series, however, 7 per cent. of ureteric stones were multiple.

Joly found 60 per cent. of renal and 80 per cent. of ureteric stones to be multiple. Brongersma (1924), impressed (as always) by the importance of infection, stated that 94 per cent. of aseptic calculi were single, compared with 73 per cent. of infected.

Multiple calculi accounted for 10 per cent. of Jeanbrau's series of ureteric stones (1914), and 6 per cent. of Braasch and Moore's (1915).

(c) <u>Size. (Table X. Fig.7).</u> Large stones are rare in the ureter (less than 2 per cent.), and relatively common in the kidney (32 per cent.). Few, however, occur in either situation, except in the operation series. The optimum condition for stone growth is a combination of mild infection and slight obstruction. Frequently, but not invariably, the very large kidney stones were infected.

(d) <u>Renal Function. (Table XI. Fig.7.).</u> In the case of unilateral stones this refers only to the side affected. Three grades of renal function are recognised on intravenous pyelography:-

1. Good: good function; normal pyelogram; no hydronephrosis.
2. Fair: some impairment of function with early or moderate hydronephrosis.
3. Poor: very little function, or none at all, or advanced hydronephrosis.

The obstructive potential of ureteric calculi has long been recognised; in fact, it is standard urological practice when renal and ureteric stones occur simultaneously, to "work from below upwards" in freeing the renal tract from stone. Information is available about renal function at diagnosis in 932 patients, and the outstanding fact which emerges is that for the entire series, kidney stone was much more harmful to renal function than stone in the ureter. The figures show that in 26.8 per cent. of 388 renal stones, function was poor, compared with 6.8 per cent. of 454 ureteric stones. In the same way, function was good in 31.2 per cent. of kidney stones, and in 56.6 per cent. of ureteric stones. These findings were more or less the same whether or not operation was performed. It seems only fair to add that the presence of 68 unilateral and 11 bilateral staghorn renal calculi made an undoubted difference, and that, if stones of comparable size alone were considered, function might well have been equally affected by renal and ureteric calculi.

Stone in the upper and middle third of the ureter was slightly more harmful than stone in the lower third.

(e) Incidental x-ray findings. Stone occurred in association with tumour in two cases only, and one of these was an adenocarcinoma. The risk of developing carcinoma at a later date seems very slight and is therefore not a convincing reason for the removal of all stones.

Unequivocal evidence of stasis, pelvi-ureteric stenosis or ureteric stricture was found in ten cases only (less than 1 per cent.).

Horseshoe kidney was present in six and pelvic ectopia in one.

These findings are discussed under "aetiology".

(10) Biochemistry.

The importance and complexity of the biochemical studies have made it necessary to consider them separately (Part VI). Information has been collected concerning urinary calcium output studies in 73 patients, blood chemistry in 210 patients and 204 upper urinary tract calculi have been analysed. This represents a considerable volume of work. Yet it will be realised that it refers to less than 20 per cent. of the total of 1,114 patients.

In passing, it may be said that hyperparathyroidism has been noted in six patients (3 per cent.). Recurrence after operation was twice as common in those with hypercalcuria as in those with a normal urinary calcium output.

Routine stone analysis has proved valuable in formulating a regime for the prevention of recurrence, particularly in the case of phosphatic, cystine and uric acid stones.

## SUMMARY OF GENERAL INCIDENCE AND DIAGNOSTIC FINDINGS.

(1) In a series of 1,114 upper urinary tract stone, roughly half (546) were treated by operation; and half (568) expectantly.

(2) The Urological Department Series represented 80 per cent. of the total, the other 20 per cent. being derived from the Victoria Infirmary Surgeons and cases treated by other Surgeons.

(3) Of the total, 70 per cent. (778) were interviewed and investigated, 20 per cent. replied to a questionnaire and 10 per cent. were untraced.

(4) During many years of observation, the mortality of the disease was less than 4 per cent.

(5) There is evidence of an increasing incidence of renal calculus.

(6) Follow-up was lengthy, 35 per cent. being followed more than ten years.

(7) The sex ratio for the total was M/F = 2/1. In the operation series it was 1.25 : 1, and in those without operation 3 : 1.

(8) The right and left side were equally affected and 13.4 per cent. were bilateral.

(9) The average age at the onset of symptoms was 39.1 and at operation 41.6 years. Most cases were aged 25 to 55 years.

(10) Pain was <u>not</u> experienced in 8 to 9 per cent.

(11) Symptoms were present for more than 5 years in 28 per cent. and more than 10 years in 16 per cent.

(12) Urinary infection was present in 50 per cent. the commonest organism being B.Coli. There was a close relationship between pre-operative urinary infection and post-operative recurrence of stone.

(13) Radiological examination showed an equal incidence of renal and ureteric stone, the principal sites being the renal pelvis, lower calyx and lower third of ureter. Single stone was commonest in the ureter and multiple stone in the kidney.

Large stones were rare in the ureter and relatively common in the kidney. Renal function appeared to suffer more harm from renal than from ureteric calculi.

(14) Hyperparathyroidism was discovered in 3 per cent. of 210 patients investigated.

## Section III. Possible Aetiological Factors.

At first sight the opportunity of interviewing and investigating 778 stone patients appeared to offer a rich field for exploration, but this purely clinical approach to aetiology has proved disappointing. The various findings are detailed in the Appendix, Table XI, page eleven.

(a) Dietary Factors.

1. Vitamin A. lack. Poor night vision was admitted by 87 of 517 patients questioned (17 per cent.). This is a very rough test of presumed vitamin A deficiency and it was difficult to believe that any of these patients had, in fact, dietary deficiency of any kind; and the same applies to the majority of stone patients seen in this country. Dark adaptation tests and estimation of vitamin A in plasma by biophotometry were impracticable. This view is in agreement with Keyser (1935) and Grossmann (1938) who reported that they could find no evidence of vitamin or other nutritional deficiency. Higgins (1936), however, was so impressed by finding II out of 16 patients vitamin A deficient (68 per cent.) that he insisted on a high

vitamin A intake in his regime for the prevention of recurrence, and still does (1952).

2. Peptic ulcer and alkali therapy. Of 335 patients questioned, 24 stated that they had at one time or another received alkali therapy for peptic ulcer (7.1 per cent.) and in most of them the therapy had been prolonged. Kretschamer and Brown (1939) found that only 1.2 per cent. of a large series of stone patients had at any time received alkali therapy, but Pyrah (1955) thinks there is a definite connection between gastric conditions and nephrocalcinosis or nephrolithiasis. On the statistical basis that 3.55 per cent. of admissions in one year had been for peptic ulcer, and 0.38 per cent. for stone, he calculated that the actual number of ulcer patients was four times the expected number and that the actual number of stone patients suffering from ulcer was three times the number expected. He stressed also the role of pyloric obstruction and vomiting with consequent hypochloraemic alkalosis in producing tubular calcification; and emphasised the "milk-drinker's syndrome" of hypercalcaemia and hyperphosphataemia which, (along with alkali therapy), might well produce widespread calcification. Pyrah found that 10 per cent. of stone patients had a peptic ulcer history.

3. Diet rich in oxalic acid, or oxalate. A handful of patients were abnormally fond of rhubarb, but none consumed excessive quantities of cocoa, strong tea, chocolates,

spinach or loganberries. In any case, endogenous sources of oxalic acid upset such calculations.

(b) Metabolic Factors.

It is sufficient to say that chemical analysis revealed one pure cystine and two pure uric acid stones.

(c) Familial Incidence.

Blood relatives had suffered from upper urinary tract stone in approximately 6 per cent. (20 in 335 questioned). It is difficult to say what significance may be attached to this without a control series. Stones occurring simultaneously in brothers are illustrated in Figs. 8 and 9 (the bladder stone was known to have descended from the kidney). In two instances a brother and sister of each patient had been affected. In the other 18 only one relative was concerned - father 6, mother 1, daughter 1, brother 9, sister 1.

The racial incidence does not require consideration since almost all of the patients were of Scottish descent. The Arab is commonly affected (even allowing for bilharizia) while the Negro is relatively immune. Both have a high enough melanin content in the skin to prevent excessive formation of vitamin D from exposure to strong sunlight. In both cases there is dietary deficiency in some respects. The American negro is more likely to develop stone than his Bantu cousin (Cony, 1937; Dodson and Clark, 1946). An understanding of racial factors might give valuable clues to the underlying aetiology.

(d) Recumbency, Low Fluid Intake, Sweating.

These factors, in combination, are neatly illustrated in the recumbency calculi associated with bone and joint tuberculosis, as Illingworth and Dick (1945) have pointed out. Stasis, low fluid intake, skeletal decalcification, vitamin D excess (from exposure to the sun) and sweating, all play their parts, as does urinary infection.

1. Recumbency. Only 39 of 891 patients questioned (4.4 per cent.) gave a history of disease causing prolonged recumbency, and Pyrah found a similar incidence (4 per cent.) The factor is an important one in orthopaedic practice and the value of frequent changes of position, forced fluids and frequent urine and x-ray examination is now widely recognised.

2. Low Fluid Intake and Sweating. This group of 35 patients occurring in a total of 335 (approx. 10 per cent.) arose in two ways:-

   i. Periods spent overseas during World War II when both factors operated. Dix (1951) certainly found ureteric stone to be common in the Middle East forces, although this was not my personal experience in over two years. Stone is common in North India, South China and the Arab countries, all of which have warm climates; yet it is relatively uncommon in Central Africa and has a remarkably low incidence in the north part of South America through which the

Equator runs (Davalos, 1945). Why is the modern Arab more prone to lithiasis than his ancestors? Very few of the mummies examined by Professor Elliot Smith contained upper urinary tract stone.

ii. Occupational - foundry workers, stokers, boilermen, bakers and those working in hot atmospheres. On the other hand, there is reason to believe that a sedentary occupation with imperfect drainage of the calyces might be just as harmful.

(e) Obstructive Factors.

| | | |
|---|---|---|
| 1. | Pelvi-ureteric stenosis and ureteric stricture | 3.3% |
| 2. | Congenital anomalies - horseshoe kidney | 2.3% |
| 3. | Bladder neck obstruction | 2.3% |
| | Total | 7.9% |

Obstructive factors therefore accounted for only 7.9 per cent. of the total.

Stasis has long been considered of great importance in stone-formation (Fig.10) and there is no doubt that a slight degree of obstruction is a contributing factor and that it should be corrected whenever possible. Owing to defective drainage, stone is said to be six times as common in horseshoe kidney as in the normal. Certainly, 50 per cent. of the horseshoe kidneys seen at the Urological department of the Victoria Infirmary, presented with stones. Having said this much, it must be pointed out that over 90 per cent. of stone cases have no evidence of such obstruction and, conversely, many cases of pelvi-ureteric following ways.

1. By damaging and eroding the papilla or straight collecting tubules:
2. By interfering with the normal physicochemical relationships of the urinary crystalloids and colloids; e.g. an alkaline infection in which calcium phosphate is precipitated; or interference with the calcium citrate complex which holds the calcium in solution. Its effect on the colloids is unknown, but the inflammatory debris may serve to bind the crystals together and may even act as the nucleus of the stone. Many workers have produced stones in experimental animals by introducing infection, e.g. into the dental canal (Rosenow, 1922) or intravenously (Hellström, 1938), or into the bladder.

In 1923 Davalos found, however, that B.Proteus only produced stones in animal bladders after the epithelium had been damaged by the instillation of salicylic acid - and this would appear to be the conclusion reached, that there can be no stone without preceding damage to the epithelium.

The incidence of infection in primary stone has been variously estimated. Rosenow (1922), Keyser (1943) and Hellstrom (1949) all thought it significant. Birdsall (1939) found infection in 189/211. Carroll and Brennan (1952) were undecided. Smith (1939) was unimpressed. Higgins found preceding pyelonephritis in 23 out of 29.

Lett found only 29 in 419 sterile. The U.S. survey (1955) thought infection "an associated factor" in 47 per cent.

(f) Biochemical Factors.

Hyperparathyroidism has been associated with 3 per cent. of 210 stone patients investigated. If the six cases in question are set against the total of 1,114, the incidence becomes less than 0.6 per cent. The moral is that hyperparathyroidism must be excluded in every case of stone. Over 40 per cent. of 67 stone patients investigated on a fixed low calcium intake have shown evidence of hypercalcuria.

Comment on Aetiology.

There is still a wide gap between scientific knowledge acquired under experimental conditions, and its application to the search for the cause in the individual patient. No one is more sorrowfully aware of this than the clinician, who attempts, to the best of his ability, and with the available knowledge, to bridge the gap. In some cases a definite factor is present - vitamin deficiency, hyperparathyroidism, obstruction, recumbency, (even infection or metabolic upset), but an impressively large group of patients is left in whom the most thorough clinical, x-ray, bacteriological, and biochemical investigations reveal (as yet) no abnormality. Their diet is normal; their urine shows no excess of crystals, nor is it infected; their urinary tracts are free from obstruction and their kidneys healthy; and studies of calcium and phosphate metabolism are normal - yet they form stones and continue to do so. The problem is a perplexing one, raising many questions which must remain unanswered meantime. It is full of apparent paradoxes and curious anomalies.

Unanswered Questions.

1. Are all stones formed on papillary lesions?
2. If so, what causes the lesion?
3. If the cause of the lesion is toxic, infective or vascular, why are only 10-15 per cent. bilateral and why do they not all recur?
4. Do specific infections produce stone or must there be a predisposing degenerative change?
5. Why is there a racial and climatic difference?

## SUMMARY OF AETIOLOGY

| F A C T S | No. | Per cent. |
|---|---|---|
| **Factors of Significance.** | | |
| Hypercalcuria | - | 40.0 |
| * * * * | | |
| Hyperparathyroidism | 6 | 3.0 |
| Horseshoe kidney and pelvic ectopia | 7 | 3.0 |
| Pelvi-ureteric stenosis | | 3.3 |
| Ureteric stricture | 10 | |
| Recumbency stone | 39 | 4.4 |

| Factors of Doubtful Significance. | Per cent. |
|---|---|
| 1. Peptic ulcer | 7.0 |
| 2. Family History | 6.0 |
| 3. Metabolic Stone (cystine & uric acid) | 1.5 |
| 4. Predisposing renal disease | 10.0 |
| 5. Urinary infection | 50.0 |
| 6. Vitamin A lack -(history of night blindness.) | 17.0 |

It is therefore apparent that a satisfactory explanation for stone-formation (apart from knowing that 40 per cent. have hypercalcuria) cannot be found in other than a small proportion - 62 of the total. The gap between the laboratory and the patient is obvious.

As old as medicine itself, the problem of stone remains unsolved. It has, however, stimulated and tantalised research workers to such an extent that a tremendous effort has been, and still is, being made, to unravel the tangled threads leading to its solution.

A broad picture has been presented of the material (source and nature); the methods of tracing, interviewing and investigating; and the facts or results accruing from this study of the entire series. This is a necessary forerunner of the three clinical sections, - natural history, recurrence and management of bilateral stone, - which follow.

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PART II.

## THE RESULTS OF CONSERVATIVE MANAGEMENT

### A Study of some aspects of the Natural History of Upper Urinary Tract Stone.

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# THE RESULTS OF CONSERVATIVE MANAGEMENT

## A Study of some Aspects of the Natural History of Upper Urinary Tract Stone.

### Section I. General Considerations.

According to Hippocrates, the good physician is a "minister (i.e. a servant) and interpreter of nature". Study of the natural history of disease is not simply an academic exercise, but has considerable practical value. Great physicians and surgeons such as McKenzie, Gairdner, Lewis and Trotter, have acknowledged this and have themselves been natural historians; yet our knowledge of this aspect of disease is fragmentary and much of this important field remains to be explored.

Once the natural history of a disorder is known, a yardstick is available by which the results of treatment may be measured, and the prognosis accurately assessed. In surgical practice the indications for operation can rarely be stated with confidence until the course of the untreated disease is known. By prolonged observation, supplemented by discriminating experimental work, the true natural historian will become accurate and confident in prognosis, sound in judgment, broad in outlook, and consistent in his assessment of the indications for treatment.

Upper urinary tract stone provides abundant material for the study of its natural history. Many stones require no treatment since they treat themselves by spontaneous passage.

Others, equally small, become lodged in a calyx, or, (according to Carr's hypothesis, 1945) in a "pouch" outside the calyx, there to lie dormant, causing neither symptoms nor damage to the kidney. More rarely, large symptomless "silent" stones are revealed as an incidental finding during some other form of radiological examination. Finally, there are the patients who are unfit for operation or who refuse it since their symptoms are not sufficiently severe.

Material. The principal group studied was the "no operation" series (568 patients). Even in the "operation" series some cases were treated conservatively for good reasons. Table III indicates broadly the treatment carried out in 1,114 patients, and it will be seen that in the "operation" series there were at least three groups who merited further study from this point of view; viz:-

(1) The stone-passers ... ... ... ... ... ... ... ... 106

(2) Some of the large stones, primary or recurrent... 26

(3) The small untreated stones ... ... ... ... ... 71

When these are added to the 568 patients not treated by open surgery, an impressive total is available for analysis. Finally, it seemed fair to incorporate patients deliberately treated conservatively for many years before operation; and even those recurrent cases for which treatment was not advocated.

Method. A questionnaire was sent as a form of introduction. Thereafter patients were interviewed and re-examined in the manner previously described. The 568 patients constituting the "no operation" series, had all initially been seen at the Urological Department, so that uniformity in their management was guaranteed. Many of them had been reviewed in 1945-46, and the resulting information was entered on their transcription cards. More than 90 per cent. were traced and followed for periods of from one to 30 years.

## The Progress and Fate of Stones Originating in the Kidney

The clinical course and termination of 1,394 renal calculi in 1,038 patients, are summarised in Table XII and Fig.14. Each stone is followed from its birthplace until it either (1) passed naturally, or (2) removed surgically, or (3) retained temporarily or permanently at some point in the urinary tract. Such a study gives a very impressive aerial picture of the natural history of the disease. Two courses are open to stones formed in the kidney:-

(1) They may be retained in the kidney. (711). This fate befell 711 (just over one half) of the 1,394 stones under consideration. Operative removal was required in 534 (75 per cent.) of these retained stones, and the remaining 25 per cent. or 177 were treated conservatively and may be divided into:-

(a) Small stones (124) with minimal symptoms, good renal function, and every expectation, in time, of spontaneous passage.

(b) Large stones (53) which had no hope of passing naturally. Expectant treatment was advocated in unilateral large stones because patients were unwilling or unfit to undergo operation; and in bilateral branched calculi because they were symptomless.

(2) They may enter the ureter. (683). For the present, only primary stones are considered. Patients may therefore pass one stone from each side and multiple stone-passers are excluded. Of the 683 stones which escaped from the kidney, only 146 (21 per cent.) required open removal (62 per cent. from the lower ureter, 12 per cent. from the middle third and 26 per cent. from the upper ureter). Spontaneous passage (in some with endoscopic assistance) occurred in 521, whilst 16 described as "retained" are still under observation.

These figures indicate that 521 of 683 stones entering the ureter eventually pass (75 per cent.); or 37 per cent. of the original total of 1,394. It is emphasised that all those which passed were confirmed by x-ray examination or were identified after passage. If allowance is made for the total number known to have been passed (1,641 stones by 521 patients) and for those cases in which a stone has presumably passed without identification, it is certain that the proportion of stones leaving the kidney is greater still - probably over two-thirds of the total. In the same way, the percentage of ureteric stones passed would be even higher than 80 per cent.

The natural history of ureteric stone is simpler than that of kidney stone and will be considered first.

## Section II. The Natural History of Ureteric Stone.

It has been observed above that some patients have the happy knack of passing their stones unaided. Further consideration of this group of 521 patients constitutes the natural history of ureteric stone.

### A Study of Stone-passers.

Of the 521 patients concerned, 415 came from the "no operation" series, and 106 from the "operation" series.(Table III).

The number of stones passed per patient is illustrated in Fig.15.,(the black columns representing stones passed by patients treated by open operation.). It is at once obvious that the majority (365) passed only one stone each, but several patients who showed special aptitude, passed more than seven stones each. One patient, in fact, passed the astonishing total of 560 stones. The total number of stones passed is considered in Table XIII. Needless to say, not all of these have been confirmed radiologically and diagnosis depends on the patient having observed the stone after passage. The mammoth total of 1,641 was unfairly influenced by including the patient who passed 560 stones, but even if he is omitted there remains a total of 1,081 stones.

Fallacies Exposed by these Figures. (1) It was stated earlier that slightly more than half (711) of 1,394 stones were retained in the kidney, and slightly less than half (683) entered the ureter. If the grand total (1,641) of stones passed is taken into consideration, it is clear that two-thirds or more make their escape from the kidney. (2) Many of the good results of endoscopic intervention would have been achieved in any case by "watchful waiting".

Particularly significant is the fact that 365 patients (70 per cent.) passed one stone only - an isolated lapse from grace. The remaining 156 passed more than one, and if, hypothetically, this is regarded as a "recurrence", 30 per cent. were thus affected (Table XIV). This must be regarded as <u>recurrence due to the disease itself</u>. It would be expected therefore that open operation would have at least this recurrence rate; and such indeed proves to be so in the case of uretero-lithotomy (31.4 per cent.).

In the operation series of 106 stone-passers (25 per cent. of 403 interviewed), the process started after operation in 12 per cent., stopped after operation in 44 per cent., and occurred with impartiality before and after in 44 per cent., i.e. operation appeared to start it in 12 per cent., to terminate it in 44 per cent., and to have no effect either way in 44 per cent. (Table XV). (Detailed information about this group of 521 stone-passers is available in the Appendix, Table XII, page 12).

<u>Factors influencing the passage of Stones.</u>

Patients vary widely in their ability to pass stones. In general, women appear to be more expert than men, but even within the sex there are individual differences. One lady (Fig.16) passed a large ureteric calculus while she was under observation in a maternity hospital. Another (Fig.17) whose stone was smaller, but easily palpable per vaginam, required operative treatment. One patient, a shipping clerk, who has already been mentioned, produced a bag containing 560 stones, which he claimed to have piloted from his left kidney to the exterior over a period of ten years. Nephrectomy was performed for widespread large renal calculi and the process stopped at once.

Time and again one is struck by the ease with which some patients pass irregular stones of 1 cm. diameter, whilst others have great difficulty in expelling stones half that size. Stone-passers merit further study to determine the important factors facilitating or hindering stone passage. If it may be assumed that there is equality among patients in respect of the muscular expulsive power of the renal pelvis and ureter, there is then left for consideration the stone itself, and the passage it must traverse. The subject is, of course, highly speculative and the remarks which follow are only impressions based on incomplete information. This can hardly be otherwise, since, to be completely informed, it would be necessary to follow the stone from its earliest days by serial radiography until it has been trapped in the kidney for certain, or had been passed and was available for measurement, weighing and analysis.

(a) <u>The Stone</u>.

1. <u>Size</u>. Assuming for the moment that there is no

constriction at the calyceal neck or pelvi-ureteric junction, the critical factor is the size of the stone when it is lying freely in the renal pelvis waiting to be passed. If it has been liberated from the plaque, pouch or surface on which it has formed before its diameter has exceeded 1 cm. it still has a reasonable chance of passing naturally. Above that size the prospect becomes more remote, although assistance can be given in the lower ureter by endoscopic manoeuvres. The largest stone in this series recorded as passing spontaneously, was 1.4 cm. in diameter (see Fig.16) but this is most unusual. The average stone is less than 0.5 cm. and the usual measurement given is 5 x 3 x 2 mm. On the other hand, Dourmashkin (1945) was able to produce from his very large series of cases, 503 examples of lower ureteric stone of greater diameter than 0.5 cm. Phosphate or mixed oxalate-phosphate stones achieved the greatest size. Pure oxalate stones in the main were smaller. Analysis of 52 stones passed naturally showed that 28 were composed of pure calcium oxalate and that 80 per cent. of the total contained <u>some</u> calcium oxalate. This was not the experience of Kretschmer (1942). In his series of ureteric stones, 45 were composed principally of calcium phosphate, and 35 of calcium oxalate.

2. <u>Nature of Stone</u>. Obviously the smooth non-irritant stone has a much better chance of passing than the one with an irregular surface which readily causes spasm. Swift Joly (1929) thought that the majority of stones passed naturally consisted of uric acid or urates, because of their smooth surfaces.

In this series only one urate stone has been noted. The largest, heaviest and smoothest stones were made of calcium phosphate; the smallest, lightest and roughest, of calcium oxalate.

(b) The Passage.

What may be termed the normal points of narrowing, occur at the calyceal neck, the pelvi-ureteric junction and the intra-mural portion. Once the stone has entered the ureter it is most likely to travel at least as far as the bladder wall. Pathological obstruction has not proved to be common in this series, either in respect of the aetiology of stone production, or of hampering the progress of the stone once it has been formed. It is, however, obvious that the "dysuric" calyx, or pelvi-ureteric stenosis, or an aberrant renal artery, or ureteric stricture, may all play a significant part in a small group of cases, as may congenital abnormalities like the six cases of horseshoe kidney noted previously.

Comment on Stone-passers.

It has been noted that two-thirds of those who pass stones, do so only once. If it is assumed that these stones form on a papillary plaque, it must be possible for such a plaque to heal. In the same way, if the stones are caused by some upset of the urinary physiochemical relationships, this upset must be reversible. These patients portray an uncomplicated picture of stone-formation in its earliest and mildest form. If modern radiological biophysical and biochemical techniques were applied to the problems of calculous disease at this stage when the departure from normal is least obvious, it would be possible to learn more about underlying aetiology than can ever be achieved by animal experimental studies.

Conclusions.

(1) In a group of patients with ureteric stone, surgical removal was required in 146 (20 per cent.) and in 521 (80 per cent.) the stone eventually passed (30 per cent. with endoscopic assistance). This is a conservative estimate of the proportion passing naturally since a total of 1,641 stones was passed by the 521 patients concerned. Calculation on the basis of this large figure indicates that approximately 90 per cent. passed naturally.

(2) Endoscopic intervention was successful in 80 per cent; but in the light of the last statement this has no particular merit and the method should be used with discrimination.

(3) "Recurrence" or the passage of a second stone, occurred in 30 per cent. This is the natural progress of the disease. Likewise, 70 per cent. of the 521 patients passed only one stone, and many of this group had experienced no symptoms, passed no stones, and were clear on x-ray examination when they were reviewed after intervals of one to thirty years.

(4) The majority of the stones passed were small and contained oxalate (80 per cent.). In the absence of repeated attacks of colic, hydronephrosis or severe infection, and providing it shows a satisfactory rate of progress and no increase in size, there is every justification for a conservative

attitude to the smooth, ureteric calculus less than 1 cm. in diameter.

## Surgical Management of Ureteric Stone.

Although it is far removed from the natural history, the surgical management of ureteric stone deserves some comment at this point, since it becomes necessary when expectant treatment fails.

(a) Open Surgery. Operative removal was performed in 146 of 683 ureteric calculi (21 per cent.). The stone was arrested in the upper third of the ureter in 26 per cent., in the middle third in 12 per cent., and in the lower third in 62 per cent. of these 146 patients. In 1932 Ravich stated that only 11.2 per cent. of ureteric stones in his care were removed by open operation. In a series of 274 cases, Kittredge and James (1954) treated all stones in the upper and middle ureter surgically, none passing naturally, whilst 21 per cent. of those in the lower ureter required operative removal. In the absence of repeated colic, hydronephrosis, or infection, there is much to be said for an expectant attitude to the ureteric calculus of moderate size and reasonably smooth contour. Steady progress along the ureter, with frequent x-ray confirmation of the stone's position, should encourage one to continue in this way. Precipitate surgical action is called for only in bilateral stone where obstructive anuria is potentially imminent until at least one ureter is cleared. In unilateral cases, surgical action is indicated when there is complete arrest of progress with marked increase in size, leading to hydronephrosis; or where symptoms become intolerable, or severe infection supervenes. Dourmashkin (1945) was impressed by the number of patients with large stones in the lower ureter who could continue for long periods without suffering renal damage. Closer inspection of the stones showed grooves or channels along which urine could trickle. The ureter itself developed a little pocket-like dilatation round the stone. The patient exemplified in Fig.18a retained a fairly large calculus for one year without colic or hydronephrosis, and is still under observation. By contrast, and without apparent explanation, the stone in Fig.18b is not significantly larger, yet hydronephrosis developed at an early stage and operative removal was indicated.

(b) Endoscopic Surgery. Indications for its use were present in 193 of the 521 patients who eventually passed stones. The procedures employed and the results are detailed at some length in the Appendix Table XIII, page 13. Briefly, 80 per cent. success was attained in 135 of 168 patients traced. The merit of this is difficult to assess once it is realised that approximately the same figure obtains for untreated ureteric stone. "Recurrence", or the passage of a further stone after successful endoscopic treatment, was recorded in 12.5 per cent. This is the "recurrence" of the disease itself, and is the very least that may be expected after open operation. Many American Urologists attach great importance to "cystoscopic recovery of the stone", and claim success in achieving this in a high percentage of all ureteric stones encountered. Squires (1930) reported 87.3 per cent. and Ravich (1932), 83.6 per cent. In fact, Ravich stated that only 6.3 per cent. of ureteric stones passed spontaneously. In the present series, endoscopic assistance to stone-passage was found necessary in only 30 per cent. The commonest method employed was the passage of one or more ureteric catheters which were left in place for several hours. Ureteric meatotomy, diathermy coagulation to the orifice and Dourmashkin's ureteric bougies were less commonly used. Examples of cases treated by these methods are illustrated in Figs. 18e and 18f. The dangers associated with forcible extraction by wire baskets and snares, have been emphasised by Kretschmer (1942), Ormond (1940) and Dourmashkin (1945). When it is realised that 50 to 90 per cent. of ureteric stones pass naturally, there is little credit in achieving figures within the same range by endoscopic methods. Barney and Chute (1931) very reasonably make the point that the natural force of an obstructed stream can scarcely be equalled by dragging downwards. Dourmashkin (1945) held that simple passage of ureteric catheters was valueless, and that forcible extraction by wire baskets was positively dangerous. He felt that cystoscopic dilatation of the ureteric orifice by metal bougies was effective and safe.

The subject teems with problems, calling for sound judgment based on a wide experience of handling ureteric stone patients. One of the best ways of gaining a balanced outlook is a careful review of those patients who pass stones without surgical assistance, i.e. the stone-passers previously considered.

## Section III. The Natural History of Stone Retained in the Kidney.

Isolated examples of large, symptomless, slowly-growing stones have occurred at one time or another in the experience of most urologists. They are sufficiently rare that the individual surgeon can scarcely hope to accumulate enough information on which to base a confident prognosis, and very little help is forthcoming from the literature. Swift Joly's (1949) view was that sooner or later a stone destroyed the kidney; and even worse, if infection were present, the stone-forming process spread to the other side, after the manner of tuberculosis. He categorically stated that the most conservative treatment of a stone in the kidney was its early removal and found no indication for conservative management, apart from a brief period of observation in very small stones. The only comparable review of conservative management comes from Priestly and Brousch (1937) who followed 177 untreated stone cases for 11 years. Symptoms occurred in a high proportion. Those stones originally "silent" caused symptoms in two-thirds, those originally harmful, in almost 100 per cent.

Large stones were worse than small; calyceal stones better than those in the pelvis. In their opinion, kidney calculi, even if silent, were serious and progressive.

Problem Stone Cases.

These views appear sufficiently definite to exclude further argument; yet it is the actual experience of many urologists that cases of large unilateral or bilateral stone remain symptomless and in good health for long periods. It is felt by these urologists that, apart from the radical step of nephrectomy, surgical interference might worsen the situation. Conservative operations, in their opinion, might not ensure complete removal. They are quite likely to impair further the function of the kidney and in more than half are followed by recurrence, itself more painful and harmful than the original stone. A lesser version of the same problem is presented by calyceal stones for which calycectomy is recommended (Stewart, 1952), yet conservatively-minded surgeons feel reluctant to make this sacrifice of healthy kidney tissue unless the stone is increasing rapidly or causing symptoms sufficient to interfere with work.

There is general agreement that the obstructive stone should be removed, and in the last event the degree of obstruction is much more important than the size of the stone. The other point which must be assessed is whether the stone or its surgical removal will be more harmful.

## Studies of various Groups of Patients with Kidney Stones treated Conservatively.

In an effort to arrive at some broad conclusions which might be helpful in managing these problem cases, the natural course of the disease has been studied in seven groups of patients suffering from kidney stone - all treated conservatively:-

(1) Stones treated conservatively for more than 10 years (156 patients).

(2) Small untreated calyceal stones (156 patients).

(3) Large untreated pelvi-calyceal stones (68 patients).

(4) Stones treated conservatively for some years before operation (34 patients).

(5) Untreated bilateral calculi (53 patients).

(6) Mild post-operative recurrences, where secondary operation was not indicated (43 patients).

(7) Severe post-operative recurrences unfit or unwilling to have secondary operation (29 patients).

### Group I. Kidney Stones treated Conservatively for more than ten years.

This group of 156 patients is approximately one quarter of the "no operation" series. It represents a mixture of 106 "stone-passers" who had passed a stone and were known to be clear, and 50 "stone-retainers". Their progress is contrasted in the Appendix, Table XIV, page 14, and summarised below:-

Originally clear, having passed stone (106 patients).

Progress: 87 have remained clear and had no symptoms (85%)
15 have passed further stones.
4 have formed fresh stones (small).

Stone originally present (50 patients).

Progress: 18 remain unchanged, no symptoms (36%)
3 have passed further stones.
3 have formed further stones.
1 (bilateral, large) died from urinary causes.
16 have increased - no operation.
9 have had operative treatment.

It is obvious, therefore, that a more sanguine prognosis can be given to the patient who has passed one stone and whose urinary tract is clear than to those retaining the stone. In the latter, 32 of the 50 (64 per cent.) had symptoms and 29 (58 per cent.) had progressed.

Conclusions.

(1) Of the 106 stone-passers followed for more than 10 years, 85 per cent. have had no further evidence of stone-formation. It will be remembered that this applied to only 70 per cent. of the total group of stone-passers. The difference is not a marked one, but it does seem that the longer they survive without passing stones, the less likely this is to happen.

(2) Where stones are retained in the kidney, symptoms occur in 64 per cent. and the disease progresses in 58 per cent. of patients. The results, therefore, although not good, are not so depressingly bad as those reported by Priestly and Braasch (1937).

## Group II. Small untreated Calyceal Stones.

Symptoms were absent or minimal in the 156 patients studied. The stones were small, less than 1 cm. in diameter, usually incarcerated in a calyx, and had a good chance of passing naturally if they were freed into the pelvis. Pyelography showed no evidence of renal damage. In these circumstances, surgical removal would probably have been more harmful than the condition itself. Partial nephrectomy seemed a rather extravagant method of extirpating such small calculi.

The progress of 156 untreated small calyceal stones is given in detail in the Appendix, Table 15, page 15. The patients were followed for periods ranging from one to 30 years. Tracings of some examples of the latest pyelograms are illustrated in Fig.19, the number in the renal pelvis indicating the length of time each has been followed. It is obvious that hydronephrosis is not a common sequel.

The decision not to operate imposes on the surgeon a strict moral obligation to review the patient at regular intervals of not more than one year to ensure that the stone is not making rapid progress.

The progress of the cases may be summarised thus:-

(a) Now clear, having passed the stone - 12 (7.7 per cent).

| | | | |
|---|---|---|---|
| Alive | - | no symptoms .... | 9 |
| Died | - | other causes ... | 3 |

(b) No increase in size - 111 (71.2 per cent)

| | | | |
|---|---|---|---|
| Alive | - | no symptoms ... | 74 |
| Alive | - | symptoms ... | 30 |
| Died | - | other causes ... | 7 |

(c) Increase in size (all alive) - 33 (22.1 per cent).

| | |
|---|---|
| No symptoms ... ... ... ... ... | 1 |
| Symptoms, no operation ... | 13 |
| Operation required ... ... | 19 |

Hence: (1) 33 had become larger.

(2) 30 had mild symptoms without becoming larger.

(3) 10 had died from other causes.

(4) 83, or more than half, were symptom free.

Urine examination showed no infection in over 80 per cent. Pyelograms have remained normal in over 75 per cent. Those who have come to operation for symptoms, or increase in size, or hydronephrosis, have lost nothing by the period of observation, and technically, removal of the stone has been easier.

Conclusions.

1. Failure of a small stone to progress does not mean (as Swift Joly thought) that it is lodged in a functionless kidney.
2. Small calyceal stones, unless causing pain or kidney damage, should be treated expectantly.
3. The absence of urinary infection in 80 per cent. is surprising.

Comment. These small calyceal stones may originate in a dilated and obstructed lymphatic pouch outside the calyx, as Carr (1954) has described. If they do not ulcerate into the calyx, it is natural that they should remain small. They may, however, form on a papillary erosion or plaque (Randall, 1932). In this case they constitute a surface on which crystals may be deposited and they ought therefore to increase in size. The fact that many of them do not grow may mean that the neck of the calyx is constricted (the "dysuric" calyx of Twinem, 1940) so that the stone cannot escape. Subsequently, the mechanical irritation caused by the presence of the stone may fibrose the straight collecting tubules, so that urine no longer enters the calyx and the stone is now imprisoned in a "urine-tight" compartment. Advances in radiographic technique might be of great benefit in investigating these small calyceal stones which represent an early and important stage in the life history of a stone which eventually grows large enough to require surgical treatment.

## Group III. Large Untreated Kidney Stones.

The progress, particularly the symptomatology, has been studied in 68 patients with large untreated kidney stones. They represent a heterogeneous collection derived from the "operation" and "no operation" series, the common features being the size and conservative treatment. Those in the operation series represent original untreated stones, the patient being unwilling or unfit, or of advanced age. Of the 68, 44 were unilateral and 24 bilateral. The term "large" indicates that they were large enough to have no chance of passing naturally, so that, normally, operation would have been advised. It does not indicate that they were all huge, branched stones.

Some of the grosser examples of large untreated stone are illustrated in Fig.20, in which the number under each kidney represents the period in years each patient has been followed. The patient whose pyelogram is shown in Fig.21, had experienced no pain, in spite of the presence of multiple large discrete stones in a non-functioning right kidney. He had bronchiectasis and was unfit for operation. It will be noted that there has been no involvement of the opposite side in spite of an infected (B.Proteus) urine for most of these 16 years.

The progress of the 68 patients with large untreated stones has been detailed in the Appendix, Table 16, page 16.

The outstanding points are:-

(1) Symptoms were experienced by 22 of the 68 patients, i.e., only 32 per cent. In some of the larger stones the absence of symptoms was undoubtedly due to poor remal function. The kidney was "too ill to complain".

(2) Deaths were due to urinary causes in 9 of the 20 that occurred.

(3) Operation was required in 15 of the 48 alive.

(4) Of the remaining 33, only 11 have symptoms (33 per cent.).

Conclusion.

It is difficult to draw any firm conclusion from study of this group, particularly as the patient's age or unfit condition may make the decision for the surgeon. The large unilateral stone in a non-functioning kidney ought, other things being equal, to be treated by nephrectomy. It is hardly a matter of extreme urgency, however, unless pyonephrosis is superimposed. In the last event, the clinician has to be guided by the thought that a conservative attitude (or operation) is only truly conservative when it is in the patient's best interests.

Comment on manner of growth of Large Branching Stones.

A large coral calculus may start:-

1. In the renal pelvis and grow upwards against the urinary stream.
2. In a calyx on a plaque, and spread outwards.
3. Multifocally in the pelvis and calyces, later coalescing to fill the entire pelvi-calyceal system.

In order that growth may be maintained, the ideal condition is a combination of mild obstruction and slight infection. If the stone impacts in the pelvis, the kidney will rapidly be destroyed, and the kidney must retain some function to provide material for stone-formation.

## Group IV. Kidney Stones treated conservatively before operation.

This group has been included since it gives additional information about the course of the untreated disease. The progress of 34 patients with kidney stones treated conservatively for some years before operation is given in the Appendix, Table 17, page 17. In 16 patients the stones were large, and in 18 they were of medium size. Patients were followed for periods up to 30 years. A conservative attitude had been adopted in 30 because symptoms were mild or absent, in two because they were unfit, and two refused operation.

Progress was rapid in only three patients (9 per cent.) The remaining 31 had slowly growing stones, 18 of which were calyceal and 13 branched. Eventually, one half of the patients had conservative operations and the other half had nephrectomy.

Initially, bilateral stone was present in nine, so that 25 were unilateral. During the period of observation none had "spread" to the opposite side in spite of the almost universal infection and the presence amongst the group of staghorn calculi, for 4, 7, 8, 11, 15 and 20 years.

The patient illustrated in Fig.22 is typical of the group. He had very mild symptoms, yet radiological examination showed a staghorn calculus in a functionless left kidney. The opacity on the right side was shown by intravenous pyelography to be outside the urinary tract. For business reasons he refused operation for three years, during which time he had no symptoms and the stone did not enlarge.

Some present with atypical urinary symptoms, such as frequency or pyuria, or even albuminuria. Others are incidental findings during radiological examination for a different complaint. Symptoms are mild or absent. Kidney pain may never have been experienced or, to the confusion of the patient, and the embarrassment of his medical attendant, may be present on the opposite side. In many cases it is quite obvious that the condition has developed slowly over several years.

Conclusion:

(1) Spread to the opposite side has not occurred in 25 unilateral stone cases followed for periods of several years.

(2) Progress has been slow in the majority (90 per cent.) even when kidney function has been good.

(3) No common aetiological factor has emerged.

(4) Many are so "silent" that it is difficult to imagine that they might ever be detected at an earlier stage.

Cases illustrating some of the features of large renal stones, treated conservatively.

The natural history of the large, or moderately large, renal calculus has been discussed above in groups 3 and 4. Some of their salient features are best illustrated by referring to specific examples. Circumstances prevented operative treatment being carried out at first in the following three cases which have therefore been followed without operation for 11, 7 and 4 years:-

Case 1. Male, Aged 19 years.

10.1.44. Referred by the Recruiting Board with albuminuria and six attacks of right renal colic in the previous six months.
Intravenous pyelography showed a considerable stone in the right renal pelvis with marked hydronephrosis. The left pyelogram was normal. (These films are not available.)
Urine: Acid, frequent leucocytes, B.Coli.

28.1.44. Operation was advised and refused.

28.9.55. He was seen in the course of this review. Operation had still not been performed. He had no urinary symptoms and his general health was good. He worked as a labourer.
Intravenous pyelography showed a large irregular stone of triangular shape in the right renal pelvis with extension into the lower calyx. Some function was still present, but hydronephrosis was advanced (Fig.23).
Urine: Acid, no R.B.C. or W.B.C., sterile.
Studies of calcium and phosphorus metabolism were normal. The urinary calcium output (on a fixed low intake) was 0.18 gm. in 24 hours.

29.11.55. Right nephrectomy was performed.
Histologically there was dilatation of all the calyces with compression of medullary tissue, but no significant degree of inflammatory cellular tissue. Stone analysis showed mixed calcium oxalate and phosphate.

Comment. The previous films are not available for comparison, but it is obvious that growth has been slow, and kidney damage gradual during these eleven years. The sterile urine, lack of inflammatory cells histologically, and failure to spread to the opposite kidney, are all worthy of note. This patient's main trouble now is to convince the Labour Exchange that he is fit to return to heavy work, which he is quite capable of undertaking.

* * * * *

Case 2. Male. Aged 20 years.

6. 8.47. Incidental discovery of left staghorn calculus during chest screening for cough. No urinary symptoms.
General health good.
I.V.P.: Large left branched renal stone. Function was only fair but there was no dilatation. (Fig.24a).
Urine : Alkaline, phosphate crystals, frequent W.B.C., B.Coli.
Operation was advised, but he was reluctant, and was advised to return if he had further symptoms.

25.11.53. One attack of left renal colic and haematuria of three hours' duration.
I.V.P.: Stone much the same size. Kidney now functionless. (Fig.24b & c).
Urine : Amphoteric, frequent W.B.C., B.Coli.
Biochemistry: First Stage Biochemical Osteomalacia:- Serum Calcium 9.7 mg. per 100 ml. Serum Inorganic Phosphorus: 2.22 mg.per 100 ml. Serum Alkaline Phosphatase: 5.7 K.A.units per 100 ml. Plasma Total Protein 7.2 gm. per 100 ml.
Blood Urea: 33 mg. per 100 ml.
Sulkowitch: Normal.

31. 8.54. Left nephrectomy.
Stone analysis: Mainly magnesium ammonium phosphate with traces of magnesium and calcium carbonate.

6. 3.56. Review: In very good health.
Urine : Alkaline, no W.B.C. or R.B.C., sterile.

Comment. This stone was symptomless from the start, apart from one brief colic six years later, in spite of a constant urinary infection. He was 20 years of age when first seen with a staghorn calculus, which must therefore have been present for many years, perhaps from early childhood. This is the type of case which, if bilateral, is best treated conservatively.

* * * * *

Case 3. Male. Aged 35 years.

10.10.51. His complaint was of left renal colic with haematuria of two days' duration. Had never experienced pain on the right side.
I.V.P.: Irregular stone in right renal pelvis, with collection of small stones in lower calyx and single stone in middle calyx. Poor function and hydronephrosis. (Fig.25a & b).
Urine : Amphoteric, few W.B.C., sterile.
Operation was advised but he was unable to attend for admission for business and domestic reasons.

14. 9.55. Reviewed. No urinary symptoms and general health good.
I.V.P.: Irregular stone right renal pelvis with calyceal stones as before. Not much increase in size. Fairly marked hydronephrosis as in 1951. Regarded as borderline case for partial nephrectomy. (Fig.25c & d).
Urine : Acid, frequent W.B.C., B.Coli.
Blood Chemistry: Normal.
Urinary calcium output (on intake of 0.15 gm. per day) was 0.22 gm. per day (just above the upper limit of normal).

23.11.55. Right nephrectomy.
Stone on analysis showed mixed calcium oxalate and phosphate.

13. 3.56. Reviewed. No symptoms.
Urine: Acid, no W.B.C., sterile.

* * * * *

Interesting common factors in these three cases.

(1) Failure to involve the opposite kidney after 11, 7 and 4 years.

(2) Slow rate of growth, probably due to poor kidney function.

(3) Youthfulness when discovered - ages 19, 20 and 35: yet, judging by the size of the stone the condition had been present for many years.

(4) Absence of any gross aetiological factor; no pelvi-ureteric stenosis, hyperparathyroidism, or urea-splitting infection.

## Group V. Untreated Bilateral Calculi.

The surgical management of patients with bilateral calculi is beset with so many problems and difficulties that it has been given separate consideration at a later point in this work. Cases treated conservatively are more appropriately dealt with in this part.

In general, the presence of stones on both sides indicates a more advanced and serious stage of the disease (size, amongst other things, being equal). Even small bilateral calculi are potentially dangerous since they may lead to calculous anuria. It would therefore seem that there is very little place for expectant treatment when such a threat to life and health is present. Closer inspection of the problem, however, soon reveals that only bilateral obstructive stones are dangerous, and the calculi under consideration are not of that type.

Of the 53 patients concerned, 42 presented with small stones on both sides, eight with large stones on both sides and three with a large stone on one side and a small stone on the other.

### (a) Bilateral Unbranched Calculi.

Patients in this group (42) had small non-obstructive calyceal stones. Their progress is described in detail in the Appendix, Table 18, page 18. The findings on re-examination may be summarised as follows:-

| | | |
|---|---|---|
| Both sides now clear | ... | 14 |
| One side now clear | ... | 14 |
| Stones still present on both sides ... | ... | 9 |
| Condition unknown | ... | 5 |
| | | 42 |

There was evidence of improvement in 28 of the 37 patients traced, and half of those improved were completely clear. Conservative treatment in suitable cases was therefore completely justified.

(b) Bilateral Branched Calculi.

Operation was not advised in some who were unfit and in others who were symptom-free. The progress of these cases is detailed in the Appendix, Table 18, page 19. In brief, three have died from urinary causes, one is untraced, and four are alive 5, 5, 8 and 17 years later. One of the four has mild symptoms. Comparison with the results of operation (Table XVI) shows that there is little to choose between the two sets of results, as only 10 of the 23 undergoing operation are known to be alive (9 having died from the disease, 1 from other causes and 3 are untraced). All ten have stones and five have symptoms.

The problem is a very difficult one. Each case should be judged on its merits and operation should be undertaken only for severe pain or unilateral infection.

The ten years' survival rate following treatment of bilateral staghorn calculi has been studied by Priestley and Dunn (1949). They came to the conclusion that removal of the stones gave more favourable results than conservative management. They appreciated that practically every operation would be followed by recurrence sooner rather than later, but still considered that operation was the treatment of choice. In their opinion a painless case was a hopeless case.

The following case is described in some detail since it is such a striking example of the opposite side of the picture:-

<u>Bilateral Symptomless Branched Calculi Treated Conservatively for 16 Years.</u> (Fig.26).

| | |
|---|---|
| 1940. | Female, aged 37, seen by Mr.T.L.Chapman's senior, Mr.J.Russell, with minimal symptoms and bilateral stone, already branched on the right side, and developing calyceal extensions on the left.<br>Conservative treatment was recommended. |
| 6. 3.46. | Occasional haematuria and pyuria. Passed two stones.<br>I.V.P.: Bilateral staghorn calculi. Total function fair.<br>Urine : Alkaline, frequent W.B.C., B.Coli and Proteus Vulgaris. |
| 9. 6.48. | Very slight backache and tiredness.<br>I.V.P.: Stones even larger.<br>Blood Urea: 40 mg. per 100 ml. |
| 7. 3.51. | Routine follow-up. No symptoms. "Never felt better".<br>I.V.P.: Stones larger still, but total function fair.<br>Blood Urea: 36 mg. per 100 ml. |
| 25.3.53. | Haematuria, tiredness, and aching pains in the legs.<br>I.V.P.: Still further increase in size of the stones.<br>Urine : Persistent Proteus infection in alkaline urine.<br>Blood Urea: 36 mg. per 100 ml. |
| 25.4.55. | Admitted with uraemic symptoms. Blood Urea 100 mg. per 100 ml. Settled with chemotherapy and correction of electrolyte imbalance. |

3. 8.55. Felt better than she had done for years. No urinary symptoms. Only complaint was of tiring easily and dyspnoea on hills.
Blood Urea: 43 mg. per 100 ml.

20.4.56. Routine follow-up. Occasional haematuria and pyuria. General health good apart from tiredness at night and dyspnoea on effort.
I.V.P.: Enormous staghorn calculi. No obvious renal function, and a rather poor concentration of dye in the bladder. The renal outline however indicated that, at places, there was a fair thickness of parenchyma.
Urine : Proteus infection persists.
Biochemistry: Serum Calcium: 10.4 mg.per 100 ml.Serum.
Inorganic Phosphorus: 4.4 mg.per 100 ml.Serum.
Alkaline Phosphatase:10.9 K.A.units per 100 ml.
Plasma Total Protein: 7.5 gm.per 100 ml.
Blood Urea 27 mg.per 100 ml.

Comment. This case is a classical example of the combination of mild chronic urea-splitting infection combined with slight obstruction. She was reported by Mr.Chapman in the discussion on stone at the 1948 Meeting of the British Association of Urological Surgeons, and was contrasted with another case of bilateral staghorn calculi in a male treated surgically. Post-operative x-ray examination of the latter showed no residual fragments, but about a year later he had attacks of colic and passed stones. He died from uraemia three and a half years later.

(c) Unilateral Branched, Unilateral Unbranched Calculi.

No helpful conclusions emerge from consideration of three cases. Two have died from other causes 4 and 7 years later. The third is alive and symptom-free 2 years after refusing operation.

Conclusions.

(1) Conservative treatment was completely justified in small bilateral non-obstructive stones since improvement was noted in 60 per cent. on review.

(2) Bilateral branched stones should be treated conservatively

if symptomless. Operation is only indicated for severe pain or unilateral infection. There is little to choose between the results with and without operation in these cases.

## Group VI. Mild Post-Operative Recurrences Treated Conservatively.

Recurrence is regarded as "mild" when stones are small, symptoms few, and secondary operation not indicated. During a review of the late results of operation in 1949, evidence of mild recurrence was discovered in 43 patients and their progress has been studied seven years later. Tracings of some examples of the latest pyeolograms are shown in Fig. 27, where it will be noted that the number in the renal pelvis indicates the length of time since the recurrence was detected. It is obvious from the pyelograms that the kidneys show no evidence of hydronephrosis.

The progress of the 43 patients is indicated in the Appendix, Table 19, page 20, which may be summarised thus:-

| | | |
|---|---|---|
| Improved, having passed stones | - | 13 |
| Unchanged | - | 25 |
| Operation required | - | 2 |
| Died - other causes | - | 3 |
| | | 43 |

Conclusions.

(1) Mild recurrences have the same hopeful prognosis as small untreated calyceal stones.

(2) Operation was required in two patients. It is imperative that they be reviewed regularly in case they grow rapidly and damage renal function beyond any hope of recovery. Expectant treatment can only be advised with a clear conscience if facilities are available for such a follow-up. The ideal method is a Stone Clinic.

## Group VII. Severe Post-Operative Recurrences Treated Conservatively.

The group to be considered consists of 29 patients who developed severe recurrence.

Recurrence is regarded as "severe" when secondary operation is indicated. The late results and sequelae of operative treatment, hardly constitute the natural history of the disease, but having acquired fresh stones, the 29 patients in question were treated expectantly for the following reasons:- Unfit (10), unwilling (10), waiting for operation (2), and untraced (7). Some were unfit in the sense that their general condition was too poor or their age too great. In others the presence of a branched stone in a solitary kidney prevented operative intervention owing to the risk of kidney failure. A typical example is shown in Fig.28 where a branched stone occupies the remaining portion of the right kidney, nephrectomy having been performed on the left side and resection of the lower pole of the kidney on the right. The patient is alive six years after operation, enjoys good health and has a blood urea of 45 mgm. per 100 ml. Seven were untraced and 22 have been followed for periods up to 22 years, 6 having died (5 from other causes; 1 from urinary cause). The results are not good (Table XVII). Kidney function is fair in 6 and poor in 12, i.e. impaired in 18 out of 22. General condition when first detected was good in 18, poor in 11. Symptoms were present in 20 of the 29 patients.

Comment and Conclusion.

An impression is gained that there is a difference in behaviour between large unilateral or bilateral stones arising de novo and those developing as post-operative recurrences. The recurrent stones progress more rapidly. Many of them have Proteus or Staph. Aureus infections, but this is not the sole determining factor as others may develop without urea-splitting organisms.

The gloomy picture presented makes one wonder that Priestley and Braasch thought recurrence of so little moment that they were prepared to take the risk of performing bilateral conservative operations, after which recurrence is acknowledged to be very common.

Infection in Renal Calculi Treated Conservatively.

The results of urine examination at the first visit and at subsequent review, have been analysed and compared in 223 patients treated conservatively. When first seen, 168 patients had sterile urines. At review the figure had risen to 180 of the 223 (80 per cent.). In the same way, of 55 patients who had infected urines when first seen, only 43 were infected at review.

The incidence of infection in the various clinical groups is closely related to the presence or absence of stone, e.g., where patients are free from stone only 10 per cent. are infected; where they continue to pass stones, 16 per cent.; where small stones are present, 40 per cent. and large stones are practically all infected.

Once again B.Coli predominated in 32 out of 43 (75 per cent.). Proteus was present five times in association with large branched stones.

## Conclusions.

Urinary infection does not necessarily develop in all cases treated conservatively. It is commonest where large stones are present.

The results are presented in detail in the Appendix, Table 20, page 21.

## Rate of Growth of Renal Calculi.

Joly considered that phosphatic stones grew most rapidly followed by cystine, uric acid and oxalate, in that order. He thought that the main factor in determining the rate of growth was the amount of stone-forming substance in the urine; that small stones grew less rapidly than large since there was a smaller surface area for deposition; and(for the same reason) that single stones grew more slowly in terms of total weight than multiple. Other factors to be considered are (1) Obstruction, particularly when slight and intermittent; (2) Infection, particularly when it is urea-splitting; and (3) Hyperparathyroidism, although this applies to a very small fraction of the total. Joly remarked that the best combination of circumstances for rapid stone growth was mild infection and slight obstruction.

The all-important point that emerges from this is that size by itself is not the main consideration. Within reason it does not matter how rapidly stones grow or recur. What does matter greatly is how much damage they cause to the kidneys, and in this sense the medium-sized, tightly-impacted stone is much more dangerous than the large, symptomless, mildly infected, non-obstructive staghorn calculus. The large stone is quite often found in a kidney with fairly good function, whereas the smaller obstructive stone leads to complete destruction of the kidney.

## An Appraisal of some of Joly's Statements.

Our knowledge of stone has been advanced so considerably by Joly's work, and such great authority attaches to all his writings, that it is with some reluctance that the following rather dogmatic statements of his are queried. In respect of large impacted stones there is a great deal of truth in them; but in the light of the present natural history studies, all of them require to be qualified to some extent, particularly in the case of small calyceal stones. The following observations appear on pages 192 and 194 of "Stone and Calculous Disease of the Urinary Organs":-

(1) "The majority of these stones become infected in the course of time." This is completely true of large branched stones but only 40 per cent. of small stones were infected when reviewed.

(2) "If a renal calculus is left untreated it sooner or later destroys the kidney in which it lies." While this is more or less true of large stones, it is definitely not true of small calyceal stones followed for many years.

(3) "Renal Calculus is a serious menace to life." In a series of 1,114 stone cases, 39 urinary deaths were recorded, 23 post-operative and 16 from uraemia, i.e., less than 4 per cent. of the total series died from the disease.

(4) "A stone that is not increasing in size is always lodged in a functionless kidney and cessation of growth is a bad instead of a good sign." This statement is undoubtedly true in respect of large branched stones or obstructive smaller stones, but it is doubtful if Joly would have been quite so emphatic about smaller stones had intravenous pyelography been available as a test of individual kidney function.

(5) "The most conservative treatment of renal calculus is an early removal of the stone." This very bald statement gives the impression that Joly thought operative treatment indicated in practically every stone. There would be no argument with his statement if the words "potentially obstructive" were inserted before "renal calculus".

It will hardly be disputed that the most conservative treatment of the <u>obstructive</u> or <u>potentially obstructive</u> stone is its early and complete removal by the least traumatic method. On the other hand, it is felt that there is a definite place for conservative management, with careful supervision, in the following groups of cases:-

(1) Small symptom-free calyceal stones with normal pyelograms.

(2) Large symptomless bilateral branched stones.

(3) Ureteric stones which are making satisfactory progress, providing there is no hydronephrosis, repeated attacks of colic, or severe infection.

## SUMMARY

Stimulated by the lack of information available, the natural history of upper urinary tract stone has been studied in a series of 568 stone patients not submitted to operation and in suitable cases,(also untreated) from the operation series.

1. The clinical progress of 1,394 stones formed in the kidney showed that 711 were retained in the kidney, while 683 entered the ureter.
2. Of 711 stones retained in the kidney, operative removal was performed in 534 (approximately 75 per cent.).
3. Of 683 stones entering the ureter, 521 passed, 146 (21 per cent.) required operative removal and 16 were under observation.
4. If the total number of stones passed is considered, it is

probable that more than 80 per cent. pass naturally. Watchful waiting is therefore recommended.

5. In a total of 521 stone-passers, 136 or 30 per cent, passed more than one stone.

6. The recurrence rate following endoscopic manoeuvres is 12.5 per cent.

7. Renal cases treated conservatively for more than 10 years showed that only 15 per cent. of those whose urinary tract was free from stone at first, had further symptoms, compared with 64 per cent. of those who retained stones.

8. Small calyceal stones in more than 50 per cent. of cases remained symptom free, only 20 per cent. increasing in size. Pyelograms have been normal in 75 per cent. after several years and in most the urine has remained sterile. An expectant attitude is therefore recommended for small calyceal stones if symptoms are absent and the pyelograms normal.

9. Of 33 large stones treated conservatively before operation, progress was slow in 30 (90 per cent.). There was no spread to the other side in the 25 unilateral calculi.

10. There is little to choose between the results of operative and expectant treatment in bilateral branched stones. In the absence of pain or severe unilateral infection a conservative attitude is advocated.

11. Small <u>recurrent</u> calyceal stones behaved in much the same (fairly benign) way as small primary calyceal stones. Large

recurrent stones had a worse prognosis than the corresponding primary calculi.

12. Urinary infection was present in only 10 per cent. whose urinary tract was clear, in 16 per cent. of those who continued to pass stones, in 40 per cent. with small stones and in 100 per cent. with large stones.

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PART III.

# THE RESULTS OF OPERATIVE TREATMENT OF UPPER URINARY TRACT STONE.

With special reference to

POST-OPERATIVE RECURRENCE.

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PART III.

## THE RESULTS OF OPERATIVE TREATMENT OF UPPER URINARY TRACT STONE.

The relative merit of any operative procedure may best be judged by the immediate post-operative course, in which the mortality and complications are the main considerations, and by the late results.

Recurrent stone-formation is one of the most important problems in the after-care of patients who have undergone surgical treatment for calculous disease. According to Joly (1929) the late results depend on:-

(1) Recurrence of the stone.

(2) The functional value of the kidney.

(3) Post-operative infection.

These three factors are so closely related and inter-dependent that the study of recurrent stone leads inevitably to consideration of the other two.

The patient submitting himself for operative treatment may reasonably anticipate relief from his symptoms; but this is, at best, of temporary benefit, unless steps can be taken to prevent the development of further stones, themselves requiring treatment. The thoughtful stone patient has every right to ask the following two questions:-

(1) How often do stones recur?

(2) What can be done to prevent recurrence?

In spite of the considerable volume of research devoted to the subject in the last 30 or 40 years, it is still difficult to give him an accurate answer about the incidence of recurrent stone, and even more perplexing to reply convincingly about its prevention. It is the object of the present investigation to attempt to answer the first of these questions, the other being considered in Part IV of this work.

## Section I. Method of Review.

Stone patients treated by operation were reviewed in 1949, 1951, and 1955. On each occasion fresh material was added until the present total of 546 patients was reached. Table XVIII indicates that 323 (60 per cent.) were treated in the Urological Department, 161 (30 per cent.) in the General Surgical Wards, and 62 (10 per cent.) elsewhere.

It is desirable that as many patients as possible should be interviewed and re-examined. Every effort was made to trace patients by postal questionnaire, Social Service Department visits, and by letters to their doctors. Once contact had been established, they were invited to attend for an interview and a simple examination.

Many of the patients treated by the Victoria Infirmary Surgeons had last been seen 20 or 30 years previously. It is therefore greatly to the credit of all who assisted in tracing them that only 38 of the total of 546 could not be found. This means that information of some sort is available for over 90 per cent. of all cases. In the Urological Department Series, in which only 10 patients were untraced, the follow-up is even better, - 96 per cent.

Even so, the important point is the number re-examined. In spite of the careful follow-up technique mentioned above, only 403 of the 546 patients (74 per cent.) were personally seen and investigated. This is a common and unavoidable factor in reviews of the present type.

Patients seen for the first time within the last year (32) have been excluded. Post-operative deaths numbered 23 - an incidence of 4.2 per cent. Information concerning 50 patients gained from questionnaire forms, Social Service visits, or letters from relatives, is valuable in terms of symptoms, but not helpful in assessing the incidence of recurrence, and it has therefore been omitted.

The present investigation is based on the 403 patients interviewed and re-examined. Of this total, 246 had been treated in the Urological Department, 99 by the Victoria Infirmary Surgeons, and 58 by surgeons elsewhere.

It is at once clear that the most reliable figures will come from the Urological Department series since all have been under the care of one surgeon and 80 per cent. have been interviewed (compared with 60 per cent. of the Victoria Infirmary Surgeons' patients). The group of 58 treated elsewhere, reported only when compelled to do so by symptoms. They therefore introduce a considerable bias towards recurrence - another reason for believing that the figures for the Urological Department are more accurate than the total. The other two groups provide valuable information, however, and are included. Throughout the part of this work devoted to post-operative recurrence, the results for the total number of cases re-examined (403) and the Urological Department series (246) will be compared and contrasted.

During the extraction of relevant data from case records, prolonged search was made for information on three vital points: (1) An immediate post-operative radiograph of the urinary tract to exclude stones left behind at operation; (2) an early post-operative urine examination; (3) stone analysis. Only in isolated instances had these investigations been carried out before 1945, but shortly thereafter they became established as standard practice in the post-operative management of patients.

The interview was conducted on the lines indicated earlier. The length of follow-up (interval since operation) was more than five years in 64 per cent., and more than ten years in 35 per cent. of those investigated.

The minimum investigations carried out were (1) a plain x-ray film of the urinary tract, and (2) bacteriological and cytological examination of the urine. Where symptoms or x-ray evidence of recurrence were present, more detailed investigation was undertaken on radiological and biochemical lines. A vigorous effort was made to investigate each case with pains-taking thoroughness so that not even the smallest recurrent calculus would escape detection.

## Section II. Operations Performed.

The operations performed fall into six well-defined groups designated as follows:-

(1) Pyelolithotomy: the stone was removed by a simple incision in the renal pelvis.

(2) Nephrolithotomy: this implies all operations in which renal parenchyma was incised. Hence it includes pyelonephrolithotomy in which a small cortical incicision down to the stone was made against the counter-pressure of a finger introduced through the renal pelvis; nephrostomy with removal of stones and drainage of the kidney; and pyélotomie élargie (Marion) in which the incision in the pelvis extended into kidney substance.

(3) Partial Nephrectomy: The upper or lower calyx was resected.

(4) Nephrectomy:

(5) Ureterolithotomy:

(6) Indefinite: precise information about the nature of the operation was not available.

Pyelolithotomy, nephrolithotomy and partial nephrectomy together, represent "conservative renal operations".

(A more detailed account of the operations performed is available in the Appendix Table 21, page 22.)

### The Incidence of Different Operations in Three Decades.

The number of operations performed per decade has steadily increased due, possibly, to a true increase in the incidence of the disease. This was noted by Hellström (1949) whose figures are reproduced in Fig.1 (See Volume II.). In the present series a total of 680 operations was performed in 546 patients. The numbers for the decades 1926-35, 1936-45, and 1946-55, were 105, 249 and 326 respectively.

The percentage incidence of the various types of operation is indicated in Fig.29, each column representing the percentage incidence of the particular operation in its own decade. Analysis is best achieved by individual consideration of the operative procedures.

Pyelolithotomy: It was with some surprise that a percentage decrease in the last decade was noted. The percentages in chronological order, 1926-35, 1936-45, 1946-55 (which is followed throughout) were 39.2, 41.8 and 28.5. One explanation is that partial nephrectomy is now the operation of choice for a dendritic calyceal stone or for a "nest" of small stones in a calyx. Another is the recent expectant attitude to borderline stones (less than 1 cm. in diameter) which would previously have been treated by pyelolithotomy, but which now impact in the upper ureter and require ureterolithotomy.

Nephrolithotomy: The steady decrease in the popularity of nephrolithotomy over the three decades (18.0, 14.0, and 3.4 per cent.) indicates the growing appreciation of the traumatic nature of the operation and the high recurrence rate associated with it. Hellström (1949) also made this point, and the operative techniques employed in Sweden over the period 1911-1947 are shown in Table XIX.

Partial Nephrectomy: The last decade has witnessed the advent of partial nephrectomy as an operative measure which offers a happy medium between simple removal of the stone and nephrectomy. It is indicated in patients who have a large dendritic stone or a collection of small stones in a calyx, and was used in 9.2 per cent. of cases.

Ureterolithotomy: The increasing use of ureterolithotomy through the decades (15.2, 20.4 and 25.5 per cent.) is probably due, as suggested above, to the expectant treatment of stones less than one cm. in diameter. Those with a rough surface become impacted and require removal. (In the upper third of ureter this may be accomplished through the triangle of Petit without division of muscles, Fig.30).

Nephrectomy: Much will be written later about modern trends in conservative renal surgery: but the percentage incidence of nephrectomy has risen in three decades from 16.2 and 13.0, to 26.0 per cent. The anomaly is due to the number of secondary nephrectomies necessary in patients found to have severe recurrence during this investigation.

Operations performed in the cases interviewed.

A total of 437 primary operations has been performed in the 403 patients interviewed, 34 having bilateral operations (Table XX) - 26 on both kidneys, 2 on both ureters, and 6 on one kidney and the opposite ureter.

## Section III. Early Results of Operation.

### Post-operative mortality.

The incidence was 4.2 per cent., 23 deaths occurring in 546 patients. Six occurred on the day of operation, 13 within four weeks, and 4 at later dates. In brief, 19 were urinary in origin, in the sense that they were due to operative shock, haemorrhage, or renal failure, and 4 were due to causes outside the urinary tract. The incidence in relation to the type of operation was:-

| | | | | | Per cent. |
|---|---|---|---|---|---|
| Pyelolithotomy | 4 | in | 238 | operations | 1.7 |
| Nephrolithotomy | 10 | in | 128 | do. | 8.0 |
| Ureterolithotomy | 5 | in | 150 | do. | 3.3 |
| Partial nephrectomy | 2 | in | 134 | do. | 1.5 |
| Nephrectomy | 2 | in | 30 | do. | 6.6 |

(Each post-operative death is detailed in the Appendix, Table 22, pages 23 and 24.)

### Comment.

The mortality associated with nephrolithotomy is another good reason why it should lose favour. Liberal incisions into renal substance cause considerable destruction of functioning nephrons, and secondary haemorrhage from infection is still a possibility, in spite of antibiotics. The International Congress of Urology in 1924 found (according to Joly) that the mortality from nephrolithotomy was 10.3 per cent., compared with 2.4 per cent. from pyelolithotomy.

The total post-operative mortality in this series (4.2 per cent.) is in agreement with that reported by Joly (1929) - 4.9 per cent; Barney (1922) 3.5 per cent; Quinby (1933) 3.3 per cent; Twinem (1937) 3.4 per cent; and Winsbury-White (1954) 4.6 per cent.

Early Post-operative Complications.

The common and important complications are:-

(1) Urinary leakage (35). Leakage occurred in 22 after uretero-lithotomy, 7 after pyelolithotomy and 6 after partial nephrectomy. Dix (1951) reported urinary leakage after 10 per cent. of ureterolithotomy for stone in the lower third and the experience in this series confirms that this is the worst point, since it occurred in 14 per cent. of patients undergoing lower ureterolithotomy. A fine continuous catgut suture is now used in an attempt to achieve watertight closure of incisions in the renal pelvis and ureter. In consequence, there has been less leakage after pyelo-lithotomy, but an appreciable number still leak after lower ureterolithotomy.

(2) Secondary nephrectomy for haemorrhage (5) - three after nephrolithotomy for the reasons mentioned above.

(3) Secondary nephrectomy for persistent fistula (8).

(4) Wound infection (15).

(5) Pseudo-recurrence (32).

(6) Pleural injury (5). Rapid lung expansion occurred in all.

(7) Injury to inferior vena cava (1) - with recovery.

(8) Lumbar hernia - only 2 of the 403 interviewed were affected.

The post-operative complications are listed in detail, according to the operations performed, in the Appendix, Table 23, page 25).

## Section IV. Late Results of Operation.

The principal complications encountered at a later date are:- (1) recurrence of the stone; (2) impaired renal function; and (3) urinary infection. The initial aim of this investigation in 1949 was an accurate assessment of the incidence of post-operative recurrence and of the factors related to it. It was hoped that the information obtained might have a practical application in the prevention of recurrence.

### Results of other investigations.

At the Annual Meeting of the British Association of Urological Surgeons in 1948, Professor John Hellström remarked that there had been surprisingly few investigations in recent years to determine the frequency of recurrence after operations for renal lithiasis. Table XXI indicates that the most modern studies of all aspects of recurrence before World War II were conducted by Twinem (1937), Oppenheimer (1937) and Spence and Baird (1939), who must have been given considerable food for thought by the fact that some 15 to 20 years had elapsed since the well-known investigations of Cabot and Crabtree (1915), Barney (1922), Braasch and Foulds (1923) and Brongersma (1924), without any significant reduction in recurrence rate. Swift Joly (1929) considered that Brongersma's report to the International Society of Urology in 1924 was the most complete and convincing review of the late results of the various operations for renal stone, and in many respects this is still true. His figures are worth recalling. Following 38 cases of pyelolithotomy, recurrence was present in 23.6 per cent. of sterile cases, compared with 50 to 54.8 per cent. of those infected. Hunner (1928), an enthusiastic advocate of urostasis and ureteral stricture as causes of stone-formation, followed 78 of 302 cases and found 9.5 per cent. recurrence after kidney operations. Higgins (1936) reported that his recurrence rate had been reduced from 16.4 to 4.7 per cent. by a strict dietary and follow-up regime. In a recent Hunterian Lecture Hamilton Stewart (1952) described the progress of 101 partial nephrectomies performed in the 13 years prior to the early part of 1950: he re-examined 87 of these and found recurrent calculi in only six (6.8 per cent.).

The very wide variations that may be expected from one investigation to the next is emphasised by the high incidence in two recent British papers which were in fairly close agreement (Sutherland, 1954 and Pyrah, 1954) and the very low rate found by Kairis, (1955).)

<u>Reasons for Widely-varying Recurrence Rates Reported in Different Investigations.</u>

In any careful and objective follow-up of stone patients, the accurate assessment of recurrence depends on the following five points:-

(1) The thoroughness of the investigation. It will be shown later that one-third of patients with recurrence are symptom-free and would therefore have been missed without radiological examination. In 1923 Braasch and Foulds depended largely on questionnaire follow-up, and it is significant that their recurrence rates are much lower than those of the other investigators of their day (Table XXI).

(2) The Length of time for which cases are followed. Oppenheimer (1937) followed his own cases for an average of 4 years only, but considered that a 10 or 15 year period would give more accurate figures. In this series, 17 per cent. of recurrences were detected after 10 years.

(3) The percentage traced and re-examined. Hunner (1928) re-examined 78 out of 302; Twinem (1937) 115 out of 252; and Kairis (1955) 39 out of 1,676; and their recurrence rates were all low (Table XXI). In the case of those dying since operation, the cause of death should be verified from the family doctor. In the present investigation 80 per cent. of the Urological Department cases have been re-examined.

(4) The exclusion of pseudo-recurrence. This may only be done by x-ray examination before the patient leaves hospital; otherwise there is no method of distinguishing at a later date between fresh stones and residual ones.

(5) The criteria of recurrence. Oppenheimer (1937) regarded a colic followed by the passage of a stone as a recurrence. Others maintain that this is recurrence due to the disease

and not to the operation. There can, however, be no certain way of distinguishing. All stone-formation after operation must therefore be regarded as recurrence.

Conclusion.

The greater the percentage traced, the longer the follow-up, and the more thorough the investigation, the higher is the recurrence rate.

It is obviously an unattainable ideal to trace, interview and investigate 100 per cent. of cases after 10 to 20 years, and invariably be able to distinguish between true and false recurrences; but the more those standards of perfection are approached the more accurate will recurrence rates be. The fact that his patients do not return complaining of colic or haematuria undoubtedly gives the surgeon a false sense of security. Kairis (1955) for example, re-examined only those who returned with symptoms. Only by regular review and thorough re-examination of as many cases as possible may an opinion be passed of the relative merits of the various operations and post-operative regimes.

The Incidence of False or Pseudo-Recurrence.

The reported incidence varies widely from one investigation to the next and depends entirely on the performance in every patient of a plain film of the urinary tract before they leave hospital. At one end of the scale Barney (1922) reported 45 per cent. and Nay (1928) 30 to 40 per cent; at the other end Quinby (1933) found only 3.3 per cent. and Braasch (1917) 4.4

per cent. There is even a hint of fatalism in the suggestion that all recurrences are due to tiny portions left behind at operation. This may be true enough in the sense that microscopic tubular calcification, microliths, and plaques remain behind, but immediate post-operative x-ray showed no opacity in 87.5 per cent. of cases in this series. False recurrence is taken to mean an opacity which can be appreciated naked-eye on a plain film. Benjamin (1931) who reported 25 per cent. pseudo-recurrence, found that it was quite possible to leave behind stones greater than 1.5 cm. in diameter.

The evidence of pseudo-recurrence in this series has been assessed by careful re-examination of x-ray plates taken immediately after operation in 175 patients (or roughly one-third of the 546 treated surgically). Stones had been left behind in 38 patients (22 per cent.). A fairer estimate was made by adding all patients who showed no opacity on x-ray examination several years after operation, and who had passed no stone in the intervening period. Under these circumstances it seemed unlikely that they had left hospital with residual stones, even though there was no immediate post-operative plate to prove it. This brought the total reviewed to 305 and the incidence became 38 in 305, or 12.5 per cent. (Table XXII). The incidence was 16 per cent. for stones in the kidney, and 6 per cent. for stones in the ureter. In the 403 patients interviewed, only 21 showed evidence of pseudo-recurrence, but information was available for less than 200 (10 per cent.).

The incidence of recurrence and its relationship to the various types of operation is stated in detail in the Appendix, Table 24, page 26. Briefly, the relationship of recurrence to different operations is:-

| | | |
|---|---|---|
| Pyelolithotomy | : | 12 in 119 (10 per cent.) |
| Nephrolithotomy | : | 13 in 44 (30 per cent.) |
| Partial nephrectomy | : | 4 in 27 (15 per cent.) |
| Ureterolithotomy | : | 6 in 104 ( 6 per cent.) - (five in the lower third of ureter.) |

<u>Cases illustrating Pseudo-recurrence.</u>

Pyelogram tracings before and after operation (Fig.31) illustrate four examples of pseudo-recurrence. Two merit discussion.

<u>Example (a).</u> A boy, aged 12, had a pelvic stone of moderate size, and scattered small calyceal stones in a poorly functioning pain-free kidney. Sacrifice of the whole kidney seemed too radical; removal of all the stones by resection of the lower calyx did not seem practicable, and the compromise was a series of cortical incisions against the counter-pressure of the little finger inserted into the calyces through the renal pelvis. A small fragment has been left and he may eventually come to nephrectomy.

<u>Example (b).</u> A paraplegic man, aged 45, had a gross scoliosis to the right side with a narrow ilio-costal space.

An approach via the twelfth rib bed was not particularly helpful. Small stones were scattered throughout all the calyces with a larger collection in the lower calyx, which was therefore resected. Through the renal pelvis and the neck of this calyx the kidney was thoroughly explored to the extent of a further incision through renal cortex, over the middle and upper calyces. X-ray control was not available in theatre or it might have been possible to locate and remove the remaining fragments.

Conclusions.

1. Pseudo-recurrence has been detected after 12.5 per cent. of the operations performed for upper urinary tract stone. In this respect nephrolithotomy has the worst record, the incidence of residual stone after it being 30 per cent. The surgeon tries to spare the kidney by conservative removal of multiple scattered stones. In the end, nephrectomy may be necessary on account of further large stones developing on the basis of pseudo-recurrence.
2. There are some cases in which it is humanly impossible to remove all the stones. It is wiser therefore not to make the attempt. Consideration of the radiograph of a kidney after removal in Fig.32 will at once make clear the difficulty of removing every tiny fragment of stone.
3. Radiographic confirmation that all stones have been removed is helpful (but technically bothersome) in the operating

theatre. During the operation it may give valuable guidance on reaching a decision regarding the operation indicated. Even with x-ray control, complete removal of the stones shown in Fig.32 would be impossible and the attempt to achieve it would be very damaging to kidney function.

4. All stone patients should have a plain film of the urinary tract before they leave hospital or, if this is omitted, when they report for check-up. Only in this way can pseudo-recurrence be distinguished.

Terminology of Recurrence.

True recurrence indicates fresh stone-formation since operation. False or pseudo-recurrence refers to stones left behind at operation. Contralateral recurrence means the development of fresh stones on the opposite side after operation. It does not include those present on the opposite side at the time of operation.

True recurrence has been further divided into mild and severe recurrence.

"Mild" and "Severe" Recurrence.

The disability caused by recurrence varies enormously from case to case and much the same applies to the subsequent progress ot those suffering from it. Some patients have no backache or haematuria, enjoy good health, and have a perfect work record. Those less fortunate are crippled by repeated bouts of colic or the passage of stones. Others require one or more secondary operations, ending sometimes in the loss of a kidney, or more rarely, in complete renal failure. On clinical grounds at least there has therefore seemed some justification for classifying recurrence as "mild" and "severe".

In the sense in which it is used in this investigation, severe recurrence indicates that secondary operation has in fact been performed, has been advised and refused, or has been considered unwise on account of the patient's general condition.

The patient illustrated in Fig.33 had bilateral severe recurrence, a staghorn left renal, and a massive right lower ureteric stone. His blood urea was 95 mg. per cent., and he leaked urine through bilateral lumbar sinuses, having had two conservative operations elsewhere on each kidney. Naturally, no surgical action was undertaken.

Size by itself is not necessarily the main index of the severity of recurrence. The medium-sized stone which is liable to become impacted in the ureter, leading to frequent bouts of colic, or hydronephrosis, or even anuria, is considered more serious than the large, immobile, symptomless, staghorn calculus, although the latter is also regarded as a severe recurrence.

The patient shown in Fig. 34 had a right pyelolithotomy and later a right nephrectomy for recurrent stone before she reported to the Urological Department with left renal colic. The plain film showed three medium-sized calculi, all of a suitable size for impaction in the ureter with the development of anuria. There was no hydronephrosis, but pyelolithotomy was performed as a matter of urgency.

Mild recurrence indicates one of the following possibilities:-

(1) Radiological demonstration on the side of operation of a stone (or stones) small enough to stand a reasonable chance of passing naturally. Where some doubt has existed about a shadow on the x-ray plate it has been regarded as a recurrent stone, particularly if the patient has experienced significant symptoms. Most commonly these tiny stones are locked away in a calyx, causing minimal discomfort to the patient, damage to the kidney, or threat to life. They are so small that the possibility of impaction in the ureter, with consequent anuria, is a remote one. Tracings of recent pyelograms exemplifying mild recurrence are shown in Fig.27.

(2) The development of similar calculi on the opposite side.

(3) The passage of a stone from either side since operation.

Summarising, then: Severe recurrence calls for secondary operative treatment. Mild recurrence does not.

Criteria of Recurrence.

Oppenheimer (1937), as already mentioned, had very strict criteria of recurrence. A colic followed by the passage of a stone was regarded as a recurrence, even if x-ray examination subsequently proved negative. Every effort has been made in this investigation to emulate these high standards.

Not all follow his example, however. Some feel that the passage of a stone on the opposite side cannot be considered a true recurrence due to operation. They maintain that such sequelae represent the appearance of the same disease elsewhere

(Kairis, 1955, Douillet, 1933). In their opinion, this fraction of recurrence is inevitable, in much the same way as cystoscopic treatment of lower ureteric calculi is followed by recurrence in 12.5 per cent. Nevertheless, to preserve uniformity of observation, they should be included in recurrence figures, since they constitute fresh stone-formation since operation.

Reliability of figures in various groups studied.

Before the incidence of recurrence and the factors related to it are discussed, attention is drawn once more to the differences that exist between the Urological Department series and the other groups (Victoria Infirmary Surgeons and Other Surgeons). A summary of the percentage true recurrence for the three groups in terms of patients, and of operations, will at once make the point clear.

| Percentage Recurrence | Urological Series. (246) | Vict.Infy. Surgeons. (99) | Other Surgeons. (58) | Total Series. (403) |
|---|---|---|---|---|
| Per operation | 26.0 | 51.4 | 71.4 | 39.4 |
| Per patient | 30.0 | 52.5 | 70.0 | 41.7 |

The favourable results in the Urological Department are not claimed to be due to any superiority in treatment, one hastens to add. The reasons lie elsewhere:-

(1) The Victoria Infirmary Surgeons' patients have been followed for longer periods and fewer have been traced.

(2) Patients treated by Other Surgeons have reported only when compelled to do so by symptoms. It is natural, therefore, that over 70 per cent. should prove to have recurrence.

(3) Urological Department cases have been followed more completely, but for shorter periods.

(The results shown above appear in greater detail in the Appendix, Table 25, page 27).

The Total Series (403 patients) represents a cross-section in that its recurrence rate lies between that of the Urological Department and the Victoria Infirmary Surgeons. The figures for the Urological Department Series and the Total Series run in parallel and will be studied throughout the remainder of this section.

## Section V. Post-Operative Recurrence.
## (Incidence and Relationships)

The following factors appear to be related to the incidence of recurrence:-

I. The type of operation performed.

II. The decade in which the operation was performed.

III. The development of contralateral recurrence.

IV. The presence of bilateral lithiasis.

V. The sex of the patient.

VI. The number who have symptoms with recurrence.

VII. The interval between operation and recurrence.

VIII. The size of the stones.

IX. The number of stones.

X. Pre- and post-operative urinary infection.

XI. Post-operative renal function.

XII. The composition of the stone.

XIII. Hyperparathyroidism.

XIV. Urinary calcium output.

The subject of recurrent stone involves many complex statistical analyses. Histograms have been constructed to make the arithmetical presentation as lucid as possible, without sacrificing accuracy. More detailed information is available in the Appendix, pages 21 to 47.

I. Relationship to the type of operation.

There is general agreement that the best operation is the one which ensures complete removal of the stones with as little damage to the kidney as possible and which is associated with a low recurrence rate. The results in the Total Series and in the Urological Series are presented separately so that comparisons can be made and general conclusions reached about the relative frequency of recurrence after the various operative procedures.

(a) Total Series. There were 437 primary operations in 403 patients (34 having had bilateral operations). If 21 pseudo-recurrences are omitted, 416 operations remain for study of the true recurrence. Fig.35 indicates the percentage incidence of no recurrence, mild recurrence, severe recurrence and total recurrence (i.e. the sum of mild and severe) following the different operations. The salient features are:-

(1) <u>The total recurrence</u> (shown at the extreme right) which may be summarised thus:-

| | Per cent. |
|---|---|
| All operations (including nephrectomy) ......... | 40.0 |
| Pyelolithotomy .............................. | 48.1 |
| Nephrolithotomy ............................. | 64.0 |
| Partial nephrectomy ......................... | 6.0 |
| Ureterolithotomy ............................ | 31.6 |
| Nephrectomy (contralateral recurrence).......... | 12.9 |
| Conservative operations (excluding nephrectomy). - not shown in Fig.35. | 46.0 |

(2) <u>Severe recurrence</u> closely parallels total recurrence, and is commoner than mild recurrence.

(3) <u>Mild recurrence</u> remains at a stable level apart from nephrectomy and partial nephrectomy.

(b) <u>Urological Series</u>. In similar fashion, there were 260 primary operations in 246 patients (14 having had bilateral operations). Omission of 14 pseudo-recurrences leaves for consideration of true recurrence, 246 operations.

The salient features of Fig.36 are:-

(1) <u>Total Recurrence</u>:- after:-

| | Per cent. |
|---|---|
| All operations (nephrectomy included) .......... | 26.0 |
| Pyelolithotomy .............................. | 34.0 |
| Nephrolithotomy ............................. | 50.0 |
| Partial nephrectomy ......................... | Nil |
| Ureterolithotomy ............................ | 27.5 |
| Nephrectomy (contralateral recurrence) ......... | 7.9 |
| Conservative operations (nephrectomy excluded).. | 31.0 |

The percentage incidence for conservative operation, i.e., all except nephrectomy, once again does not appear in Fig.36.

(2) This time, <u>mild and severe recurrence</u> both run parallel to the total recurrence and mild recurrence is, if anything, the commoner.

(Statistics relating to the two series are given in much greater detail in the Appendix, Tables 26, 27, 28 and 29, pages 28, 29, 30 and 31.)

In passing, a striking similarity is noted between the recurrence rates of the Urological Series and those lately published by Pyrah (1954). He found recurrence in 34.9 per cent. after pyelolithotomy, 60 per cent. after nephrolithotomy and 20.9 per cent. after ureterolithotomy.

<u>Conclusions and Comparisons</u>. (Recurrence rates for the Total Series are always quoted before those for the Urological Series.)

1. In accordance with the experience of other investigations, nephrolithotomy had the highest recurrence rate (64 and 50 per cent.). The reasons are obvious. Greater trauma is inflicted during the operation and quite considerable areas of parenchyma lose their blood supply when deep mattress sutures are used to control bleeding and coapt the edges of the wound in the kidney.
2. Pyelolithotomy (48 and 34 per cent.) was slightly better, but not outstandingly so. Ureterolithotomy (32 and 28 per cent.) was in the same category.

3. Partial nephrectomy had a low incidence of recurrence (6 per cent. in the Total Series and none in the Urological Series). This depended on the proper selection of cases and the complete removal of the calyx and all the stones.
4. If nephrectomy is excluded, and the remaining five operations are regarded as "conservative operations" the recurrence rates were 46 and 31 per cent.
5. The figures for the Urological Series were better for reasons which have already been discussed (p.102), and severe recurrence (requiring secondary operation) was less common in it. No matter which series is considered, the results present a gloomy picture, and study of them does not leave much room for complacency. It is no consolation to say that they were discovered because of the strict standards observed in the investigation.
6. A further possible explanation for the higher rates in the Total Series is that the older cases did not then have the benefit of many of the facilities now taken for granted. Few of them had routine post-operative urine examinations and at that time modern antibiotics were not available. Urinary infection must therefore have persisted for years unchecked. Biochemical departments were in their infancy and little attempt was made to detect and correct known aetiological factors, e.g., metabolic upsets and hyperparathyroidism. Cases were seen after operation only if symptoms recurred, and routine follow-up was not practised. This contributing

factor is emphasised when we consider:-

II. Relationship to the decade in which the operation was performed.

The incidence of recurrence following 416 primary operations (21 pseudo-recurrences having been excluded) was studied for the three decades 1926-35, 1936-45 and 1946-55. The results are given as histograms for the various types of operation (Fig.37). (More detailed figures appear in the Appendix, Tables 30 and 31, pages 32 and 33).

Results.

Analysis of Fig.37 shows that, apart from ureterolithotomy, there has been a marked decrease in post-operative recurrence in the last decade, (percentages are given in the chronological order - 1926-35, 1936-45, and 1946-55 all through).

Total operations: 55.6; 55.2; and 18.7 per cent.

Conservative renal operations, (i.e., pyelolithotomy, nephrolithotomy and partial nephrectomy combined); 67.4; 71.9; and 25.8 per cent.

Ureterolithotomy: 20.0; 52.6; and 18.2 per cent.

Nephrectomy: 41.7; 22.0; and 6.0 per cent.

The only anomalous and unexplained finding was the sudden increase in the recurrence rate for ureterolithotomy for the decade 1936-45.

Conclusion.

Even allowing for the shorter period of follow-up, there has been a definite reduction over the years, and particularly in the last decade. This is attributed to:-

(1) the arrival of chemotherapeutic and antibiotic methods of treating urinary infection,

(2) a deeper appreciation of aetiological factors and the need for regular follow-up, and

(3) the adoption of some type of post-operative prophylactic regime.

III. Contralateral recurrence.

There are certain cases of upper urinary tract stone in which there is no difficulty in deciding that nephrectomy is the correct operation. This is so where a staghorn calculus occupies the pelvis and most of the calyces of a non-functioning kidney, or where advanced pyonephrosis or hydronephrosis has supervened in lesser degrees of stone-formation. Conversely, there are many cases of stone in which pyelolithotomy is just as obviously the ideal procedure. Between these clearly defined extremes there are quite a few border-line cases in which it is by no means easy to decide which is the correct course to adopt. Is it better to remove the kidney in the hope that this will end the stone-forming process or should the 40 per cent. risk of recurrence shown to accompany conservative procedures be taken so that functioning renal tissue may be conserved? In the past the tendency has been to advocate nephrectomy for these doubtful cases, since it was believed that contralateral recurrence rarely, if ever, occurred.

Consideration of the Appendix, Table 32, page 34, and of the summarised version below will show how unfounded is this impression.

| <u>Total Series.</u> | <u>Per cent.</u> |
|---|---|
| Contralateral recurrence after conservative operations | 9.2 |
| Contralateral recurrence after nephrectomy | 12.9 |
| <u>Urological Department Series.</u> | |
| Contralateral recurrence after conservative operations | 7.7 |
| Contralateral recurrence after nephrectomy | 7.9 |

Pyrah (1954) found 15.4 per cent. after conservative operations and 15.9 per cent. after nephrectomy.

The widely differing figures reported by other investigators are shown in Table XXIII. Oppenheimer (1937) found involvement of the opposite kidney in 15.1 per cent. after conservative operations and in 14.8 per cent. after nephrectomy, and Hellström (1933) in 6 to 15.5 per cent. after conservative operation and 10 to 11 per cent. after nephrectomy, results that agree fairly closely with those of this series.

Most writers state that bilateral stone is present in 10 to 30 per cent. of their cases. The original stone-forming factor is therefore at work on both sides in a fair proportion of cases, and this makes it easier to accept the fact that contralateral recurrence is almost as common after nephrectomy as after conservative procedures. It is equally difficult to reconcile the low contralateral recurrence rates (0 to 4.2 per cent.) reported by some (Brongersma, 1924; Rovsing, 1924; and Twinem, 1937), with the high recorded incidence of bilateral stone (10 to 30 per cent.). In Oppenheimer's words: "Why is recurrence after nephrectomy so low, then, if the incidence of bilaterality is so high?"

The work of Eliot (1910) and Cahill (1935) who studied cases of calculus anuria, provides further indirect evidence that recurrence after nephrectomy is not so uncommon as was at one time thought. Eliot found that 23 of his 32 cases (72 per cent.) had previously been subjected to nephrectomy, and Cahill that the same applied to 128 out of 377 of his cases (34 per cent.).

Conclusion.

Ablation of the kidney is no guarantee of immunity from recurrence. Where doubt exists it is therefore wise to err on the conservative side. Partial nephrectomy quite often appears to offer a happy intermediate solution to this difficult problem.

IV. Relationship to Bilateral Calculi.

Bilateral stone constitutes a perplexing problem which has such highly characteristic and individual features that its management is considered in detail in Part V. of this work. The incidence of post-operative recurrence in bilateral calculi is considered at this point to serve as a contrast to the unilateral cases.

Operation was necessary in 96 out of a total of 149 bilateral stone patients. Primary operations totalled 130, i.e., 34 patients had bilateral operative treatment.

Not all of the patients had bilateral calculi when first seen or submitted to operation, e.g., "recurrence after nephrectomy" indicates that nephrectomy was performed when the opposite side was free from stone, and the recurrence developed later in this remaining kidney.

Summary of Results.

Recurrence followed conservative renal operations in 72.4 per cent., ureterolithotomy in 37.5 per cent., and nephrectomy in 53.0 per cent. The corresponding figures for the Total Series were 46.0, 31.6 and 12.9 per cent. respectively - a much lower rate. The results are represented in Fig.38, the percentage recurrence rates being printed at the head of each column. (See also the Appendix, Tables 33 and 34, pages 35 and 36.)

Conclusion.

The recurrence rates are very much higher than for the Total Series. This is not in the least surprising, since bilateral stone represents an advanced state of the disease in which it is not uncommon to find the patient, sooner or later, with recurrent stones in a solitary kidney. Calculous anuria is then a constant threat, particularly if the stone is of a suitable size to produce obstruction. The point is well illustrated by the following example:-

Case History of Calculous Anuria after Multiple Stone Operation.

| | |
|---|---|
| | Male, aged 44. |
| 5. 4.44. | Left pyelolithotomy. |
| 25. 4.44. | Right pyelolithotomy. |
| 16.11.47. | Right pyelolithotomy. |
| 22.11.49. | Reviewed in this investigation. Small stones were present in both lower calyces, those on the left side being larger (Fig.39a). Function was good on both |

sides and the pyelograms were normal (Fig.39b). Left inferior calycectomy was advised and refused. Persistent Staph.Aureus urinary infection was present.

14. 5.51. Admitted with left renal colic. A large branching pelvi-calyceal stone and scattered small calyceal stones were present in the left kidney which was now functionless (Fig.40c). A reversed albumin/globulin ratio suggested the advisability of sternal marrow puncture and radiography. Both appeared to confirm the presence of multiple myelomatosis. For this reason, treatment was expectant.

16. 1.56. Reviewed (after his doctor had confirmed he was still living). Skeleton now normal. No change in the calculi.

20. 3.56. Left nephrectomy.

2. 8.56. Admitted with calculous anuria. The small stone on the right side had escaped from the lower calyx and was now impacted in the upper ureter (Fig.39d). Immediate ureterolithotomy and drainage of the kidney was performed (his fifth operation). Studies of calcium metabolism in convalescence suggested the possibility of hyperparathyroidism. He will be admitted for further investigation.

Comments.

(1) Earlier partial nephrectomy might have saved the left kidney. If he had been seen at six-monthly intervals the rapid progress would have been noted. The need for a Stone Clinic in which thoughtful and leisurely follow-up can be conducted, is apparent.

(2) The radiological and haematological evidence of multiple myelomatosis cannot be explained.

(3) He may represent a missed case of hyperparathyroidism. If so, removal of the adenoma may be expected to prevent further recurrence and halt the deterioration of renal function associated with hyperparathyroidism (Albright and Reifenstein, 1948).

## V. Relationship to Sex.

Reference to Figs. 40 and 41 shows at once the marked sex difference. In general, men are affected by recurrence twice as frequently as women. The difference is least marked after conservative operations (Male:female = 55.7 : 41.5 per cent. in the Total Series, and 39.7 : 22.6 per cent. in the Urological Series), and most marked after ureterolithotomy (Male:female = 38.6 : 14.3 per cent. in the Total Series and 36.7 : 5.0 per cent. in the Urological Series). (Detailed figures are given in the Appendix, Tables 35 and 36, pages 37 and 38.)

Conclusion.

Recurrence is almost twice as common in men as in women. The finding is a constant one for the two series studied and the same tendency is shown, in greater or lesser degree, for each operative procedure. It was also reported in a previous investigation (Sutherland, 1954) when fewer patients had been studied. There has been no change as the number investigated has increased.

Further reflection suggests that this sex incidence of recurrence is anomalous in two respects:-

(1) It has been shown previously (page 20) that 60 per cent. of women with stone require operative treatment, compared with 40 per cent. of men. In spite of this higher initial potential in women, fewer of them develop recurrence than men.

(2) Upper urinary tract infection is commoner in women, and infection plays an important part in recurrence. Women ought therefore to develop recurrence more frequently than men.

Bladder neck obstruction could hardly have been responsible for the higher male incidence as two-thirds of the men were in the age groups, 25 to 55.

VI. Relationship to Symptoms.

The fact that just over one-third were free from symptoms is demonstrated in Table XXIV.

Information was available concerning 132 patients with recurrent stone (60 with mild and 72 with severe recurrence). Almost exactly the same percentage in each group was symptom-free, and it is therefore obvious that information gained by questionnaire is of very little real value. Hellström (1949) also found that one-third of his recurrences had no symptoms.

The patient illustrated in Fig.42 is a good example of "silent" recurrence. A single stone had been removed from the left renal pelvis 28 years previously. There was no reason to think that the removal had been anything other than complete. Reviewed in April 1956, he had no urinary symptoms and enjoyed good health. A single stone of moderate size was present in the left renal pelvis and two smaller stones lay in the left upper minor calyces. How long these stones had been present it was impossible to judge. In any case, kidney function was good and the pyelograms were within normal limits, in spite of the presence of stones for some years. Operation was advised, even although he was symptom free, because the stone in the renal pelvis was potentially obstructive. With some reluctance he consented and resection of the upper calyx combined with pyelolithotomy was performed.

The outstanding features of this case are:-
(1) The total absence of pain; (2) the length of time the stones had been present; (3) the unimpaired renal function, and (4) the fact that he would have been overlooked had he not been reviewed.

Conclusion.

Approximately one-third of recurrences are symptomless and would be missed without radiological examination. Follow-up by questionnaire reply is therefore unreliable.

VII. The Interval between Operation and the Detection of Recurrence.

Accurate determination of the interval between operation and recurrence is almost impossible without serial radiography at monthly intervals, because one-third of the recurrences are symptomless. All that can be stated with confidence at present is the interval between operation and the detection of recurrence.

Results.

This interval has been calculated in 161 of the 167 recurrences, and presented in histogram form in Fig.43. The majority of recurrences have been brought to light by the end of seven years, but appreciable numbers elude discovery for periods up to 30 years. The actual figures are that 74 (46 per cent.) are discovered after five years and 27 (16.8 per cent.) after 10 years. Greater detail is provided in the Appendix, Table 37, page 39.

Conclusions.

(1) There is therefore no evidence in this series to support the theory that the optimum time for recurrence is between the first and third post-operative years (Higgins, 1938), and that the likelihood becomes less thereafter.

(2) If the period of follow-up had been less than five years, 46 per cent. of the recurrences would have been missed; and if it had been less than 10 years, nearly 17 per cent. would have escaped detection.

To emphasise this point, two cases, both symptom-free in spite of recurrence, are discussed. The first is an example of very early recurrence, the second of very late recurrence. Neither would have been diagnosed without re-examination.

Example of Early Bilateral Recurrence.

By contrast, the patient illustrated in Fig.44 shows early extensive bilateral recurrence, again quite symptomless. On 3.4.55 a single phosphatic stone was removed from the left renal pelvis. There was no radiological evidence of pseudo-recurrence. Studies of calcium and phosphorus metabolism revealed no abnormality and his urine was sterile.

Routine review on 15.3.56 showed bilateral branched recurrent stones, more extensive on the left side. (Fig.44). Kidney function was poor on both sides. Urine examination showed infection with B.Proteus.

Comment. The Proteus infection undoubtedly has had much to do with the rapid recurrence. The infection is almost certain to persist until the stones are removed, but operative removal might in this instance do more harm than good. Treatment will therefore be expectant unless he has pain or unilateral infection.

The problem of recurrent stone in a solitary kidney is one of the most difficult in Urology.

<u>Example of very Late detection of Recurrence.</u>

Male, aged 70 in 1955.

1906. Stones had been removed from the left kidney. He was then aged 20, and was informed that the stones had been completely removed.

1936. Thirty years later, having had no urinary symptoms meanwhile, investigation of "lumbago" revealed recurrent left calculi.

27. 2.52. First seen at the Urological Out Patient Department complaining of painless haematuria. There had been no lumbar pain or colic since 1936. Moderately active chronic fibroid phthisis was present:
I.V.P. showed several medium-sized stones in the left pelvis and calyces, which were slightly distorted and dilated. Function was good, and there was no hydronephrosis in spite of the fact that the stones were likely by their size to become impacted in the ureter. (Fig.45a - only plain film available.)
Urine: Alkaline, frequent R.B.C., no increase in W.B.C., sterile.

Operation was not advised on account of his age, chest condition, and relative freedom from symptoms.

16.11.55. Asked to attend for review. No pain, haematuria, or stones passed. General health excellent. Now aged 70. I.V.P. showed little change in the size or number of the stones. Kidney function was still good, but the hydro-nephrosis was a little more advanced. (Figs.45b and 45c). Urine: Amphoteric, frequent leucocytes, Staph.Aureus. Blood chemistry normal.

<u>Comment.</u> This patient represents the longest follow-up of the series. It is now 50 years since his operation, and he has been known to have recurrent calculi, causing minimal symptoms for the last 20 years, and they may

well have been present for many years before that. The stones were first detected 30 years after operation, and, had it not been for the "lumbago" and painless haematuria would have been completely overlooked. They have done very little damage since 1936, and there has been very little change in the pyelogram in the last six years. The absence of pain and hydronephrosis is most striking in view of the size of the stones.

VIII. Relationship to Size of Stone.

Information regarding the incidence of recurrence is available in 355 patients in whom the size of the stone was known. It is detailed in the Appendix, Table 38, page 40, and represented as a histogram in Fig.46.

Results. If the total of 355 is considered, recurrence affected only 27.9 per cent. of large stones, compared with 39.4 per cent. of small. The fallacy in this assessment lies in the fact that many of the large stones were treated by nephrectomy. When conservative operations alone are considered, recurrence affects 51.2 per cent. of large, compared with 40.9 per cent. of small stones.

Conclusion.

There is evidence that large stones are more likely to recur than small ones, but the difference is less marked than might have been expected.

It is possible to imagine circumstances in which either small or large stones might be associated with recurrence, but these introduce extraneous considerations, e.g., number of stones, presence of urinary infection, and many of the other factors at present under discussion.

## IX. Relationship to Number of Stones.

In the same 355 patients information was obtained regarding the relationship of recurrence to the number of stones. This is represented in histogram form in Fig.46, from which it is obvious that there is a steady increase in percentage recurrence as the number of stones per patient rises. This time the recurrence rates for the total operations and for conservative operations ran parallel. In brief, the percentage recurrence in all operations was 31.3 for single stones and 45.9 for multiple stones; and in conservative operations it was 37.2 for single stones, compared with 59.4 for multiple.

(See also the Appendix, Tables 39 and 40, pages 41 and 42.)

### Conclusion.

The incidence of recurrence increases in direct proportion to the number of stones present. Difficulties always arise with a broad generalisation of this nature. A single large branching stone occupying a calyx might easily be a fruitful source of recurrence unless treated by partial nephrectomy.

Oppenheimer (1937) found recurrence after pyelolithotomy in 12 per cent. of single stones, and in 23.5 per cent. of multiple stones.

## X. Relationship to Urinary Infection.

### (a) Pre-operative Urinary Infection.

Reference has already been made to the significance of pre-operative urinary infection. (Part I, page 39 ) and it has been shown (Table VII, Vol.II.) to have a definite relationship to post-operative recurrence. Only 20.3 per cent. with initially sterile urine recurred, compared with 45.1 per cent. who had urinary infection.

(b) Post-Operative Urinary Infection. (Appendix Table 41, p.43).

1. Early. Examination of 149 patients soon after operation, and at long—term follow-up, confirmed that only 8.5 per cent. of those with a sterile urine recurred compared with 61.2 per cent. of those with infection. Conversely, only 25 per cent. of those with no recurrence had early post-operative urinary infection, compared with 85.4 per cent. of those with recurrence.

2. Late. Urine examination at follow-up confirmed these findings in 350 patients who were interviewed: Of those with sterile urine only 17.3 per cent. had recurred, compared with 66 per cent. of those with infection. Conversely, infection was present in 19.8 per cent. with no recurrence, compared with 68.8 per cent. of those with recurrence.

Conclusion.

There is a close relationship between pre- and post-operative urinary infection and the incidence of recurrence. From the practical viewpoint it is apparent that early eradication of infection makes the possibility of recurrence less likely.

Other Views Regarding Significance of Infection in Recurrence.

Joly regarded urinary infection as of greater importance even than recurrence itself.

Brongersma (1924) was so impressed by the importance of infection in recurrence that he classified his cases as sterile and infected. Recurrence after pyelolithotomy was found by him in only 16.6 per cent. of sterile cases compared with 50 per cent. of infected cases, and after nephrolithotomy in only 16.1 per cent. of sterile cases compared with 54.8 per cent. of infected. Oppenheimer (1937) reported 12.5 per cent. recurrence in sterile stones, and 33.3 per cent. in those grossly infected. In 1929 Hellström detected recurrence on the side of operation in 11.4 per cent. of sterile cases and in 45.5 per cent. of infected, and Rovsing (1924) stated that 68.8 per cent. of his recurrences were associated with urea-splitting infection and that only 15.9 per cent. occurred in the presence of a sterile urine.

(c) The Infecting Organism.

In 161 instances where organisms were grown, B.Coli was present alone in 88, and in 50 of these 88, recurrence took place (just under 60 per cent.). Alone or in mixed infection, B.Coli was present in 111 patients. Proteus was associated with recurrence in 16 out of 19 (90 per cent.) and Staph.Aureus in 13 out of 17 appearances, (80 per cent.). These observations are given in detail in the Appendix, Table 42, page 44.

Conclusions.

(1) Numerically, B.Coli is of significance, and it is associated

with recurrence in 60 per cent. of its appearances.

(2) The urea-splitters, Staph.Aureus and Proteus, were less frequent - 35 out of 161; but when they did appear they were associated with recurrence in 80 to 90 per cent. Fig.47 illustrates the type of staghorn calculus associated with unchecked B.Proteus infection. Five years previously (when operation had been refused) the stone was of moderate size and confined to the lower calyx.

Views of other Investigations on Significance of Organism.

Opinion is sharply divided on the importance of B.Coli infection in stone-formation, original and recurrent. Joly stated that he had never known of any case in which recurrence was associated with B.Coli infection alone. Twinem (1937) found that B.Coli was the commonest organism in his series, followed by Proteus and Staphylococci. In the 10 severest recurrences, however, Proteus was the organism responsible in six. Illyes (1934) considered that B.Coli was capable of initiating coral stones, but Rovsing (1924), Swift Joly (1929) and Winsbury-White (1936) failed to confirm this finding. Some strains of B.Coli are urea-splitting according to Hellstrom (1938), who qualifies this by adding that most B.Coli infections in stone cases are secondary to the Staphylococci which can be found in the organic nucleus. He advocates that the centre of each calculus should be stained for organisms during chemical analysis.

The importance of the urea-splitting Proteus and Staph.

Aureus in recurrence has long been recognised (Higgins, 1939; Heyser, 1934; Rovsing, 1924; and Twinem, 1937). Higgins found that Proteus and Staph. Aureus were the commonest organisms in 54 infected cases in a series of 72 recurrences. Smith (1937) described B. Proteus as "Public Enemy Number One".

## XI. Post-operative Renal Function.

The impression that the size of a recurrent stone is the main criterion of the severity of the recurrence is very far from the truth; in point of fact, the small obstructive stone can do more harm, in a much shorter period, than the larger non-obstructive stone. By the same token, operative treatment has failed in its primary purpose or has been carried out too late, if renal function does not speedily return to normal thereafter.

Renal function post-operatively was determined by intravenous pyelography in 196 patients, approximately one half of the 403 interviewed. The results are presented in detail in the Appendix, Table 43, page 45, and a Summary to that Table appears on page 46 of the Appendix.

### (a) Relationship of Post-operative Renal Function to Recurrence.

Four grades of renal function were recognised:-

1. Normal.
2. Early hydronephrosis; function good.
3. Moderate hydronephrosis; function fair.
4. Severe hydronephrosis; function poor.

**RESULTS.** The results are summarised as percentages below:-

TABLE XXV. RELATIONSHIP TO RECURRENCE.

| | | Normal | Early Hydroneph. | Moderate Hydroneph. | Severe Hydron. or Poor Function. |
|---|---|---|---|---|---|
| No recurrence | 100% | 84.8 | 7.6 | 6.3 | 1.3 |
| Mild recurrence | 100% | 70.7 | 12.2 | 4.9 | 12.2 |
| Severe recurrence | 100% | 19.7 | 7.9 | 18.4 | 54.0 |

Analysis and Conclusions.

(1) Large percentages of those with no recurrence, or mild recurrence, had normal pyelograms (84.8 and 70.7 per cent. respectively).

(2) Poor function was found in 54 per cent. of severe recurrence, compared with 1.3 per cent. with no recurrence.

(3) The fact that 12.2 per cent. of so-called mild recurrences had poor function led to their being re-classified as severe recurrences (even though the stone was small), and in some instances to corrective surgical treatment. Mild recurrences with normal pyelograms and no symptoms, on the other hand, have been treated expectantly.

(b) Relationship of Post-operative Renal Function to Operation Performed.

The results are detailed in the Appendix, Table 43, page 45, and summarised below in Table XXVI. This time the results are expressed as numbers (not percentages).

RESULTS.

TABLE XXVI. RELATIONSHIP TO TYPE OF OPERATION.

| Operation | Total Number | Normal | Early Hydroneph. | Moderate Hydroneph. | Severe Hydroneph. or No Function. |
|---|---|---|---|---|---|
| Pyelolithomy | 108 | 61 | 8 | 12 | 27 |
| Nephrolithotomy | 29 | 10 | 5 | 7 | 7 |
| Partial Nephrec. | 18 | 12 | 1 | 1 | 4 |
| Ureterolithotomy | 41 | 28 | 3 | 1 | 9 |

Analysis and Conclusions.

(1) Ureterolithotomy caused least damage to renal function.

(2) Pyelolithotomy and nephrolithotomy were more harmful; after each of them poor kidney function was noted in 25 per cent of patients.

(3) Partial nephrectomy was disappointing in 4 out of 18 cases, and had obviously been used ambitiously but unwisely to treat cases for which nephrectomy was indicated.

(c) Relationship of Renal Function to Calculous State.

Table XXVII is included to show the effect on the kidney of the presence or absence of stones. Severe recurrence had already taken place. Some were cleared by open operation; others had small stones still present in the kidney; and others still had severe recurrence.

Conclusion.

It is at once obvious that renal function is much better in those kidneys which are now clear of stones, or have re-formed only small stones; and very much worse in those whose severe recurrence persists untreated.

XII. Relationship to Composition of Stone.

Information relating recurrence to stone composition was available in 122 patients. The results are detailed in the Appendix, Table 44, page 47, and may be summarised thus:-

Results.

| Composition of Stone. | | Recurrence per Cent. |
|---|---|---|
| Pure calcium oxalate | (44) | 22.7 |
| Pure calcium phosphate | (24) | 33.3 |
| Oxalate-containing | (84) | 19.0 |
| Phosphate-containing | (75) | 21.3 |

Analysis and Conclusions.

1. Of the total of 122, only five did not contain calcium.
2. There is slight evidence that recurrence is commoner (so far as operation cases are concerned) in phosphate stones. Twinem supported this view. On the other hand, the majority of small stones passed naturally were oxalate in type.

Other views.

The value of analysis in devising a prophylactic regime has been emphasised by Higgins (1936). Other are less confident: less than 50 per cent. of the United States' Urologists thought stone analysis of value in the recent survey (Burkland and Rosenberg, 1955).

Twinem (1937) found that recurrence was more probable with phosphate than with oxalate stones (Table XXVIII). Hellstrom (1938) emphasised that bacteriological examination of the organic nucleus was equally as important as chemical analysis of the stone. More than half of 220 stones analysed by him showed traces of ammonium magnesium phosphate. He found oxalate or oxalate-phosphate stones present in 63 per cent. of cases, phosphate in 5 per cent., infective in 22 per cent., and other types of stones in 5 per cent.

XIII. Relationship to Hyperparathyroidism.

Estimation of the serum calcium, serum inorganic phosphorus, serum alkaline phosphatase and plasma proteins was routinely performed in stone patients admitted for surgical treatment, and in as many as possible of the recurrent cases reviewed as out-patients. Urinary calcium and phosphorus output were estimated on a fixed low intake. In suspicious cases the full calcium balance in urine and faeces was carried out.

Since 1951, six cases of hyperparathyroidism have been diagnosed, and they are considered at greater length in the part of this work devoted to Biochemical Studies. The incidence of hyperparathyroidism for the complete series of 1,114 stone patients is therefore 0.5 per cent. Biochemical studies have been performed in only 210 patients, however, and the incidence in them is 3 per cent. The six patients in question all had post-operative recurrence (mild in two, and severe in four), and 76 cases with recurrence were examined biochemically. The incidence in recurrence is therefore 8 per cent.

Conclusion.

Hyperparathyroidism has a definite relationship to recurrence, but the patients affected by it represent only 8 per cent. of those with recurrence.

XIV. Relationship to Calcium Hyperexcretion (Idiopathic Hypercalcuria).

During their convalescence from operation the urinary calcium excretion of stone patients was measured for three consecutive 24 hour periods, after they had been six days on a fixed low-calcium intake. On an intake of 150 mgm. of calcium per day, a urinary output in excess of 200 mgm. is regarded as significantly increased (hypercalcuria).

Results.

A detailed account of these appears in Part VI (Biochemical Studies of Stone).

Information is available about 62 patients submitted to operation:-

Of 22 cases without recurrence, 11 or 33 per cent. had hypercalcuria.

Of 29 cases with recurrence, 15 or 52 per cent. had hypercalcuria.

Seven patients with recurrence had a raised urinary calcium, judged by the (admittedly rough) Sulkowitch test. If these are added it means that 22 out of 36 recurrent cases (i.e., 61 per cent.) had hypercalcuria.

Conclusions.

(1) There is a definite relationship between hypercalcuria and

stone-formation in general. It is commoner in patients with post-operative recurrence than in those who have no recurrence.

(2) Apart from six cases of hyperparathyroidism, no cause was evident for the raised calcium output (idiopathic hypercalcuria).

(3) It is impracticable to treat them with calcium and vitamin D as recommended by Albright and Reifenstein (1948), since this might produce further stones.

## Discussion on the Incidence of Recurrence and the Relative Importance of the Various Related Factors.

This seems a suitable moment at which to stand back from the mass of figures relating to post-operative recurrence, in order to view the whole picture and form some general impressions.

The outstanding point is the high recurrence rate revealed by the investigation; but when it is recalled that our knowledge of the underlying aetiology of stone is exceedingly scanty, the wonder must surely be that recurrence does not follow every operation for stone.

The factors associated with recurrence, which have been studied above at some length, advance a certain distance only along the road to the final solution of the problem. No progress will be made beyond that point until more is known of the underlying aetiology.

In the meantime, our concern must be to decide which of the factors are common, and what is even more important, which of them are capable of correction. These may then, in our imperfect state of knowledge, be described as the "aetiology of recurrence".

(1) The operation itself is important in two respects. Firstly, incomplete removal of the stones, which accounted for approximately 10 per cent. of all recurrences, is, to a large extent, preventable. Secondly, nephrolithotomy is rarely justifiable on account of its higher post-operative mortality and morbidity, and its more frequent association with pseudo- and true recurrence. It should be avoided if possible.

(2) The higher recurrence in bilateral stone is in the nature of the disease, and therefore beyond our control. The need for close supervision and discriminating conservatism is obvious.

(3) The incidence of contralateral recurrence is also predetermined. It follows nephrectomy just as frequently as it does conservative operations, dispelling the older idea that removal of the kidney would extirpate the disease.

(4) The fact that recurrence is becoming less common, in spite of an increase in the incidence of the disease and of the operations performed for it, shows that something can be done to influence the responsible factors.

(5) The sex relationship is quite definite, but why men should be more frequently affected is not understood.

(6) The symptomless nature of some recurrences emphasises the need for regular review.

(7) In the same way length of follow-up is important since one-fifth of recurrences are discovered ten or more years after operation.

(8) The size of the stones bears no close relationship to the incidence of recurrence. On balance, the large stone recurs slightly more often than the small.

(9) On the other hand, recurrence increases in direct proportion to the number of stones present.

(10) Urinary infection, before and after operation, has, numerically speaking, a closer relationship with recurrence than any other factor. Approximately two-thirds of those with infected urine recur, compared with one-sixth of those whose urine is sterile. The formidable array of modern antibiotics and chemotherapeutic substances available for the treatment of urinary infection, once sensitivity has been determined, may do much to explain the lower recurrence rate in the last decade.

(11) Renal function and post-operative recurrence are most intimately related. More than one half of those with severe recurrence have poor renal function, but the condition is reversible once the recurrence has been treated.

(12) The composition of the stone had no close relationship to recurrence. Phosphatic stones did recur slightly more often than oxalate. The principal value of stone analysis lies in

the assistance it gives in formulating a prophylactic regime.

(13) Hyperparathyroidism affected only a small group of patients. Six cases were found - 8 per cent. of 76 recurrences investigated biochemically. Its importance is two-fold: (a) Recurrence should cease when the parathyroid adenoma is removed and, (b) Kidney function no longer deteriorates from that cause.

(14) Idiopathic hypercalcuria was present in two-thirds of the recurrent cases, and in one-third of those without recurrence. Its significance is difficult to assess, and treatment in any case is impracticable.

(15) Like hyperparathyroidism, stasis affects only a small group, and in them it has great significance. All patients with stones in horseshoe kidneys had recurrences. It is also correctable, and therein lies its importance.

(16) Metabolic upsets (cystinnia and uric acid hyperexcretion) are even rarer, but are capable of treatment. In lesser degree the same is true of renal tubular acidosis.

"Aetiology" of Recurrence.

The various known factors related to recurrence having thus been stated in detail, it might now be helpful to collect those most intimately concerned, (particularly if they can be treated,) and give some indication of their incidence.

| Factors. | Incidence. |
| --- | --- |
| 1. Fragments left behind at operation. | 10 per cent. of all recurrences. |
| 2. Infection. | 62-85 per cent. of all recurrences. |
| 3. Hyperparathyroidism. | 8 per cent. of recurrences investigated. |
| 4. Idiopathic Hypercalcuria (treatment - nil). | Over 60 per cent. of all recurrences. |
| 5. Stasis. | Very low. |
| 6. Metabolic upsets. | Very low. |
| 7. Renal tubular acidosis. | Very low. |

It is apparent, therefore, that the aetiology of recurrence is but one aspect of the greater mystery surrounding the aetiology of upper urinary tract stone.

## Section VI. A Study of Mild and Severe Recurrence.

The unfortunate patients who have developed recurrence are themselves well worthy of study, quite apart from the rather academic considerations mentioned above. Their progress and general management are our main concern at this point. Discussion of prophylactic regimes after treatment of recurrence is postponed until Part IV.

Of 403 patients reviewed, 167, or just over 40 per cent., proved to have recurrence. Two out of every five patients were therefore affected - a sobering thought. Mild recurrence was present in 60 (one-seventh of the total of 403) and severe recurrence in 107 (one-quarter of the total). When the problem is studied in terms of patients rather than of operations,its significance becomes apparent. The figure quoted above for severe recurrence means that one patient out of every four originally undergoing operative treatment will require a secondary operation.

## Mild Recurrence.

Recurrence of this type, in which secondary operation is not indicated, affected 60 of the 168 patients with recurrent stone (36 per cent.). The progress of 43 patients with mild recurrence, followed without operation for seven years since their detection in 1949, has already been discussed in Part II, since they contribute to our understanding of the natural history of upper urinary tract stone. In the intervening years a further 17 cases have been added.

Type of Mild Recurrence. Table XXIX details the various types of mild recurrence encountered and gives some idea of the liberal interpretation of the term "recurrence" as applied to this series. Pseudo-recurrence was present in eight patients, leaving 52 true recurrences for further study. Nine patients had developed small contralateral calyceal stones, and eleven had passed stones since operation. The remaining 32 consisted of four who had a small ureteric stone after ureterolithotomy, and 23 with calyceal stone after kidney operations (17 on the side of operation and 6 on both sides).

These figures have been stated at some length to emphasise the fact that they would not have been included as recurrences by some investigators, to whom they would represent the "progress of the disease". In all probability this is true, but they must be included since they are stones newly-formed since operation.

Symptoms. Very few of these patients suffered any appreciable disability. More than one-third had been completely symptom-free since operation (Table XXX). Symptoms in the remainder were mild (11) or, if severe, (28 had colic) were brief and infrequent. All of them had returned to full employment and enjoyed good health.

Relationship to the type of operation. Table XXXI indicates that the total incidence of 52 true mild recurrences after 416 operations (12.4 per cent.) is very similar to the recurrence rate after endoscopic procedures for stone in the lower ureter (12.5 per cent.), and quite close to that for contralateral recurrence after all types of operations (10 per cent.). It may well be true, therefore, that mild recurrence, contralateral recurrence, and recurrence after endoscopic procedures are all, in fact, "the incidence due to the disease itself"; that is to say, such stone-formation would have taken place irrespective of operative intervention. If this is so, it follows that severe recurrence is the only form of recurrence due to the operation. The incidence would then be 107 in 403, or more than 25 per cent. and there would still be little cause for rejoicing.

The incidence in the three conservative operations is roughly similar, ureterolithotomy on this occasion having the highest incidence. Six of the seven recurrences after ureterolithotomy occurred in the kidney, however, which is further support for the theory propounded above.

Relationship to Urinary Infection. (Table XXXII). Only 40 per cent. were infected on post-operative urine examination. This is surprising since stone has always been considered an important cause of persistent urinary infection.

B.Coli was the commonest infecting organism. Alone or in mixed infection, it accounted for 13 out of 19 patients who had organisms in their urine. Proteus was present in 10 per cent. showing that it is not invariably associated with massive stone-formation.

Radiological Findings. These have already been considered in some detail. In round figures, function was good in 70 per cent., fair to good in 20 per cent., and fair to poor in 10 per cent. (Table XXXIII). Pyelogram tracings of mild recurrences followed for more than seven years (Fig.27.Vol. II.) showed normal outlines, with no evidence of hydronephrosis.

Biochemical Findings. (Appendix, Table 45, page 48). Hyperparathyroidism was found in two out of 26 investigated (8 per cent.). The common impression that hyperparathyroidism is associated only with multiple large bilateral calculis is shown to be fallacious.

Urinary calcium excretion was raised in 50 per cent. and normal in 50 per cent. Stone analysis showed that two-thirds were oxalate-containing.

Management. In all senses, patients with mild recurrence have the same hopeful prognosis as those with small, untreated calyceal stones. They should be reviewed at regular intervals lest there has been rapid increase in size. Stones originally localised to a calyx, may have been liberated into the renal pelvis, producing hydronephrosis or serious damage to renal function. Two of the 43 mild recurrences followed for seven years, eventually required operation.

A high fluid intake is recommended and vigorous efforts are made to eradicate any urinary infection. If the original calculus of a co-operative patients has been analysed, a suitable dietary regime may be used. Dissolution of these small stones by instilling various solutions into the renal pelvis and calyces has always seemed a logical procedure, (Randall, 1932; and Suby, 1944). Unfortunately, the results have not been consistently good. The latest solvent 2% Sequestrine (Ethylene Diamine) has proved in Suby's hands to be both painful and irritating . Suby (1955) says: "It is still the sideshow."

The fields of usefulness of hyaluronidase, aluminium gels, and the salicylates, apply more to the treatment of established stones. They are therefore considered in Part IV.

Conclusion.

Small recurrent calyceal stones in the main, seldom give rise to incapacitating symptoms, interfere with work, or damage health. The majority are not progressive, or harmful to the kidney. In these circumstances there is every reason for conservative treatment providing they are regularly reviewed. Most patients are willing to co-operate if the nature of the condition and the problems arising from it are explained in simple terms.

## Severe Recurrence.

Review and re-examination of 403 patients revealed 107 with recurrence sufficiently severe to justify secondary operation - an incidence of one in four.

Relationship to Type of Operation. Information is available concerning 112 patients (five having been included who were not interviewed). Table XXXIV bears witness to the startling fact that nephrolithotomy has been followed by severe recurrence in one out of two instances, and pyelolithotomy in one out of three. These figures, alone, indicate the importance and size of the problem of recurrence.

Treatment. The treatment of the series of 107 patients is given in detail in Table XXXV, as it affects two groups.

(a) No secondary operation. Conservative treatment of 29 cases of severe recurrence has already been considered in Part II. It is obvious that their progress is unsatisfactory and their outlook poor. The main reasons for the expectant attitude have been the unfitness or the unwillingness of the patients.

(b) Secondary operation. The operations performed are shown in Table XXXV. Unilateral surgical treatment was necessary in

55, bilateral treatment in 23 patients. The operations were conservative in 43, and in 35 they were radical. In five patients multiple bilateral operative procedures were necessary - proof, if proof were needed, of our relative impotence in preventing post-operative recurrence. It is not uncommon for a patient to undergo multiple operations, ending in recurrence in a solitary kidney. The patient in Fig.48 had a left nephrectomy in 1952, and a right pyelolithotomy in 1953. By 1954 a recurrent staghorn calculus had damaged the kidney so badly that its function was practically nil, and further intervention was too hazardous to be undertaken.

Study of the 78 Cases treated by operation.

Disposal. Fourteen had died and 8 were untraced, leaving 56 for further study. Nine of the 14 deaths were directly connected with the urinary tract, four occurring after operation, and five from uraemia at other times. (Table XXXVI). The period of follow-up extended to 30 years.

Symptoms. In 56 patients questioned, symptoms were present in only 17, or roughly one in three. Some of these patients were, however, free from stone at the time, having received treatment in the interval. Where severe recurrence was still present, 9 out of 13, or two-thirds, had symptoms (Table XXXVII).

General health was good in 35 of the 56 patients, i.e., over 60 per cent. (Table XXXVIII). This indicates that the outlook is not completely hopeless, and that severe recurrence can be treated, or tolerated. In point of fact, 32 of the 56 patients were actually free from further stone when re-examined, and only 13 still had radiological evidence of severe recurrence (Table XXXVIII).

Renal function was good in 17, fair in 2 and poor in 12, so that the kidney damage proved to be reversible in more than 50 per cent. investigated (Table XXXVIII).

Urinary infection (Table XXXIX) was present in 56 out of a group of 96 severe recurrences examined. The incidence of infection was closely related to the calculous state. Where large stones were present the incidence of infection was very high indeed. B.Coli was the commonest organism. Proteus was associated seven out of eight times with large stones.

The biochemical findings were much the same as for mild recurrence Hyperparathyroidism occurred in 8 per cent. and hypercalcuria in 60 per cent. Chemical analysis showed oxalate and phosphate stones in roughly equal proportions.

Management. Operation is indicated in cases of severe recurrence, particularly if there is a possibility of ureteric obstruction or calculous anuria. Judgment is difficult in the individual case, particularly when a large stone occurs in a solitary kidney.

Conclusions.

Severe recurrence was found in 25 per cent. of 403 patients reviewed. It followed nephrolithotomy in one half of patients and pyelolithotomy in one-third. Severe recurrence justified its name in its effect on general health, symptoms, renal function and urinary infection. In spite of all this, and with suitable surgical treatment, more than half were free from stone when re-examined. Operation is indicated particularly when there is a risk of obstruction leading to hydronephrosis, or calculous anuria.

## SUMMARY.

The results of the operative treatment of upper urinary tract stone have been investigated in 403 out of 546 patients subjected to operation during the years 1905 to 1950. All these patients attended for interview followed by x-ray and urine examinations. No case is included in which operation took place less than one year ago.

In accordance with the general increase in the incidence of the disease, more patients have received operative treatment in the last decade than in the one preceding that. Nephrolithotomy has lost any popularity it may once have possessed, and increasing use has been made of partial nephrectomy in suitable cases.

False or pseudo-recurrence has been found in 12.5 per cent. of patients investigated immediately after operation. The problem of eliminating this artificial form of recurrence has been discussed. They have been omitted from the series so that the incidence of true recurrence might be accurately assessed.

Recurrence has been graded as "mild" and "severe", depending on whether or not secondary operation has been necessary. A high recurrence rate has been noted. Of 403

patients re-examined, 167 had recurrence (42 per cent.), and secondary operation was indicated in 107 of these, (one in every four undergoing operation).

The various operations which may influence the incidence of recurrence have been closely studied. Survey of the true recurrence rates for the various operations has shown, even when circumstances were most favourable, the following rather gloomy figures (Urological series):- all operation, 26 per cent; conservative operations, 31 per cent; pyelolithotomy, 34 per cent; nephrolithotomy, 50 per cent. and ureterolithotomy, 27.5 per cent. There was no recurrence after partial nephrectomy.

The investigation has indicated that thoroughness in removal of the stones is very important, and that a conservative attitude is completely justified. Pyelolithotomy is to be preferred to nephrolithotomy. A definite place exists for partial nephrectomy, which may be combined with pyelolithotomy when stones are present in the pelvis as well as in a calyx. By careful selection of cases, nephrectomy may sometimes be avoided, and healthy renal tissue conserved. This is even more desirable since it has been shown that contralateral recurrence is just as common after nephrectomy as after conservative operations.

A significant reduction in the incidence of recurrence has been noted in the last decade, due, possibly, to an increasing awareness of the problem, to the application of some of the practical lessons learned from experience (e.g. conservatism in renal surgery) and to the advent of the newer therapeutic agents.

Recurrence has proved to be twice as common in men as in women. More than one-third of recurrences have been symptomless. For this reason, 17 per cent. have been detected more than ten years after operation, having experienced few, if any, symptoms in the intervening years.

The size of the stone has no close relationship to recurrence, but the incidence increases in direct proportion to the number of stones present.

Urinary infection and recurrence have much in common. Approximately two-thirds of those with infected urine recur, compared with one-sixth of those with sterile urine. Every effort should be made to eradicate urinary infection before the patient leaves hospital.

Recurrence has a marked influence on renal function, and the converse may well be true. More than one half of the patients with severe recurrence have evidence of impaired or poor renal function.

Hyperparathyroidism has been diagnosed in six patients, all of whom had recurrent stone. The incidence has therefore been 3 per cent. of 210 patients investigated, or 8 per cent. of 76 recurrences reviewed biochemically.

Hypercalcuria, mainly of the idiopathic type, has been found in one-third of the patients who were free from recurrence, and almost twice as frequently in those who had recurrence.

The general features and management of patients with mild and severe recurrence have been studied and discussed. Regular review of all cases has been strongly recommended, particularly where conservative treatment has been advised. The merits of a Stone Clinic have been emphasised.

Operative measures in nephrolithiasis are directed against the effect of the disease, leaving the underlying cause, in most cases still active. For that fundamental reason, recurrence may be expected to continue, in spite of a flawless operative technique, until aetiology is more completely understood. The late results show only too clearly that the management of a patient with upper urinary tract stone is a complex problem, to which surgery does not invariably provide a complete or a happy solution.

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The first question asked by the patient, "How often do stones recur?" has now been answered to the best of our ability. Our next consideration is to decide on a suitable reply to his second question, "What can be done to prevent recurrence?".

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PART IV.

# THE PREVENTION OF POST-OPERATIVE RECURRENCE OF UPPER URINARY TRACT STONE.

| | | |
|---|---|---|
| Section I | : | Early Preventive Measures. |
| Section II | : | Long-term Measures. |
| Section III | : | The Value of Hyaluronidase in the Prevention and Treatment of Recurrent Stone : Experimental work in Man and Animals. |

Summary.

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PART IV.

## THE PREVENTION OF POST-OPERATIVE RECURRENCE UPPER URINARY TRACT STONE.

The prevention of recurrence is the all-important consideration in the after-care of patients who have undergone operative treatment for stone. That the problem is large and complex has been shown in the preceding part of this work; that its solution is exceedingly difficult will be shown in this one.

It is a much simpler matter to remove a calculus than to prevent it re-forming, and it should never be forgotten that operative treatment represents only one phase in the management of a patient with calculous disease. This is so obvious that it seems unnecessary to repeat it; yet only too frequently patients leave hospital under the impression that the operation has not only removed the stone, but has, somehow or other, put an end to the stone-forming process. The only advice they are given is to maintain a high fluid intake and, apart from one visit soon after the operation, they may not be seen again until recurrence has taken place.

In the light of the high recurrence rates shown earlier, this is the wrong outlook. The surgeon who prides himself on a scientific approach to the treatment of disease will adopt a different attitude, and will not easily be satisfied until he has done everything in his power to eliminate the need for further intervention.

## Section I. Early Preventive Measures.

It is no exaggeration to say that preventive measures start as soon as the diagnosis is made, and a decision reached about operative treatment.

Operative Measures. The correct operation is the one which removes the stones completely and damages the kidney as little as possible. It is an essential precurser of the long-term measures, and gives the patient the best possible chance of success with any subsequent prophylactic regime.

For the single uncomplicated stone lying free in the renal pelvis, pyelolithotomy is the operation of choice. Nephrolithotomy is seldom used since it causes so much damage to the kidney and is associated so frequently with recurrence. Occasionally a small incision may be made through atrophied renal substance to permit extraction of a small calyceal stone which has proved inaccessible from the renal pelvis. Pyélotomie élargie (Marion, 1922) may be usefully employed to remove larger pelvic stones with calyceal extensions. Even though contralateral recurrence has been shown to occur as commonly after nephrectomy as after conservative operations, blind adherence to the dictum of conservatism is unwise in cases of staghorn calculus with superimposed hydronephrosis, pyonephrosis, or poor renal function.

Partial nephrectomy is indicated where a dendritic stone occupies the upper or lower calyx, the remaining part of the kidney being free from stone, as in Fig. 49 , which illustrates a recurrent stone localised to the upper calyx. It is radical since it removes all the stones and the diseased calyceal lining; and its increasing popularity reflects the recent conservative trend in renal surgery since it preserves as much healthy kidney tissue as possible. Although partial nephrectomy is regarded as a fairly recent development, it was first performed by Czerny in 1887, and was mentioned by Barney in 1922 as an operative step which might with advantage be combined with pyelolithotomy. Simple removal of a stone leaving behind roughened ulcerated calyceal lining is equivalent to dealing with a hydrocele without resection of the tunica vaginalis.

Thorough removal of the stones is of fundamental importance. There will always be some cases in which it is humanly impossible to remove all the stones, but radiological assistance at operation will reduce these to a minimum. Tiny fragments of stone which are lodged in calyces may be extracted with the help of an irrigation-suction apparatus, or a coagulum gel which forms a cast of the renal pelvis and calyces.

Pelvi-ureteric stenosis must be corrected and free drainage established. Hamilton Stewart (1952) insists that replacing the kidney in faulty position is an important factor in recurrence after partial nephrectomy. He recommends that the kidney be placed at the top of the renal fossa, and that the anterior and posterior layers of the perirenal fascia be sutured to act as a sling, retaining the kidney in this high position.

Early Post-operative Measures.

During convalescence from operation various investigations are carried out which have a direct bearing on the prevention of recurrence.

(1) As soon as the patient is ambulant and the stress factor is less evident, calcium and phosphorus metabolic studies are commenced. A fasting specimen of blood is taken for estimation of the serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, plasma proteins, blood urea and electrolytes. Urinary calcium output, on a fixed low calcium intake of 150 mgm. per day, is estimated on the last three days of a nine-day period. At the end of this period further blood examination is carried out. Any patient in whom these determinations give rise to suspicions of hyperparathyroidism receives separate consideration, and a complete calcium balance in urine and faeces is performed.

Idiopathic hypercalcuria or renal tubular acidosis may also be revealed by these investigations.

(2) If there is evidence of hypercalcuria or an increase of the serum acid phosphatase, the skeleton is examined radiologically to exclude metabolic bone disease.

(3) Bacteriological and cytological examination of the urine, is routinely performed to determine the pH, crystal content, and presence or absence of infection. The sensitivities of any organisms cultured are determined and the appropriate therapeutic agent administered. Infection is eradicated before the patient leaves hospital, or as soon thereafter as possible, since it plays a most important part in recurrence.

(4) A plain film of the urinary tract is taken so that pseudo-recurrence is automatically detected. When renal function has been poor before operation, intravenous urography is arranged at follow-up examination six weeks later to determine whether hydronephrosis has disappeared and whether there has been any improvement in function.

(5) Quantitative and qualitative chemical analysis of the stone is performed. The time-honoured custom of presenting the stone to the patient is a great mistake, since the chemical composition of the stone is one of the principal means of formulating a prophylactic regime on a long-term basis.

## Section II. Long-term Preventive Measures.

The patient is now ready to leave hospital. The stones have been completely removed, free drainage of the kidney ensured, urinary infection eradicated, and hyperparathyroidism and idiopathic hypercalcuria excluded. What advice shall he be given about fluid intake, diet, and medicinal treatment? How shall he best order his life from this point?

It may be said at once that it is not an easy matter to decide which regime will give the patient the best chance of avoiding recurrence, unless in the minority who have a known aetiological factor capable of correction. In the experience of most urologists, deficiency diseases in these days are rarely the underlying cause of stone. Most patients have a well-balanced diet, hence "stone-belts" are probably associated with local differences in the soil or water. Only a handful of urologists are sufficiently impressed with the part played by vitamin A that they prescribe it for all patients. Hammarsten (1937) concluded with some certainty that the amount of magnesium in the food of the populace of America, Germany and Sweden was too low. She believed that the increasing occurrence of oxalate calculi in Sweden in the last two decades is to be considered against a background of decreasing mineral in the diet. In support of this theory she found that stone rarely occurred in Finland where there was a high calcium and magnesium consumption.

The metabolic diseases, cystinuria and uric acid excess, are rare causes of stone, and their treatment is relatively simple.

The main advice given to patients is that they should maintain a high fluid intake. This is wise since it prevents supersaturation with deposition of crystals which may, according to Prien (1955) conglomerate to form the nuclei of stones.

"Dry" cider has been recommended to many patients as a very pleasant beverage. It is claimed (by the brewers) to have magical properties in preventing stone owing to its malic acid content. Stone is said to be uncommon in Normandy on account of the high cider consumption. It is interesting to note that salicylic acid is one of the other acids present in cider, since it has recently been shown to be excreted in the urine in conjugation with glucuronic acid which is known to increase the solubility of calcium phosphate (Prien and Walker, 1955).

From this point onwards the depth of our ignorance of the aetiology of urinary stone becomes increasingly apparent. In the absence of this vital information the regime advised is based almost entirely on the crystalloid content of the stone, and treatment consists of dietary and medicinal means of preventing or lessening the precipitation of the particular stone-forming substance. During the last five or six years the nature of the urinary biocolloids has been studied with increasing interest and prophylactic measures have been suggested which aim at preventing recurrence by altering the colloidal content of the urine.

## Preventive Regimes based on the Crystalloids present in the Stone.

In 1929 Meyer showed that urine was commonly supersaturated two to four times its normal aqueous solubility. Calcium is twice as concentrated in urine as in serum and phosphorus up to thirty times. Supersaturation is therefore the normal state of affairs and there must be mechanisms whereby this is maintained without precipitation of crystals. The reaction of the urine has been shown by Meyer to exert an important influence. When the pH was 5.0, uric acid was deposited; at a pH of 6.0, uric acid, calcium oxalate, and calcium phosphate; at a pH of 7.0, calcium phosphate; and over 7.0, magnesium ammonium phosphate.

### Stone analysis.

The highly refined biophysical techniques of x-ray diffraction photography and microradiography have enabled Prien and Walker (1947) and Lagergren (1956) to study the crystalloid composition and architecture of urinary calculi. The three common stones revealed were:-

(1) Calcium oxalate.

(2) Apatite (basic calcium phosphate and calcium carbonate).-

(3) Magnesium ammonium phosphate.

Prien (1955) concluded that the nucleus of most calcium stones consisted of apatite, regardless of the composition of the rest of the stone.

Mechanisms of supersaturation responsible for recurrent stone-formation.

The two fundamental mechanisma producing the supersaturation necessary for the formation of recurrent calcium stones are (Prien, 1955):-

(1) Hypercalcuria, which may result in precipitation of calcium phosphate or of calcium phosphate and calcium oxalate.

(2) Urea-splitting infection which results in precipitation of magnesium ammonium hydroxide.

In any regime devised to prevent recurrence it is important to know which mechanism is primarily responsible, and Prien believes that only by these biophysical methods of stone analysis is it possible to tell.

Hypercalcuria.

A close study of the urinary calcium output of 62 patients in this series who have undergone operation has shown hyper-calcuria in 40 per cent. In those with recurrence the figure rises to 60 per cent. The main causes (Albright, 1948) of hypercalcuria are:-

(1) Idiopathic hypercalcuria in which there is no acidosis or metabolic bone disease, the blood chemistry (in the main) is normal, and hypercalcuria is the only positive finding. Albright thought that a preceding staphylococcal pyelonephritis might have damaged the renal tubules to such an extent that they were unable to reabsorb calcium. Reduction of calcium in the diet only worsens the situation by causing even more calcium to be withdrawn from the skeleton. Administration of calcium and Vitamin D in excess is contra-indicated on account of the stone-formation. Blocking of the absorption of calcium is also undesirable. The only remaining form of therapy (apart from treatment of the Staphylococcal pyelonephritis) is stabilisation of the solubility of the stone-forming calcium substances as shown below.

(2) Metabolic Bone Disease is rare by comparison. The three main causes are hyperparathyroidism, rapidly-progressing osteoporosis and renal tubular acidosis.

## Factors responsible for Solubility of Calcium and its Salts in Urine.

(1) The pH as shown above. Calcium oxalate, or calcium oxalate mixed with calcium phosphate, commonly occurs in an acid sterile urine, whereas magnesium ammonium phosphate stones (with or without calcium phosphate) occur in an alkaline infected urine.

(2) The influence of <u>magnesium</u> was shown by Hammarsten (1937) in her memorable work on the precipitation of calcium oxalate stones in the urinary tract of rats. Urinary calculi were produced on diets deficient in magnesium whether the diets were rich or poor in vitamins A, C and D. On a diet low in mineral content and relatively deficient in vitamins A and D, there was a marked rise in the urinary calcium excretion. Administration of calcium and magnesium lowered the calcium excretion in the urine whether or not vitamins were given. She stated that a diet insufficient in calcium led to over-mobilisation of skeletal calcium, to a negative calcium balance, and hypercalcuria. Her conclusion, which appeared startling at the time, was that it was incorrect to put stone patients on a low calcium diet, but rather that they should be ordered a diet rich in calcium and magnesium in easily assimilated form with adequate magnesium and vitamins. Dulce (1956) has confirmed her work.

(3) <u>Citric Acid</u>, is present in urine in a concentration about 30 times as high as that in serum. Calcium has the property of uniting with citric acid to form a soluble, only slightly ionised complex in which calcium forms part of the anion. Flocks (1945) has shown that 15 to 40 per cent. of the urinary calcium is bound in a negative complex, emphasising the importance of citric acid in the urine. Stone patients were found to have a low citric acid concentration but Conway et al (1949) claimed that this occurred only in

patients with an infected urine. Shorr (1945) recommended oestrogens for stone patients since they cause a significant increase in urinary citric acid excretion.

(4) The colloids or acid mucopolysaccharides were claimed by Butt and his colleagues in 1952 as the means by which the supersaturated salts were prevented from precipitating. They considered that diminution in the amount of protective colloids was responsible for stone formation. It is possible, however, as Anderson (1954) points out, that it is some chemical alteration in the acid mucopolysaccharides increasing their affinity for calcium rather than actual deficiency of these substances which is the cause. An increased acidity of the acid mucopolysaccharides in cartilage develops at the transitional zone in calcifying bone, and this is considered to be one of the important factors determining the deposition of calcium in the cartilage. A similar mechanism may operate in calcium stones.

(5) Infection, by its effect on pH principally, leads to an alkaline urine in which calcium phosphate is more easily deposited.

(6) The Urinary Glucuronides increase the solubility of calcium phosphate. Salicylates are excreted in the urine with as much as 15 to 40 per cent. of the total conjugated with glucuronic acid. Prien and Walker (1955) therefore recommended the use of aspirin 10 gr., t.i.d., and found

it effective in preventing recurrence in 17 out of 19 persistent calcium stone-formers over one to one and a half years.

(7) Aluminium Hydroxide Gel. As a further indirect method of preventing the precipitation of calcium phosphate, oral administration of aluminium hydroxide gel was recommended in 1945 by Shorr. Highly insoluble aluminium phosphate is formed in the bowel, so reducing the total absorption of phosphate. Daily doses of 120 ml. appreciably reduce the urinary phosphate excretion, particularly when urea-splitting infection is present (Robinson, 1947).

Summary of Hypercalcuria.

The cause in the majority is unknown, and treatment in most cases consists of stabilising the solubility of the crystalloids by altering the reaction of the urine. Most calcium oxalate stones have a nucleus of apatite, so acidification is indicated for all calcium-containing stones and for magnesium ammonium phosphate stones. The effect of magnesium, citric acid, the mucopolysaccharides, infection, and glucoronic acid, in promoting the solubility of calcium and its salts is worthy of note, but in the last event, control of urinary pH remains the sheet anchor.

Role of Urea-splitting Infection.

Infection produces excess alkalinity of the urine with deposition of phosphate. Fortunately its treatment is a little simpler, though some strains of Proteus are still able to defy the full range of modern therapeutic agents. The practical problem here is that the presence of a stone is so often the cause of the persistent infection.

## Preventive Regimes.

Ideally, urine reaction is tested daily and the patient reports monthly. The stone having been analysed, the following regimes are recommended:-

(1) Uric Acid. The pH is maintained at 7.0 by an alkaline-ash diet and alkali therapy. The purine intake is curtailed.

(2) Cystine. An alkaline-ash diet and alkali therapy maintain the pH at 7.0. Dent (1955) has shown the importance of maintaining a 24-hour urinary dilution, and recommends that they waken once through the night to drink a pint of liquid.

(3) Calcium Oxalate. The deposition of calcium oxalate itself is constant and cannot be controlled by altering the pH. On the basis that the nucleus consists of apatite and that acidification helps to maintain the solubility of calcium salts, an acid-ash diet is recommended. Greta Hammarsten's diet is advocated (a copy appears in the Appendix, page 50) The main principle is that patients receive an adequate supply of calcium, magnesium, phosphorus and vitamins in an easily-assimilated form. Foods rich in oxalate are avoided.

(4) Calcium Oxalate and Calcium Phosphate. The same regime is recommended. (Oestrogens, aluminium hydroxide gel and

salicylates might be considered.)

(5) Calcium Phosphate and Magnesium Ammonium Phosphate.

(a) Treatment of the urinary infection is absolutely essential.

(b) The pH is maintained at 5.2 to 5.4 by an acid-ash diet supplemented by urinary acidifiers such as ammonium chloride and acid sodium phosphate.

(c) Oestrone sulphate mgm. 5-10, daily, is given orally for four weeks if hypercalcuria is a prominent feature.

(d) Amphogel (aluminium hydroxide gel) 30 to 40 ml. after meals reduces urinary phosphate excretions.

(e) Salicylate, as aspirin, gr.10 t.i.d. (or if this causes dyspepsia, as Fizrim, an effervescing form of aspirin). It is claimed by Baker and Connelly (1956) that this (1) acidifies the urine (2) increases the glucuronic acid content so that the calcium phosphate solubility is increased and (3) has a beneficial effect on the mucoprotein of the renal tubule connective tissue (proven by renal biopsy).

## Preventive Measures Based on Study of the Urinary Biocolloids.

### The nature of the Colloids.

The protective action of the urinary colloids on preventing crystalloid precipitation has long been suspected (Lichtwitz,1919), but their nature has not been defined except in general terms, viz., that they were muco-proteins or acid mucopolysaccharides of the group to which chondroitin sulphuric acid and hepanin belong. Boyce and his colleagues (1954) by a combination of dialysis, ultrafiltration and perevaporation, recovered the urinary bicolloids. In normal urine the total in 24 hours was minute, 0.09 gm; in stone disease it was five times greater. They identified two fractions (both with negative charges), one of which has iron-binding properties, forming an insoluble complex with calcium.

Origin of the Colloids.

Mucoprotein is present in all stones except calcium oxalate. The colloids have a high molecular weight, i.e., they are not filtered through the glomerus, or secreted or excreted by the tubule. Baker and his associates (1954) suggest that they originate from the connective tissue mucoprotein of the tubules; in other words, that calculi represent another form of collogen tissue disease. Tissue stains have shown a patchy increase in the mucopolysaccharides in the tubule basement membrance immediately before calcification. This was one of the reasons why they recommended aspirin; it might equally well have been cortisone or butozolidin or any of the other anti-inflammatory or anti-phlogistic agents.

Hyaluronidase.

Butt and his co-workers found in 1952 that subcutaneous injection of hyaluronidase, mixed with normal saline, "cleared" the urine of patients who previously had turbid urine with much sedimentation. They claimed that hyaluronidase acted by liberating hyaluronic acid which belongs to the acid mucopolysaccharide group. Hyaluronic acid is excreted in the urine, thus increasing the total quantity of protective colloid present. By the methods of electrophoresis, ultramicroscopy and surface tension estimation they found that diminished colloidal activity was associated with a predisposition to stone-formation, e.g., colloidal activity is elevated in the Negro race, which is relatively immune from stone. Patients harbouring stones are said to have decreased urinary colloids.

Colloidal activity is significantly increased in 80 per cent. of subjects following subcutaneous injection of Hyaluronidase (Butt et al., 1952), and the greatest response was in members of the Negro race. Women showed a more marked response than men, and this was considered consistent with the lower incidence of stone in the female sex. The increased colloidal activity was even more marked during pregnancy.

On the basis of these findings they therefore treated a group of patients, in whom kidney stones had previously formed rapidly with hyaluronidase 150 to 900 turbidity reducing units (T.R.U.) every 24 to 48 hours. They found that hyaluronidase therapy was effective in preventing stone-formation in 19 out of 24 patients, 79 per cent., during a period of 11 to 21 months.

## Effect of Hyaluronidase on Prevention of Further Stone Formation.

Stimulated by the high recurrence rate, and our relative helplessness in the face of it, a clinical trial of hyaluronidase was conducted in certain types of patients in whom surgical treatment was not indicated.

Groups studied.

1. Large primary or recurrent stones, in poor general health.
2. Large stone in a solitary kidney.
3. Small calyceal stones, primary or recurrent.
4. Those passing large numbers of stones.

Three patients were studied in each group.

Object.

The principal object was to determine whether hyaluronidase was effective in preventing further stone-formation, i.e., whether stones already present enlarged, or (if the urinary tract happened to be free from stone at that moment) whether they recurred. The appropriate regime according to the crystalloid present in the stone was also prescribed in the rather forlorn hope that this would disperse the crystals of the stone while the hyaluronidase was acting on the organic stroma.

The use of hyaluronidase was quite empirical. Apart from the work of Butt and his colleagues, no guidance was available in the literature. This was explained to the patients since it was essential to have their co-operation throughout a course of treatment lasting several months. They appreciated that they had nothing to lose and possibly something to gain.

Dosage.

In the presence of a sterile urine the dose started at 500 T.R.U. and rose (in the absence of any appreciable improvement) over a period of six months to 1,000 T.R.U. every 48 hours. With an infected urine the dose was doubled, as recommended by Butt. Prien (1955) reported rapid recurrence of a cystine stone after small doses of hyaluronidase, and considered that sensitization to hyaluronidase may actually stimulate stone-formation. Large doses were therefore used to avoid this unwelcome complication.

Adjustment of Dose.

Smiddy (1954) showed that a single determination of surface tension is valueless in normal subjects and may range from 59 to 72 dynes per ml. On the other hand he found a very close relationship between specific gravity and surface tension, in that they were inversely proportional. As a simple clinical test in patients who had no infection and minimal albuminuria, the specific gravity was used to determine the need for increasing the dose, bearing in mind the fact that most of these patients had been exhorted to drink five pints of liquid per day. A specific gravity of 1,025 was regarded as equivalent to a surface tension of 56 dynes per ml., and a specific gravity of 1020 to 59 or 60 dynes per ml. (Smiddy, 1954). The average surface tension in the white male is 65 dynes per ml. and for the white female 60 dynes per ml. It was considered advisable to produce a lower surface tension than this if possible.

Method of Study.

A specimen of urine was obtained on each visit, i.e., every 48 hours, (midstream from men, and by catheter from women). Specific gravity, bacteriology, and cytology were all performed. Radiological examination was carried out at two-monthly intervals. Routine stone analysis and biochemical studies of calcium and phosphorus metabolism had been performed in most cases.

Results in Individual Patients.

The results in individual patients are shown in short case histories in the Appendix, pages 51 to 55 inclusive. For our present purpose a summary is sufficient.

Group I. Three patients had large primary or recurrent bilateral stones, associated with severe and persistent urinary infection. Each had previously undergone operative treatment, analysis of the stones showing a mixture of apatite and magnesium ammonium phosphate (signifying urea-splitting infection). Kidney function was universally poor, as was their general condition.

Hyaluronidase therapy was continued for six to twelve months in the dosage 1,000 to 2,000 Turbidity Reducing Units by sub-cutaneous injection every 48 hours.

Improvement, of slight degree only, was noted in one of the three cases. The stone became smaller, without any corresponding improvement in renal function. The other cases were quite unaffected as far as the size of the stone was concerned. In none did the specific gravity of the urine rise above 1,020, due, probably, to the diminished renal function. It seems only fair to add that there was no increase in size of the stones during the period of observation, but this point loses its value when it is appreciated that the same held good when the cases were reviewed one year after completing the hyaluronidase therapy.

Group II. Three patients had stones in a solitary kidney, as a result of recurrence after operative treatment. They also had heavy urinary infection and the remaining kidney functioned poorly. The stones consisted of magnesium ammonium phosphate.

Hyaluronidase therapy was given in the same dose as for Group I., viz. 1,000 to 2,000 T.R.U. every two days, for a period of six to twelve months.

No case showed any appreciable change in respect of the size of the stones, or of renal function. There was no significant increase in urinary specific gravity during the therapy.

Group III. Small calyceal stones were present in the three patients in this group. All had undergone operation; in two instances the stones were pseudo-recurrences; the third was a true recurrence. Kidney function was good in all three, and the stones this time were unilateral. There was no evidence of urinary infection. Stone analysis showed calcium oxalate or mixed oxalate and phosphate as the principal constituent.

Hyaluronidase therapy in the dosage 500 to 1,000 T.R.U. was given every 48 hours for six months.

In the patient who had a true recurrence the small calyceal stone disappeared during the period of treatment, and there may be some significance in the fact that the specific gravity of his urine rose from 1,016 to 1,026. The other two small stones treated in this way were quite unchanged.

Group IV. Three patients who passed stones so frequently that the phenomenon constituted a disability were studied. Operative treatment had been necessary in all cases, and stones had been passed before and after operation. None had radiological evidence of stone when treatment started. Hyaluronidase was therefore given the opportunity of preventing recurrent stone production starting with a clear urinary tract. There was no evidence of urinary infection, and kidney function was good in all three.

Hyaluronidase therapy was given in the dosage 500 to 1,000 T.R.U. every 48 hours for six months.

The patients continued to pass stones at the interval normally experienced, in spite of the fact that the specific gravity in one case rose to 1,027.

Conclusions.

The results detailed above are not impressive bearing in mind the disadvantages of the method. Patients were given no guarantee of success; in fact they were warned against over-optimism, and in this spirit they submitted to the regime with good grace.

Slight improvement was noted in only two of the twelve patients treated with hyaluronidase. One large stone had become slightly smaller, and one small calyceal stone had disappeared; but similar results are not uncommon with forced diuresis alone.

If it may be assumed that Smiddy's observation (1954) on the inverse relationship of specific gravity and surface tension is correct, only two of the twelve patients had a specific gravity sufficiently high to suggest that the surface tension had been lowered by hyaluronidase to the optimum level of less than 60 dynes per ml. This might well be explained by (1) a high fluid intake, or (2) impaired renal function, either of which may be expected in these patients.

The dose of hyaluronidase was at least twice that recommended by Butt (1952), and even greater doses were exhibited when infection was present, Failure cannot therefore be attributed to under-dosage.

None of the stones under observation actually grew or progressed. If the criterion of success with hyaluronidase is control of stone growth, this clinical trial has been completely effective. The cases in question have, however, shown no progression when reviewed one year after the cessation of treatment, and it must therefore be deduced that their natural rate of growth is exceedingly slow anyhow, due to grossly impaired renal function. If the criterion of success is freedom from recurrent stone formation once the urinary tract has been cleared of the original stone, this clinical trial has been a failure, since those who previously passed stones continued to do so. Butt's claim (1954) that fresh stone formation is prevented by hyaluronidase therapy has not been substantiated. In any case, patients would require very lengthy periods of surveillance before such a claim could reasonably be made. It has already been shown in the studies of the Natural History of Stone (Part II) that alternating periods of quiescence and renewed activity are the rule rather than the exception in patients who pass stones.

At one time it appeared that hyaluronidase might prove as beneficial to patients with calculous disease as insulin is to diabetics. This high hope has not been fulfilled, and in the present state of knowledge it is unjustifiable to ask patients to undergo the inconvenience and discomfort of injections every 48 hours for the doubtful benefits obtained from them.

Shortly after the completion of this clinical trial with hyaluronidase, Badenoch (1954) reported complete failure with prolonged courses of hyaluronidase in eight patients with large stones corresponding to the first two groups studied.

## Animal Experimental Studies on the Value of Hyaluronidase in the Prevention and Treatment of Calcium Oxalate Stones.

Concurrently with the clinical trial, but on slightly different lines experimental studies in rats were proceeding. In view of its possible therapeutic value in man it was obviously desirable that hyaluronidase be assessed under strictly controlled experimental conditions in animals. This was particularly true of calcium oxalate stones, which occur most commonly, and present the most difficult problem of all in respect of the prevention of recurrence. Stones of this nature are easily induced in rats.

Object. The object of the experiment was to assess the value of hyaluronidase in:-

(1) Preventing the formation of calcium oxalate stones in rats on a high oxalate, low vitamin A and D diet:

and (2) Dispersing or "dissolving" calcium oxalate stones already formed on such a diet.

Work carried out by Smiddy at the same time as this animal experimental study (1954) had shown that daily subcutaneous injections of hyaluronidase did not prevent the development, or influence the size, of calculi formed on zinc pellets which had been surgically introduced into the bladders of twenty rats. These conditions are highly artificial (even although they are convenient from the experimental viewpoint). They are probably quite unrelated to the natural method of calculogenesis in man, and it was therefore considered advisable to seek other means of producing stones.

Methods of Producing Stones in Animals. Several of the innumerable methods reported by other workers may briefly be mentioned.

(1) Vitamin A lack (Higgins, 1932).

(2) Vitamin D excess (Pyrah, 1954).

(3) Vitamin lack, inadequate calcium and magnesium, with excess of oxalate, on an acid-ash diet (Hammarsten, 1937).

(4) Parathormone injections (Baker et al., 1954).

(5) Excess of ammonium oxalate and ammonium chloride with lack of vitamins A and D (Domanski, 1950).

(6) Infection (Rosenow and Meisser, 1922).

Method Employed.

Wistar strain male albino rats, aged six to eight weeks were used during the experiments. They were placed on Domanski's stone-forming diet which is detailed in Table XL. This diet was selected since Domanski (1950) claimed that it was simple, successful in over 90 per cent., and as natural as possible. Control rats were placed on the basic diet which was nutritionally adequate in all respects. The stone-forming diet was simply the basic diet without the cod liver oil (vitamin D) and vitamin A extract. Meat and bone scraps were also excluded, and ammonium chloride (2%) and ammonium oxalate (0.6%) were added. The two diets were caked and made available in excess to the animals, with drinking water containing 0.6 per cent. ammonium oxalate.

EXPERIMENT I.

Object: To Assess the Value of Hyaluronidase in Preventing the Development of Calcium Oxalate Stones in Rats on a Stone-forming Diet.

Procedure. Sixty rats were used, twenty as controls and forty for the experiment itself. The controls were divided into two groups of ten:-

(1) On the basic nutritionally adequate diet, and

(2) On the basic nutritionally adequate diet + hyaluronidase injections.

Likewise the forty employed for the main experiment were divided into two groups of twenty:-

(1) On the stone-forming diet alone, and

(2) On the stone-forming diet + hyaluronidase injections.

Large daily injections of hyaluronidase were given, since Butt and his colleagues (1952) had suggested that inadequate doses might, by sensitisation, provoke rather than retard stone formation. The actual amount was 500 Turbidity Reducing Units of hyaluronidase in 0.5 ml. of normal saline, injected subcutaneously in rotation into the four quadrants of the anterior abdominal wall to reduce the incidence of septic sequelae.

Radiological examination after 90 days showed no suggestive opacities. The kidney of the rat measures 1.5 x 1.0 x 0.75 cm., and it is an exceedingly difficult matter to be certain about early stone formation by x-ray alone. Anaesthesia is essential to abolish or minimise respiratory movements. Even then, diagnosis is not easy, since artefacts are numerous. The animal in Fig. 50 was free from stone at autopsy in spite of the suggestive shadow in the left renal pelvis. Stones were present in several of the rats after a further 45 days (135 days in all). Fig. 51 shows two opacities in the right kidney, which were confirmed as stones after the animal had been sacrificed. It was therefore considered wise to conclude the experiment at this point, sacrifice the animals, and search for stones with the assistance of a dissecting microscope.

Results. The control series (with and without hyaluronidase) were completely free from stone. The urinary tract and general condition of all twenty were satisfactory.

The results obtained in the groups on the stone-forming diet (with and without hyaluronidase), are summarised below in Table XLI. Three of the forty had died under anaesthesia before the technique had been mastered. Insufficient time had elapsed for stone formation in any of these anaesthetic casualties.

TABLE XLI.

Incidence of Stone after Stone-forming Diet and Hyaluronidase Injections.

| Groups | Total Number | Number with Stone | Per cent. with Stone |
|---|---|---|---|
| I. Stone-forming diet | 19 | 16 | 84.0 |
| II. Stone-forming diet + hyaluronidase | 18 | 14 | 77.0 |

Analysis. There is very little difference in the two groups in terms of the incidence of stone revealed at autopsy. Clinically the rats receiving the hyaluronidase injections were much the poorer group. After a few weeks several of them developed alopecia, skin eruptions, conjunctivitis, and listlessness.

The distribution of the stones is shown in Table XLII.

TABLE XLII.

Distribution of Stones Formed.

| Site of Stones | Group I | | Group II | |
|---|---|---|---|---|
| | No.of rats. | Per cent. | No.of rats. | Per cent. |
| Total rats with stones | 16 | 100.0 | 14 | 100.0 |
| Kidney | 12 | 75.0 | 10 | 71.4 |
| Kidney + ureter | 3 | 18.75 | 2 | 14.8 |
| Kidney + ureter + bladder | 1 | 6.25 | 2 | 14.8 |
| Unilateral | 6 | 37.5 | 5 | 38.0 |
| Bilateral | 10 | 62.5 | 9 | 62.0 |

Analysis. The kidney was affected in all 30 of the rats who formed stones, the ureter in five, and the bladder in only three. The incidence of bilateral stone was surprisingly high (approximately two-thirds), particularly when compared with man. There was no appreciable difference between the two groups (with and without hyaluronidase).

When the disease is bilateral the kidneys appear to be equally affected, as shown in Fig.52. Radiological examination of the kidneys after removal illustrates bilateral pelvic stones with patchy pyramidal and medullary calcification, of equal extent on the two sides. There is no suggestion here that the disease has started on one side and "spread" to the other. Micro-dissection very frequently showed papillary plaques, and many of the tiny stones had a facet corresponding to such an origin. The kidney on the right side in Fig. 53 contains two calcium oxalate stones which have arisen from two eroded renal papillae immediately to the right of them. Analysis of several of the larger stones showed that they were composed of calcium oxalate with occasional traces of calcium phosphate. The principal histological finding was mild deposition of calcium in the tubules. This occurred in all the animals which had formed stones, and in two of the seven which had not.

Conclusion. Hyaluronidase is unable to prevent the development of calculous disease in rats placed on a stone-forming diet. In approximately 80 per cent. widespread calcification and stone formation occur, and there is little to choose between the groups with and without hyaluronidase therapy.

EXPERIMENT 2.

Object: To Assess the Value of Hyaluronidase in Dispersing Induced Calcium Oxalate Stones.

Procedure: Fifty rats were given the stone-forming diet, twenty controls having been placed on the normal well-balanced diet, The primary object was the production of radiologically identifiable calculi in as many animals as possible. To this end the diet was continued for a much longer period than in the previous experiment. X-ray evidence was essential this time in order that the effect of hyaluronidase therapy might be assessed with accuracy. There would otherwise be no certainty that the credit should be given to hyaluronidase in the case of rats found to be free from stone at autopsy.

At three months no suggestive opacities were seen on radiography, and at six months only 20 of the surviving 46 had definite stones (four having died from injury and anaesthesia). It seemed premature to start therapy at this point. The diet was therefore continued for a further six months, (a total of one year), by which time much more convincing evidence of stone-formation was present. It was also apparent that the disease was at an advanced stage in some animals, since calculous anuria and renal failure accounted for seven deaths in the period between six and twelve months. Further delay in starting treatment was dangerous from the survival viewpoint alone. Accordingly the diet was stopped, so that a significant number might remain alive for study.

Radiological examination of the surviving 39 revealed that 36 (92 per cent.) had formed stones. Three who showed no opacity were kept on the stone-forming diet for a further three months, given massive doses of vitamin D, and sacrificed. All three showed widespread tubular calcification; none, curiously enough formed definite discrete calculi.

<u>The 36 stone-forming animals were treated in four groups of nine</u>:-

Group I : On a normal well-balanced diet.

Group II : On a normal well-balanced diet + hyaluronidase injections.

Group III : On the stone-forming diet.

Group IV : On the stone-forming diet + hyaluronidase injections.

The control groups continued throughout on a normal well-balanced diet.

Treatment was carried out on the lines indicated for the four groups for six months. Losses from calculous disease were heavy during this period. Autopsy was performed on all those dying during treatment, and on the survivors who were sacrificed at the end of the period of therapy.

Radiological examination was performed before sacrifice and the removed kidneys were x-rayed before micro-dissection.

The animals on hyaluronidase behaved in the manner described in the first experiment. They were less active, and after a few weeks hardly seemed to resent the injections, so that it became unnecessary to wear gloves.

Results. None of the control animals showed stone formation or any other evidence of disease (whether they were on hyaluronidase or not). The results in the survivors are shown in Table XLIII according to the treatment received by the four groups.

TABLE XLIII.

Results of Treatment of Induced Oxalate Calculi.

| Treatment in the Four Groups. | Total No. | Died during treatment. | Surv-ived. | No. with stones. | Progress of Surv-ivors. |
|---|---|---|---|---|---|
| I. Normal diet. | 9 | 2 | 7 | All | Two smaller on x-ray. |
| II. Normal diet + hyaluronidase. | 9 | 3 | 6 | All | I.S.Q. |
| III. Stone-forming diet. | 9 | 8 | 1 | All | Larger. |
| IV. Stone-forming diet + hyaluronidase. | 9 | 7 | 2 | All | Larger. |

<u>Group I</u>. (On normal diet alone).

In the course of treatment two animals died from calculous anuria. The remaining seven were the fittest of all the survivors (16). All seven had stones, however, and only two showed radiological evidence of reduction in size after treatment. The stones on the whole were larger than those found at the end of the last experiment since the diet had continued for a much longer period. The radiographic size of the stone is shown in Fig.54, in which may be seen a fairly well defined left renal calculus, and a more vaguely outlined stone on the right side. Fig.55 shows the left kidney opened, with the stone lying in the renal pelvis.

The results in this group do not confirm those of Hammarsten (1937), who was able to produce decalcification in a high percentage of induced oxalate calculi merely by restoring the animals to a diet adequate in minerals and vitamins. One of the possible reasons for this may be the length of time for which the animals in this experiment were kept on the diet, and the excessive quantities of oxalate used. It may well be that Hammarsten's results would have been confirmed if treatment had been started before the stage of excessive kidney damage.

<u>Group II</u>. (On normal diet + hyaluronidase). Except that the animals were less fit the results were much the same as in Group I. Only six survived the treatment period, and all showed stones when sacrificed. The same applied to the three who died during treatment.

The addition of hyaluronidase to the normal diet therefore made no difference to the results. The stones in both Group I and Group II rats were much the same size at the end of treatment as they were at the start (apart from the two in Group I which were slightly smaller). Therapy therefore inhibited further stone growth, even although it did not disperse the stones actually present.

Group III. (On stone-forming diet alone). It was not in the least surprising to find that only one survived the six months of treatment, the other eight having died from calculous disease at varying intervals during it. The stones in this group were larger and more widespread at autopsy.

Group IV. (On stone-forming diet + hyaluronidase). This combination proved equally disastrous, only two surviving the treatment period. Radiological and post-mortem examination confirmed that all the animals had larger stones at death than at the commencement of treatment.

Conclusions: (1) Hyaluronidase was ineffective in dispersing induced calcium oxalate calculi in rats.

(2) If anything, the results obtained by restoring the animals to a normal well-balanceddiet alone were better than those with hyaluronidase and the normal diet.

(3) It was impossible to decalcify a high percentage of the stones (leaving behind the organic stroma) as Hammarsten did in 1937 in spite of the fact that the normal, well-balanced diet used in this experiment was very similar to

Hammarsten's "therapeutic diet", which is detailed in Table XLIV.

The Verdict on Hyaluronidase.

The results of the experiments described above leave no doubt that the use of hyaluronidase should be discontinued. It does not protect those who are prone to form stones, nor does it have any appreciable effect on calculi which are already present.

Since hyaluronidase appeared on the therapeutic scene, interest in the urinary biocolloids has been greatly enhanced. In the last analysis this may prove to have been the most valuable contribution made by hyaluronidase. For the moment the balance between crystalloid and colloid has been restored, and further research into the unexplored territory of the latter may bring forth information of the greatest importance in connection with the aetiology and prevention of recurrent stone.

## SUMMARY.

The high recurrence rates noted in the preceding part of this work clearly indicate the need for a vigorous campaign against recurrence in every stone patient, particularly in those subjected to operation.

The first essential is that the correct operation be performed. This means that all the stones should be removed with the least possible trauma, and that obstructive factors should be corrected as they are encountered.

Important measures in the early post-operative period are the exclusion of hyperparathyroidism and other metabolic bone disease by calcium and phosphorus metabolic studies, the detection of hypercalcuria by estimation of the urinary calcium output, and the eradication of urinary infection at the earliest possible moment.

A high fluid intake is recommended for all patients. The diet should be well-balanced and contain adequate quantities of minerals and vitamins.

The further prophylactic management of the patient is based on the crystalloid composition and architecture of the stone. The literature has been reviewed to indicate that the two principal mechanisms of supersaturation leading to precipitation of crystals are:- (1) Hypercalcuria, and (2) Urea-splitting infection.

More than 90 per cent. of upper urinary tract stones contain calcium. The factors responsible for maintaining the solubility of calcium and calcium salts in urine have been studied at some length to explain the rationale on which the various regimes are founded.

Stone analysis, then, is still the key by which the particular regime to be employed is determined. The possibility that all calcium stones may (according to Prien) possess an apatite nucleus is important, since it means that acidification of the urine by dietary and therapeutic means should be the aim in calcium oxalate and calcium phosphate stones alike.

The fields of usefulness of oestrogens in increasing urinary citric acid excretion, of aluminium hydroxide gel in reducing the absorption of phosphate from the bowel, and of salicylates in increasing the urinary glucuronide excretion, have been discussed. They are worthwhile ancillary measures in certain types of patient, particularly those forming rapidly-recurring phosphatic calculi.

Experimental work in animals and clinical trials in stone patients have failed to confirm the value claimed by Butt and his associates for hyaluronidase in preventing recurrent stone formation or in reducing the size of stones already present in the urinary tract.

There is therefore no dramatic new answer to the question asked earlier in this part of the thesis: "How may recurrence be prevented": nor will there be, until much more is known of aetiological factors. In many instances pseudo-recurrence could be eliminated by radiological control on the operating table. There is likewise no reason why pelvi-ureteric obstruction, urinary infection, and hyperparathyroidism should persist uncorrected. The treatment of these lies in our own hands.

This still leaves a large fraction of recurrent cases for which there is no readily apparent cause; who are, in fact, different in no appreciable way from many other patients who do not develop recurrent stone. A therapeutic regime founded on stone analysis is the answer for them, the aim being the production of maximum solubility of the main crystalloid component of the stone by suitable adjustment of urinary pH.

Hyaluronidase has failed to prevent recurrence, but it has directed attention to the colloids. Recent work has suggested the possibility that urinary calculus is, after all, a collagen tissue disease, and aspirin and other anti-inflammatory medicines have been employed to prevent recurrence on this rationale.

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PART V.

# BILATERAL UPPER URINARY TRACT STONE

A Study of 149 Cases with Special Reference to Their Management.

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Section I : A General Review of the Series.

Section II : A Proposed Scheme of Management.

Summary.

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PART V.

## BILATERAL UPPER URINARY TRACT STONE.

The management of patients suffering from bilateral calculous disease is one of the most difficult problems in urological surgery. Expert opinion on the best method of treating the condition is by no means unanimous. The literature reflects these conflicting views, and is of little assistance to the busy general surgeon who encounters the occasional case, and is thus not in the position to base his treatment on the fruits of personal experience. The main object of the present part of this thesis is to evolve a policy of management which may reasonably be applied to the majority of bilateral stone patients. To this end, the clinical course of 149 examples of bilateral involvement has been studied, with particular reference to those presenting special difficulty.

Bilateral stone possesses features of special interest since the disease is now at a more advanced stage. The opportunity has therefore been taken of comparing various aspects of its incidence, treatment, and progress with that of unilateral stone. Reference to the literature has shown very few studies of this nature, and none in a series of this size.

### Section I : A General Review of the Series.

### Some Comparisons Between Unilateral and Bilateral Stone.

There is general agreement that the prognosis is worse when stone formation becomes bilateral (size amongst other things being equal). Reference to Table XLV provides ready proof of this. The figures relating to each aspect of bilateral stone have been expressed as a percentage of the whole.(1114 cases). Bilateral lithiasis represented 13.4 per cent. of all cases (149 in 1114), and this percentage provides a base line or standard of comparison. Those treated conservatively constituted 9.3 per cent. (53 in 568), while operation was required in 17.6 per cent. (96 in 546). In other words relatively fewer bilateral cases were treated expectantly, and relatively more by operation. The actual proportions coming to operation were two out of three for bilateral, compared with one out of two for unilateral. In the same way it was noted that 30 per cent. of all recurrence involved patients with bilateral stone (49 of 164), a figure quite out of proportion to the natural incidence of 13.4 per cent. noted above. These comparisons are illustrated in Fig.56, in which the varying lengths of the columns for unilateral and bilateral stone may be contrasted.

Length of Follow-Up.

One of the most valuable aspects of the present review has been the lengthy periods for which the patients have been followed. The summary at the foot of Table XLVI emphasises that over 60 per cent. have been followed for more than five years, slightly less than 40 per cent. for ten years, 20 per cent. for more than fifteen years, and 8.1 per cent. for more than twenty years. Reliable conclusions may therefore be reached about the clinical progress and late results of the various forms of management.

Sex Incidence.

No difference was shown to exist between unilateral and bilateral cases, the male to female ratio in each being two to one. Table XLVI indicates that 98 of the bilateral stone patients were men and 51 women.

Age Incidence.

Since bilateral stone represents a more advanced form of the disease, the age incidence ought to be a little higher than that for unilateral stone. This proved to be the case. The details are provided in the Appendix, Table 47, page 56, where it will be seen that three-quarters of the patients were in the age-span 30 to 60 years. In unilateral stone a corresponding number is found five years earlier, that is to say, in the range 25 to 55 years. It is obvious, therefore, that involvement of both sides takes a little longer to develop.

Simultaneity.

The term "bilateral" as applied to this series indicates that both sides were affected during the period of observation, although not necessarily at the same time. The facts recorded at the foot of Table XLVII show that only 91, or 61.1 per cent. were simultaneously bilateral when first seen, and that a further eleven developed simultaneity in the ensuing years, bringing the total to 102 patients, or 68.5 per cent. If patients lived to a sufficiently great age (during which the stone-forming process remained active) it is probable that this figure would be very close to 100 per cent.

In the remaining 47 patients the two sides were affected at different times, a serious enough condition, but not nearly so dangerous as simultaneous involvement.

Initial Urine Examination.

The results of urine examination at diagnosis in 77 patients are shown in Table XLVIII. Of 29 cases treated conservatively 13 had sterile urine, compared with eleven of 48 cases treated by operation. The total number of sterile bilateral stones was therefore 24 out of 77, or slightly less than one-third. In unilateral cases this proportion was one-half.

Even so the absence of infection in as many as 24 out of 77 examined was surprising in view of Joly's statement that he had seen only two cases of sterile bilateral stone. It was Joly's belief that the proportion of bilateral cases would not exceed one to two per cent. if infection could be entirely prevented. The results reported in Part I of this work do not support such a contention, since bilateral stone was present in 24 of the 334 sterile cases at diagnosis (approximately 8 per cent.). Infection may be intimately associated with bilateral lithiasis, but it is not the whole answer.

The relationship of initial infection to post-operative recurrence is also indicated in Table XLVIII. Recurrence developed in only 18.2 per cent. of sterile cases compared with 67.6 per cent. of those who were infected, figures corresponding fairly closely with those for unilateral stone. Conversely, and just as significantly, over 90 per cent. of the recurrences were infected, compared with 57.1 per cent. of those free from recurrence.

Radiological Findings at Initial Examination.

This subject is so complex that it has been considered advisable to present it under four headings.

(a) Size. It will be seen from Table XLIX that small or medium unbranched stones were present on both sides in 60 per cent., large or branched in roughly 20 per cent., and small on one side and large on the other side in the remaining 20 per cent. Those treated conservatively have already been considered under these headings in Part II.(Natural History).

(b) Site (or Distribution). The figures given in Table L may, with profit, be compared with Winsbury-White's findings in 100 bilateral cases (both expressed as percentages).

| Site. | Winsbury-White | Present Series. |
|---|---|---|
| Both kidneys | 70.0 | 61.1 |
| One kidney and opposite ureter | 12.0 | 19.5 |
| Both ureters | 3.0 | 8.7 |
| Both kidneys, one ureter | 8.0 | 10.1 |
| Both kidneys, both ureters | 1.0 | 0.6 |

The most interesting difference between the two sets of figures is the relatively high incidence of bilateral ureteric stone found in the present series. In a very limited number of personal cases Joly stated that he had only seen two instances of bilateral stone in the ureter. Jeanbrau (quoted by Joly) could find only eight examples of bilateral ureteric stone in a review of 220 ureteric calculi from the literature. Closer analysis of the 13 cases in the present series reveals that operation was not required in seven, and in the remaining six who came to operation, bilateral intervention was necessary in only two. It may therefore be assumed with some justification that the majority of the bilateral ureteric calculi encountered were small, and were in the process of being expelled from the urinary tract.

(c) Number. Almost 50 per cent. of the 78 patients about whom information is available had multiple stones (more than three). The corresponding figure for unilateral cases was 20 per cent.

(d) Renal Function. Intravenous urography in 76 patients showed that only 18 had normal renal function, a striking testimony to the severity of the disease (Table LI).

Biochemical Findings.

The biochemical findings in a limited number of cases is presented in detail in the Appendix, Table 48, page 57. The most significant fact was the absence of any proven case of hyperparathyroidism, although one is suspected and awaits biochemical and histological confirmation. This is contrary to the general belief that hyperparathyroidism most commonly occurs in association with bilateral rather than unilateral stone.

Hypercalcuria was noted in ten of the 19 patients examined. Three of the ten were merely at the upper limit of normal, viz. an output of 200 mgm. per 24 hours on a fixed low intake of 150 mgm. of calcium.

Stone analysis in 33 cases disclosed some interesting points. It is commonly taught that the majority of bilateral calculi originate in an alkaline infected urine, and for that reason are composed of magnesium ammonium phosphate. In this series only two of the 33 stones examined were of that nature. The majority (20) were oxalate-containing and 16 of these consisted of almost pure calcium oxalate, an incidence very similar to that for unilateral stone. Seventeen of the stones were phosphate-containing, eleven being composed almost entirely of calcium phosphate (apatite).

Treatment.

A broad outline of the treatment carried out in the 149 patients is given in Table LII. Conservative management was applied to 53 cases, whose progress has been closely studied and reported in Part II. Good reason has been brought forward for an expectant attitude to bilateral small calyceal stones which are symptomless and are associated with normal pyelograms.

Operative treatment was necessary in roughly two-thirds of the total, (96 out of 149). The corresponding figure for unilateral cases was 50 per cent. Bilateral primary operations were performed in only 34 cases, and the nature of these is indicated in the summary at the foot of the Table. Once only was a bilateral simultaneous operation considered necessary or desirable. The fact that only 34, or one-third, of the 96, had operations on both sides may occasion some surprise, but there is much truth in Winsbury-White's statement that "the best results are obtained if the surgeon is content with small measures."

The Operations Performed.

Details of the various forms of operative treatment are shown in Table LIII. A total of 165 operations in 96 patients, 130 primary, and 35 secondary, is a further index of the severity of bilateral stone. With the exception of nephrolithotomy, the incidence of the various operations is much the same as for unilateral stone. Nephrolithotomy accounted for 20 per cent. of all primary operations, for the simple reason that conservation of functioning renal tissue was imperative in cases of this type, in whom a very narrow margin of renal reserve remained. In the same way resort was had to nephrectomy in only five of the 35 secondary operations performed.

Post-operative Mortality.

Seven of the patients died as a result of operative treatment, an incidence of 7.3 per cent. The statistics in Table LIV reveal that the mortality rate was lower for cases having unilateral and primary operations, than for bilateral and secondary procedures. Reported figures vary from 2 per cent. to 60 per cent. e.g., Rafin, 60 per cent; Kuster, 35 per cent; and Legueu, 12.5 per cent. - all quoted by Winsbury-White (1954). When the almost inevitable urinary infection, impaired renal function, and poor general condition of many of these patients are recalled, it is by no means surprising that the post-operative mortality is higher than in unilateral cases.

## Post-operative Recurrence.

The results have already been considered at some length in Part III, where the general conclusion was reached that the prognosis was worse than in the case of unilateral stone. The simple fact that patients with bilateral stone constitute only 13.4 per cent. of all stone cases, whereas those with recurrence represent 30 per cent. of all recurrences, is ample proof that this statement is no exaggeration. In plain figures, 49 of the 96 patients undergoing operation had recurrence (one in two): and of the 49, severe recurrence was present in 36, while 13 had mild recurrence.

## Contralateral Recurrence.

Contralateral recurrence after operation on a patient with unilateral stone is one of the forms of bilateral calculous disease in that the condition has spread to the opposite side. It was observed in 29 of the 96 patients (30 per cent.). The incidence in conservative renal operations, nephrectomy, and ureterolithotomy, is shown in Table LV. This should not be regarded as the true index of contralateral recurrence, which is very much lower. The cases in question have been included merely because the development of contralateral recurrence converts them into examples of bilateral stone. It will also be observed that they form part of the group discussed earlier in which the stones do not occur simultaneously on the two sides.

The Late Results and Progress of Bilateral Stone Treated by Operation.

Patients have been studied in three groups according to the size of the stones, and corresponding to the groups considered under conservative management in Part II of this work.

(a) Bilateral Unbranched Calculi. Operation in these patients was undertaken because the stones were too large for natural passage, and therefore were potentially or actually obstructive. The results parallel those for unilateral stone so closely that there is no need to repeat them at this point. They are described in the Appendix, Table 49, page 58.

(b) Unilateral Branched, Unilateral Unbranched Calculi. This group, consisting of 26 patients, is considered in detail in the Appendix, Table 50, page 59, and summarised in Table 51, page 60 of the Appendix.

Information was available about 22 of the original 26 patients followed for periods ranging from one to 42 years. At the latest review only seven were found to be free from stone; five still had large original stones, and the remaining ten had recurrent stone (four small, and six large). Recurrence therefore had affected approximately half of the 22 patients studied. One point of great interest was that only seven of the 15 in whom stone was still present had symptoms. The seven patients who were free from stone also had no symptoms. Hence of the 22 studied only seven (one-third) had symptoms.

(c) Bilateral Branched Calculi. The 23 patients in this category are quoted individually in the Appendix, Table 52, page 61. The results, which have already been studied in connection with expectant treatment of bilateral branched calculi (Part II), are summarised in Table LVI. Of the total of 23 patients, three were untraced, leaving twenty for further study. Ten of these had died (six post-operative deaths, three from uraemia at other times, and one from other causes). Ten were alive, but not one of them was free from stone. The present condition of the surviving ten was rather unimpressive. Five had bilateral recurrence; three had unilateral recurrence, and two had recurrence in a solitary kidney. These results are no improvement on the conservative management of similar types of case, in which eight patients were studied. Three had died from urinary causes, one was untraced, and four were alive (all with stone of course), 5, 5, 8, and 16 years later, only one of the four having symptoms of any degree.

Conclusions on the Post-operative Progress of Bilateral Stone.

The best results are obtained in small or medium bilateral unbranched calculi producing obstruction. The larger stones present many problems which will shortly be considered. Priestley and Dunn (1949) considered that only 50 per cent. of large bilateral stones survived longer than five years without operation, compared with 95 per cent. of those in whom bilateral conservative operations were performed. The selection and physical fitness of the particular cases could easily influence the results to produce figures of this kind. In the last event a decision must be made as to whether the renal inadequacy is due to irreparable damage (in which case the outlook is hopeless), or to obstruction (when early operation is clearly indicated).

## Post-operative Urinary Infection.

The results are detailed in the Appendix, Table 53, page 62, and in the Summary to this Table on page 63 of the Appendix. It is at once obvious that those patients who have a primary or recurrent stone present have a much higher incidence of infection. Conversely, the incidence of primary or recurrent stone is very much lower in those who have sterile urine. Fifty of the 90 cases studied had urinary infection, the commonest organism being B.Coli. Proteus and Staph. Aureus were much less common, but were almost invariably associated with stag-horn calculi.

## Section II : A Proposed Scheme of Management.

The subject of bilateral calculi and their management bristles with difficulties. Aetiology is obscure, and confusion therefore persists about the best method of treatment. The clinical picture is often misleading in respect of symptoms, which may be mild with large stones and severe with small ones. Often the kidney which has suffered the greater damage has ceased protesting, and is therefore "silent" and functionless. Many of the cases have the narrowest margin of reserve tissue and are bordering on uraemia. And to render almost impossible that which is already very difficult, post-operative recurrence may be expected in one-half of the cases. Other factors which must be considered are age, general condition, and a previous history of multiple operative procedures for stone, any of which may influence to a great degree the decisions made about therapy.

When calculous disease involves both kidneys the clinical types produced may indeed be protean. There can therefore be no hard and fast rule covering every possible combination and permutation. In the last event each case must be resolved on its merits. A broad statement of this nature is, however, of very little value to the surgeon who wants to know the answer in a particular case. His main concerns are (1) whether to treat conservatively or by operation; (2) whether to deal with one or both sides; (3) which side to tackle first; and (4) which operation to perform.

To a fortunate few the answer is delightfully simple. In the words of Joly (1929): "In bilateral calculi (which are small and aseptic) an operation is the only means of saving the kidneys and should be performed at once." To others the solution does not come quite so easily, and several writers have suggested with varying emphasis that certain types of case are better left alone, particularly those which are large and symptomless (Collings, 1950; McDonald, 1936; and Tait, 1949).

Where, then, does the truth lie?

## Clinical Course of Upper Urinary Tract Stone.

It may be of assistance in reaching a few broad conclusions on which the management of these problem cases may be based if two well-defined types of stone-formation are considered:-

(1) The rapidly progressing, obstructive, form, in which there is great destruction of renal tissue from severe back-pressure. Prompt and effective treatment is essential if the kidney is to be saved. Curiously enough the stones responsible for this state of affairs are often small or moderate in size, and are found to be impacted in the pelvi-ureteric junction or upper ureter.

(2) The slowly progressing, large, branched, stone which appears to allow fairly adequate urinary drainage. The stone slowly enlarges by a combination of slight obstruction and mild infection over a period of many years, and kidney damage is correspondingly gradual.

## General Principles in Management.

With these clinical types in mind, certain general principles in the management of bilateral calculi may be stated.

(1) Conservatism is very strongly advocated in this particular form of renal disease. A decision about the desirability of operative intervention may best be reached by considering which will harm the kidney more - the continued presence of the stone, or the operation by which it is removed. Conservatism implies action in the patient's best interests by

sparing healthy renal tissue whenever possible, and if this can be combined with total removal of the stones so much the better. It does not signify a rigid adherence to therapeutic nihilism, as, for example, where pyonephrosis is allowed to persist with grave effects on general health from prolonged and unrelieved sepsis.

(2) The obstructive or potentially obstructive stone should be dealt with first. If stones of this type are present on both sides, that which is producing the greater degree of back-pressure should be given priority. For the same reason ureteric calculi should be removed before those in the kidney. The potentially obstructive stone may be small enough that there is still a reasonable prospect of natural expulsion. In this case there should be no hesitation in recommending expectant treatment, providing the pyelogram on this side is normal, and the strictest precautions are taken to review the situation at very short intervals, to guard against the possibility of calculous anuria. Once the obstructive stone has passed or has been removed, the other side should be treated on its merits.

The usual dictum is that the "good side" or "the side on which pain was last felt" should be treated first, where a small obstructive stone is present on one side and a large non-obstructive stone occupies the remaining kidney. The "good" side is usually the obstructive side since it is the small stone which more readily produces back-pressure. The exception to this rule is said to be the presence of advanced pyonephrosis in association with the large stone. Other exceptions might be:- (a) Severe pain on the side of the apparently non-obstructive large stone; but this is unusual, unless in the presence of severe infection. (b) Unfitness for operation, or advanced age; and (c) Multiple previous operations causing reluctance on the part of the patient to submit to further treatment.

(3) Where bilateral symptomless stag-horn calculi of non-obstructive type are present there is much to be said for an expectant attitude, in which treatment is directed to overcoming the grosser manifestations of infection and to correcting electrolyte imbalance. The only exceptions to this conservative outlook might be:- (a) Persistent and disabling pain, (b) severe infection, (c) dangerous haematuria, and (d) early signs of renal failure.

Simultaneous bilateral calculi pose a much greater problem than stones which occur on the two sides at different times, and it is with the former group that we are now principally concerned.

Summary of these Principles.

The principles enunciated above suggest that there are really only two categories into which any case may fall, and that in each of these operation may or may not be indicated. The categories are:-

1. The OBSTRUCTIVE in the majority of which operation is indicated. Possible exceptions may be due to advanced age, poor general condition or reluctance on

the part of a patient who had undergone many previous operations for stone.

2. The NON-OBSTRUCTIVE in the majority of which operation is not indicated. The only indications for operation in large bilateral stones of this kind are severe continued pain, unilateral infection, dangerous haematuria, or rapidly progressing renal failure, particularly if detected at an early stage.

These points are illustrated in the various examples provided in Fig.57 which are discussed at greater length below, and amplified whenever possible by relevant histories of patients who presented that particular picture.

Example (a) in Figure 57 - Bilateral Small Potentially Obstructive Stones.

This is one of the classical ways in which calculous anuria is produced. Urgent removal of the right upper ureteric calculus is indicated. This may or may not have been the side on which pain was last experienced, but it certainly is the side showing the effects of early obstruction with early clubbing of the calyces. Furthermore, the stone on this side is larger and less likely to pass naturally than the relatively small stone depicted on the left side.

The plain films from the case in question are shown in Fig. 58. The patient, a male, aged 40, complained of brief right renal colic and intravenous pyelography (which produced unsatisfactory films) suggested the presence of bilateral upper ureteric calculi, a fact which was readily confirmed by retrograde pyelography, Fig. 58 (a). A stone of moderate size lay over the tip of the transverse process of the third lumbar vertebra on the right side, an ascending pyelogram of which showed early hydronephrosis. On the left side a smaller stone was present immediately below the transverse process of the same vertebra, and the pyelogram on this side was normal. The symptoms settled after the ureteric catheterisation, but since the stones had made very little progress when x-ray was repeated two weeks later, Fig. 58 (b), operation was considered essential to avert the possibility of calculous anuria. The right upper ureteric calculus was therefore removed through the triangle of Petit. Three months later he had a short left renal colic followed by the passage of the stone from that side. Intravenous urography confirmed that the urinary tract was free from opaque calculus, and that renal function was normal, the right hydronephrosis having settled.

Example (b) in Figure 57. Combination of Obstructive and Non-Obstructive Stones of Moderate Size.

This type of case occurs quite commonly, and causes the least concern of all. There would be general agreement here that the obstructive stone on the right side should be removed first, because it has very little chance of passing naturally, and already it has produced a minor degree of calyceal clubbing. Thereafter the "nest" of small stones in the left lower calyx are considered from the viewpoint of partial nephrectomy.

Example (c) in Figure 57. Unilateral medium Obstructive, Unilateral Stag-horn Non-Obstructive.

A stag-horn calculus is present in a right poorly functioning kidney, in combination with a potentially obstructive stone of moderate size in the left renal pelvis, thus far unassociated with hydronephrosis. The left is the "good" side, and it is much more likely to be the side on which pain is experienced. The right is the "bad" side, but pain of any severity is unlikely in the absence of acute infection with intermittent obstruction leading to pyonephrosis. Most surgeons prefer to deal with the obstructive stone first, so that at least one kidney is healthy. Fortunately this is in accord with the patient's symptoms. Once this has been achieved right nephrectomy may be performed with an easier mind. A different opinion has been expressed by Cumming (1950), who feels that an operation on the "good" side may induce temporary cessation of function, during which the "bad" side may not be sufficiently active to support life. The fallacy in this argument is that the same or even worse will surely obtain when he later comes to deal with the "good" side which is then a solitary kidney, its partner having been removed, or damaged to some extent by a fairly extensive conservative operation.

The general principles involved in this type of case are clearly illustrated by the patient whose plain films are shown in Fig. 59. At the age of 50 a large stone had been removed from his left lower ureter, re-implantation into the bladder proving necessary on account of extreme narrowing immediately distal to the site of the stone. Five years later he was reviewed in the course of this investigation, having experienced no symptoms in the interval, and was found to have an early stag-horn calculus in a practically functionless right kidney (Fig. 59 (a) ), and two large left lower ureteric calculi, (Fig. 59 (b) ), function on this side being practically nil. His general condition was poor. Mild azotaemia was already present, and his abdominal wall was extremely flabby, but it was considered reasonable to remove the obstructive stones at the lower end of the left ureter in the hope that some function would be restored to this side. Naturally the ureter proximal to the stones was greatly dilated and the slightest alteration of the patient's position shot the stones up into the kidney, from which, however they were easily milked down by a hand introduced into the peritoneal cavity.

The examples discussed to this point have all involved obstructive stones on one side or the other, and the decisions have been relatively easy so far as their management has been concerned. When we turn to consider the non-obstructive group the situation becomes much more complex.

<u>Example (d) in Figure 57.</u> <u>Bilateral Small Calyceal Non-Obstructive.</u>

The good prognosis accompanying these stones has already been shown in Part II where it has been noted that 28 out of a total of 42 have actually improved during the period of observation. Therefore treatment is indicated only for persistent and severe pain, or in the rare instance in which they come to lie free in the renal pelvis, producing hydronephrosis.

A clinical example of this type is provided by the case illustrated in Fig. 60, which shows bilateral stones of medium size scattered throughout both kidneys. Operation was delayed for eight years on account of poor general health and the patient's failure to report. The latest x-ray examination has shown no change in the size and number of the stones, and renal function has not deteriorated.

Example (e) in Figure 57. Large Bilateral Non-Obstructive Calculi.

The classical example of this type has already been shown in Fig. 26, the patient having been followed for 16 years with progressive enlargement of the stones, absence of symptoms, and fairly good kidney function. Example (e) in Fig. 57 is of the same type, and the general conclusion reached is that expectant treatment gives better results than operation, which is indicated only for severe pain or unilateral infection. The correct procedure under these circumstances is removal of the stone followed by irrigation with solution "G" through a nephrostomy tube.

Two sub-groups may be identified, one with a large stone on one side and a small stone on the other, the second with large bilateral painless stones.

(a) Bilateral Non-Obstructive; Large on One Side, Small on Other.

Where symptoms are absent or minimal, conservative management is still to be preferred. The patient featured in Fig. 61 was first seen in 1937. After eight years of conservative management the stones had not altered appreciably, and his general condition and renal function were good. He has been untraced since that time.

The development of pyonephrosis is one of the signals for early action. The patient shown in Fig. 62 (a and b) had a tender mass in the right loin, and nephrectomy became necessary for a non-functioning kidney with multiple calculi. The small stones in the left inferior calyx require no operative treatment since kidney function is good (Fig. 62 (b)), and she is aged 65.

The other indication for surgery is pain of incapacitating degree. Fig. 63 (a) is a plain film of the urinary tract showing a staghorn calculus in the left kidney, and a dendritic stone in the right upper calyx. The left side is non-functioning, (Fig. 63 (b)) but the right side shows surprisingly little damage in spite of the presence of a fairly large stone. Had this woman been free from pain no action would have been taken. As it happened, she had frequent bouts of right renal colic, and resection of the right upper calyx was performed. Her pain is difficult to explain since the stone was clearly not an obstructive one, and there was no gross evidence of urinary infection.

(b) <u>Bilateral Non-Obstructive;</u> <u>Large on Both Sides.</u>

Once every so often a case of this nature is revealed as an incidental finding during radiological examination of gastrointestinal or orthopaedic cases. The bilateral stag-horn calculi in Fig. 64 represented the only positive findings of a barium enema examination. Massive recurrence after conservative renal operations may also be "silent", as was the case with the very dense recurrent calculi shown in Figure 65., the sequel to an operation on the right kidney many years previously.

The indications for operation are the same as in the previous group. The bilateral calculi in Fig. 66 (a) required treatment for recurring attacks of severe pain on both sides. On the left side an upper calycectomy was performed, and the stones in the right kidney were dealt with by nephrolithotomy. Seven years later she has evidence of multiple scattered calculi of moderate size on the right side, the left side remaining clear. Infection, particularly if it is unilateral is also a reason for surgical intervention. The patient in Fig. 67 was first seen on account of painless haematuria, and was found to have large stones in both kidneys, the left being functionless, and only the upper half of the right kidney containing useful functioning tissue. Expectant treatment was recommended in the first instance, but the development of pyonephrosis on the right side (the one on which his life depended) indicated the need for early action. The right kidney was drained for several weeks, the stones having been removed at the same time, and there is no doubt that this, together with correction of electrolyte imbalance, proved life-saving. (Fig. 67 (c) ).

<u>Conclusions Regarding the Management of Bilateral Calculi.</u>

The most important practical lesson which may be learned from the study of this series is that each patient presents a different problem, or different aspects of the same problem. Each therefore requires separate assessment after a very full investigation. The aim throughout should be to do the greatest good to the patient, and the least possible harm to the kidneys. The general policy devised from consideration of the numerous examples in the preceding pages is that obstructive stones with very few exceptions require early surgical treatment if the kidney is to be saved. If there is no clear evidence of obstruction, and symptoms are absent, many kidneys occupied by multiple large stones or stag-horn calculi are better left alone. Joly thought that large "silent" calculi should be treated by nephrostomy, but application of this policy to the lady in Fig. 26, who was followed for 16 years, would have meant that she would have been burdened through all those years with a nephrostomy tube. The only exceptions to expectant management of large non-obstructive bilateral stones are persistent and severe pain, unilateral infection, dangerous haematuria or progressive signs of renal failure.

No sooner has a policy been agreed upon than a case is sure to turn up which has atypical features and does not readily fit any of the categories enumerated. It is felt, however, that such anomalous cases will be reduced to a minimum if the simple criterion of obstruction is constantly kept in the front of one's mind. There can never be any hard and fast ruling, and each case should be judged on its merit. For those who drift steadily into renal failure, kidney transplantation from a donor would be a life-saving measure, and it may well prove that the technical difficulties involved may be overcome long before the mystery surrounding the cause of kidney stone has been solved.

## SUMMARY.

A general survey of bilateral calculous disease has shown that it is more serious than unilateral stone in many respects, the most important being the greater post-operative mortality, and the poorer long-term results.

A series of 149 patients with bilateral stone has been studied to determine the broad principles on which their management should be founded. The late results of operative treatment indicate a poor prognosis in all types of case apart from small obstructive stones.

A policy of management has been stated on the basis of two clearly defined forms of stone-formation:-

(1) The obstructive which lead to rapid and complete destruction of the kidney, and

(2) the non-obstructive, which are often large and symptomless, yet are associated with very gradual deterioration of renal function.

Numerous examples have been quoted to illustrate the applications of these principles. Inevitably there are

exceptions to the general rule, and these have been clearly stated.

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## PART VI.

# BIOCHEMICAL STUDIES

of

# UPPER URINARY TRACT STONE

Section I : Stone Analysis.

Section II : Urinary Calcium Output Studies.

Section III : Blood Chemistry.

Section IV : Hyperparathyroidism.

Summary.

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## PART VI:

## BIOCHEMICAL STUDIES OF UPPER URINARY TRACT STONE

A recurring theme throughout this work on upper urinary tract stone has been the role of biochemical disturbance (particularly that of calcium) in the aetiology of primary and recurrent stone. The practical application of such knowledge to the prevention and treatment of calculous disease has always seemed highly desirable; but this is possible, so far, in only a minority of patients, due almost entirely to our lack of concrete information about aetiology. If biochemical studies can do anything to unravel the mystery surrounding the cause of stone they will have made a major contribution to our understanding of the subject.

In this investigation the importance of calcium and phosphorus metabolic studies was appreciated from the outset, and every opportunity was therefore taken of carrying them out. Ideally, each of the 778 patients reviewed should have been investigated from this angle, but it was manifestly impossible to add this volume of work to an already overburdened Biochemistry Department. Smaller numbers have therefore been studied in greater detail, and much information has been assembled about the following group of patients:-

(1) Operation Cases:

Those admitted to hospital for operation or observation were studied intensively during the period of convalescence. Stone analysis, either quantitative or qualitative, was routinely performed. As soon as patients were ambulant, calcium and phosphorus metabolic studies were commenced. The urinary calcium output over 24 hours was determined on the seventh, eighth and nine days of a nine-day fixed low calcium intake (150 mgm/24 hours). At the beginning and end of this period, fasting blood was taken for estimation of the serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, plasma proteins, blood urea and electrolytes. If the findings were equivocal the blood examination was repeated.

(2) Patients with Recurrent Stones.

In the course of the investigation many recurrences were detected, and it was obviously desirable that hyperparathyroidism be excluded. Blood chemistry was accordingly examined; stones preserved from the date of operation, or passed since then, were analysed; and the calcium content of their urine was roughly assessed by the Sulkowitch test.

(3) Patients with Bilateral Stone.

Although we no longer believe that hyperparathyroidism is necessarily commoner in bilateral lithiasis, the latter does represent a more serious form of the disease, thoroughly meriting biochemical survey. Similar investigations to those mentioned above were therefore performed in all outpatients suffering from bilateral stone.

(4) Patients Passing Multiple Stones.

The repeated passage of stones constitutes a great disability to the patient and indicates a more active state of calculus formation at an early stage. It was hoped that biochemical study would prove profitable in demonstrating the reason for such activity.

It is significant that six new instances of hyperparathyroidism have been revealed since these biochemical examinations were extended to as many stone patients as possible. Even so, only 200 patients have been biochemically "screened", and it is probable that more complete investigation of the remaining 900 patients of the total series of 1,114 would bring to light further examples of hyperparathyroidism.

The value of chemical analysis of calculi in determining the correct regime for the prevention of recurrence has already been discussed.

The significance of hypercalcuria is not yet known in the majority of the patients in whom it occurs, but it is obviously an important factor in calcium-containing stones, and further study of it is necessary.

## SECTION I. CHEMICAL ANALYSIS OF URINARY CALCULI.

It is with considerable diffidence that the results of stone analysis by chemical techniques are presented here, since modern emphasis is almost entirely on refined biophysical techniques. These employ x-ray crystallography to determine the chemical nature and physical state of the crystalline components of the stone; and the information gained is supplemented by microradiography and x-ray microdiffraction to define the topographical relationships of the various substances present.

Neverthless, much valuable information about the structure and composition of calculi has been discovered by the older and well established biochemical method, and a great deal of the modern biophysical work is based on these older studies.

The present study is based on the quantitative and qualitative chemical analysis of 204 upper urinary tract stones by the Biochemistry Department of the Victoria Infirmary. The principal reason for analysis of calculi is the assistance afforded the clinician in providing the patient with a preventive regime. It will be interesting in due course to compare the results obtained by the older chemical methods with those of the newer highly refined biochemical techniques.

<u>Methods of Chemical Analysis of Urinary Calculi.</u>

The quantitative method employed in the Victoria Infirmary is detailed in the Appendix, pages 74, 75 and 76. It is time-consuming but gives an extremely accurate impression of the various components and their relative porportions. Ninety of the total of 204 stones have been analysed in this way, the remaining 114 having been studied by less accurate qualitative methods.

Prien and Frondel (1947) objected to "ordinary chemical methods of stone analysis", which they considered unsatisfactory for the following reasons:-

(1) There was confusion as to the exact nature of the reactions which took place in the procedures used in chemical tests; (2) interfering organic substances of unknown composition

might invalidate these reactions; (3) the complex nature of the phosphates in calculi was not amenable to resolution by chemical methods alone, and (4) the small size of many calculi made complete chemical examination impossible.

Results of Chemical Analysis of Urinary Calculi.

(a) Analysis of 204 Calculi. The stones were analysed by quantitative methods in 90 instances, and the results will be given in greater detail shortly. The remaining 114 stones were analysed by the ordinary qualitative routine. Primary stones accounted for 174 of the total, and the other 30 were recurrent calculi. The results for the series of 204 are shown in the Appendix, Table 54, page 64.

In the discussion which follows the terms "calcium phosphate" and "apatite" are regarded, for practical purposes, as being synonymous, although it is appreciated that in strictly accurate terms, apatite is a mixture of calcium carbonate and calcium phosphate.

If all the stones composed of apatite and calcium phosphate are incorporated under the one heading, and if apatite and triple phosphate stones are taken together the results of the Table might thus be summarised:-

| Stone | Number | Per cent. |
|---|---|---|
| Calcium Oxalate | 77 | 38 |
| Calcium Oxalate + Apatite | 57 | 28 |
| Calcium Oxalate + Triple Phosphate | 6 | 3 |
| Apatite + Triple Phosphate | 59 | 29 |
| Uric Acid | 3 | 1 |
| Cystine | 1 | 0.5 |
| Others | 1 | 0.5 |
| | 204 | 100.0 |

The points of interest arising from this summary are:-

(1) Only ten of the total of 204 stones did not contain calcium. In other words, at least 95 per cent. were calcium stones. The significance of this fact in terms of the prevention of recurrence has already been discussed at some length in Part IV of this work.

(2) "Pure" oxalate stones (77) represented more than one-third of the total, and oxalate-containing stones (140) almost two-thirds.

(3) Phosphate-containing stones numbered 122, approximately 60 per cent of the total. Only 42 were "pure", (38 calcium phosphate, and 4 apatite). In the "recurrent stone" group of 30, phosphate stones were commoner, 24 out of the 30 concerned having some phosphate in their composition.

(4) Magnesium ammonium phosphate ("triple" phosphate) was present in only 23 stones, or slightly more than one-tenth of the total. This implies that urea-splitting infection, on the whole, was relatively uncommon.

(5) The incidence of uric acid, urate, and cystine stones was exceedingly low.

(b) Relationship to Recurrence.

The relationship of the composition of the stone to recurrence has already been discussed in Part III of this work. It has been possible to study this in greater detail in 122 cases, as shown in the Appendix, Table 55, page 65.

If the same terminology and grouping is followed the results may be summarised thus:-

| Stone | Total | Recurrence | Recurrence Per Cent. |
|---|---|---|---|
| Calcium Oxalate | 44 | 10 | 23 |
| Calcium Oxalate + Apatite | 36 | 6 | 17 |
| Calcium Oxalate + Triple Phosphate | 4 | 0 | - |
| Apatite + Triple Phosphate | 35 | 10 | 30 |
| Uric Acid | 2 | 0 | - |
| Cystine | 1 | 0 | - |

It is therefore obvious that phosphate (or apatite) stones recur more readily than oxalate but the difference is not greatly marked. Strangely enough magnesium ammonium phosphate stones, as well as being relatively rare, do not show, in this very small series, any great tendency to recurrence. Triple phosphate was present in some measure in 13 stones, only two of which were associated with recurrence (roughly 16 per cent.).

(c) Incidence of Different Types in "Operation" and "No Operation" Series.

This may also be determined by consultation of Table 55, page 65 in the Appendix. The outstanding point is that calcium oxalate in "pure" form constitutes 54 per cent. of stones treated conservatively, compared with 36 per cent. of those for which operation is required.

Oxalate-containing stones, i.e. not necessarily pure oxalate, constituted almost 80 per cent. of the group treated conservatively, 40 of the 52 being of this nature. Stones composed of apatite with or without triple phosphate occurred a little more commonly in the operation series. They require operative treatment on account of their more rapid rate of growth, which causes them to be trapped in the kidney at an earlier stage of their clinical career.

(d) Relationship to Urinary Infection.

This may also be determined by consideration of the Appendix, Table 55, page 65. It was possible to relate the composition of the stone to the presence or absence of urinary infection in 147 of the 174 stones analysed. The results may be summarised, as previously, for the four main groups.

| Stone. | Sterile (No) | Infected (No) | Per cent Infected |
|---|---|---|---|
| Calcium Oxalate | 36 | 22 | 38 |
| Calcium Oxalate + Apatite | 20 | 21 | 50 |
| Calcium Oxalate + Triple Phosphate | 2 | 4 | 67 |
| Apatite + Triple Phosphate | 11 | 28 | 70 |

The points of interest arising from these figures are:-

(1) The incidence of aseptic and infected stones was almost equal, a point which corresponds exactly with the incidence of infection in 665 patients at the initial examination.

(2) As we proceed from oxalate stones, through mixed oxalate and apatite, to apatite with or without triple phosphate, the incidence of infection steadily rises.

(3) The third point of interest in connection with magnesium ammonium phosphate stone now emerges. It is surprising that any of the stones containing this compound should be sterile as the mere presence of magnesium ammonium phosphate is indicative of urea-splitting infection. In point of fact it was associated with sterile urine in four of the 18 stones in which it was present.

## Quantitative Analysis of Urinary Calculi.

Quantitative analysis of 90 upper urinary tract calculi has been performed in the Biochemistry Department of the Victoria by the method mentioned earlier. (Shown in detail in the Appendix, pages 74 to 76). It has been used in this series of cases over the period from 1951 to 1955. The cases are not consecutive, but most of those seen in that period are included.

The results are indicated at some length in the Appendix, Table 56, pages 66 and 67, and it may be helpful in digesting this mass of figures if they are prefaced by the following explanatory remarks.

(1) Calcium Content. It has been noted earlier that practically all stones contain some calcium, apart from those composed of pure cystine, uric acid, or magnesium ammonium phosphate. The calcium percentage in the stone was estimated in 54 of this series of ninety. Only four showed complete absence of calcium, i.e. over 90 per cent. were calcium-containing. Stones containing anything from 20 to 40 per cent. of calcium may be regarded as composed

chiefly of calcium salts, and this applied to 44 of the 54 examined (over 80 per cent.). Theoretically the calcium content of a purely oxalate stone is rarely higher than 27 per cent. and in the case of phosphate or apatite it seldom exceeds 40 per cent. The highest percentage of calcium in an oxalate stone in this series was 29.3 per cent., and in the phosphate-apatite series 40 per cent.

(2) The Percentage Ash. The quantity of ash depends on the relative proportion of organic and inorganic constituents. The higher the organic content the lower the ash since organic compounds are converted to water and carbon dioxide on burning. The main components of the ash are therefore calcium, phosphorus, and possibly carbon and sulphur. One patient passed many small stones composed of a complex polysaccharide; on analysis they showed practically no ash due to the high organic content.

Oxalate stones, for similar reasons, have a lower ash than phosphate or apatite stones. The theoretical ash in pure oxalate stones is 40 per cent., and in phosphate stones 100 per cent., but due to the presence of minute quantities of organic and other inorganic materials these figures are never obtained. It is, after all, impossible to have a stone composed of crystals alone, however greatly such a conception may appeal to the exact mind of the analytical biochemist. Colloidal matter is necessary in some quantity for the production of a calculus. As the Table shows most oxalate stones have an ash percentage in excess of fifty.

(3) Theoretical Findings on Principal Constituents.

It is generally agreed that there is no such thing as a "pure" calculus. In this series the highest percentages of the compounds were:- Oxalate - 98.6 per cent: Phosphate - 54 per cent: Cystine - 79 per cent. and Uric Acid - 91 per cent. It is of considerable assistance to the clinician to know what the theoretical findings in pure stones would be, and reference to the charts in Table 56(a), page 67(a) of the Appendix shows the theoretical composition of pure stones with some typical results. These charts have been prepared by Mr. A. J. Kenny of the Biochemistry Department of the Victoria Infirmary, and await publication.

Even with such a guide at hand it is not always easy to state clearly and simply which are the principal constituents of any given stone, for the very good reason that many contain two or more compounds. From the clinical viewpoint the nature of the main constituent is the all important consideration. That is one reason why advanced biochemical and biophysical examinations of calculi appear quite often to confuse rather than to clarify the issue.

In this Table the following rough rule has been observed:- Stones containing more than 60 per cent. of calcium oxalate or more than 20 per cent. of calcium phosphate have been regarded for practical purposes as being pure. Where the oxalate content in a mixed stone has been lower than 20 per cent. and the phosphate less than 10 per cent., they have been disregarded.

When the magnesium in the ash approached 9.8 per cent. and was associated with ammonium and a phosphate of 20 per cent. or more, the stone has been regarded as mixed apatite and magnesium ammonium phosphate. The greatest difficulty has arisen in deciding which of the 90 should be regarded as composed of mixed oxalate and phosphate. In general terms, when the oxalate lay between 20 and 60 per cent., and the phosphate between 10 and 20 per cent. (in combination), the stone was considered to contain a mixture of roughly equal amounts.

With these very rough criteria as a guide the 90 stones proved to have the following composition:-

| Composition. | Number. | Per Cent. |
|---|---|---|
| Calcium Oxalate | 34 | 38 |
| Calcium Oxalate + Apatite | 21 | 23 |
| Calcium Oxalate + Triple Phosphate | 2 | 2 |
| Apatite + Triple Phosphate | 27 | 30 |
| Uric Acid | 1 | 1 |
| Cystine | 1 | 1 |
| Insufficient material | 4 | 5 |
| | 90 | 100 |

Biophysical and Biochemical Methods of Stone Analysis Compared.

It is opportune at this point to compare the results obtained by the older biochemical methods with those by the newer biophysical techniques. For the sake of uniformity and simplicity the stones are grouped in the compositions already encountered in this section, and the results of the following four series of analysis are studied and compared:-

(1) Chemical analysis of 204 stones by qualitative methods.
(2) Chemical analysis of 90 stones by quantitative methods.
(3) Biophysical analysis of 600 stones (Lagergren, 1956).
(4) Biophysical analysis of 1000 stones (Prien, 1949).

The first two series are those from the Victoria Infirmary which have already been discussed. Table LVII shows the percentage incidence of the various types of stone in the four series.

TABLE LVII.

Comparison of Biophysical and Biochemical Methods.

| Composition of Stone. | Percentage Incidence | | | |
|---|---|---|---|---|
| | Biochemical Methods | | Biophysical Methods | |
| | Qualitative (204) | Quantitative (90) | Lagergren. (600) | Prien (100) |
| Calcium Oxalate | 38.0 | 40.0 | 15.0 | 36.0 |
| Calcium Oxalate + Apatite | 28.0 | 24.0 | 44.0 | 31.0 |
| Calcium Oxalate + Triple Phosphate | 3.0 | 2.0 | 4.0 | 2.0 |
| Apatite + Triple Phosphate | 29.0 | 31.0 | 32.0 | 21.0 |
| Uric Acid | 1.5 | 1.5 | 4.0 | 6.0 |
| Cystine | 0.5 | 1.5 | 1.0 | 4.0 |
| | 100.0 | 100.0 | 100.0 | 100.0 |

Analysis of Table LVII.

1. In spite of Prien's doubts about the value of ordinary chemical methods there is an impressive degree of similarity between his results and those of the Victoria Infirmary Biochemistry Department.

2. In striking contrast, the two series in which biophysical methods were used show great variations in the results obtained, illustrating the difficulties of interpretation when multiple constituents are present in a stone.

3. These differences are more apparent than real. They arise mainly from doubt about what constitutes a mixed oxalate and phosphate (apatite) stone. If the first two lines of the Table are added to give the total for oxalate and mixed oxalate and apatite stones the figures from left to right will read 66, 64, 59, and 67 per cent. respectively, indicating a reasonable degree of harmony.
4. The incidence of cystine and uric acid stones is higher in Prien's series, and this seems to coincide with a lower percentage of apatite and magnesium ammonium phosphate stones.

Conclusion.

Crystallographic studies of stone composition and architecture are of great value from the viewpoint of research, but offer no more information to the clinician than do biochemical methods of analysis. In both, the emphasis is directed almost entirely to the crystalline components, and at present it would appear that aetiology is unlikely to be solved from that direction alone. This in no way implies that such studies are without value. By indicating how the components of calculi conglomerate it is possible that they may provide valuable clues leading to the solution of why this occurs.

Practical Value of Stone Analysis.

The principal value of stone analysis lies in the assistance it affords the clinician in devising a regime for the prevention of recurrence. This has already been considered in such great detail elsewhere that there is no need to repeat it at this point, except to stress its importance in every case in which a stone is passed by the patient or removed surgically.

## Section II. Urinary Calcium Output Studies.

In any consideration of calcium and phosphorus metabolism it is highly artificial to separate the chemical findings in the blood from those in the urine, since they are complementary and reflect different aspects of the same subject. For our present purpose, which is the presentation of results, it is convenient, and in extenuation of the practice it is pointed out that the two will be brought together from time to time to show how the one influences the other.

Studies of urinary calcium output have been conducted principally in patients admitted to hospital for operative treatment of calculi. The average 24-hour output of calcium, phosphorus, and creatinine on a standard low calcium and phosphorus intake has been estimated in 73 patients, six of whom had hyper-parathyroidism, and a rough assessment of the urinary calcium on an ordinary diet has been gained from the Sulkowitch test in a further 19 patients.

### Method.

The low calcium and phosphorus diet shown in Table LVIII was given for six days before the collection of specimens to allow for the stabilisation of the urinary calcium excretion. The ideal diet recommended by Albright (1948) contains only 100 mgms. of calcium, but this is practically impossible in Britain at present owing to the fortification of flour with calcium carbonate. The nearest one can hope to get to this ideal calcium intake is 150 mgms. per day. The patient should be ambulant while the test is in progress to minimise mobilisation of calcium from the skeleton, and the stress factor associated with operation should have subsided. For these reasons the diet is started on the fifth post-operative day, continued for six days, and for three after that, on each of which the 24-hour specimen is collected. The specimens are pooled and the 24-hour calcium output is determined by a modification of the method of analysis of the calcium content of animal foodstuffs reported in Technical Communication No.9 of the Imperial Bureau of Animal Nutrition (1937).

On the strict low calcium intake of 100 mgm. per day, anything over 150 mgms. urinary calcium excretion is regarded as above the upper limit of normal; but with the rather uncertain intake that may be achieved (in spite of all precautions) on the present British diet, it is safer and more accurate to raise the upper limit of normal to 200 mgms. in 24 hours, (Albright, 1948 Anderson, 1954). On a fixed low intake of 0.50 gm. per day the urinary phosphorus excretion should not exceed 0.50 gm. per day.

Results.

The average urinary 24-hour excretion of calcium, phosphorus, and creatinine has been estimated in 67 stone patients, cases of hyperparathyroidism being omitted from the study for the moment. The individual results are shown in Table 57, on pages 68 and 69 of the Appendix. Accepting 0.15 gm. of calcium per 24 hours as the upper limit of the normal urinary calcium excretion on a standard low calcium intake, 42 had hypercalcuria (63 per cent.). This figure is remarkably close to that of Flocks (1939) who was greatly impressed by the importance of hypercalcuria in his own cases (15 out of 23 cases or 65 per cent.). We have, however agreed that it is unwise to place the upper limit of normal as low as 0.15 gm. per 24 hours. If it is moved up to 0.20 gm. the number with hypercalcuria becomes 28, (as is indicated at the foot of page 69 of the Appendix), and the percentage drops to 41.8. There is doubt about the exact level at which hypercalcuria becomes significant, especially in relation to stone formation, but few would deny that a level of 0.30 gm. per 24 hours is excessively high on such a low intake. Eight patients showed outputs above 0.30 gm., i.e. 50 per cent. above the upper limit of normal; two above 0.40 gm. per 24 hours., i.e. twice the upper limit of normal; and one was actually above 0.50 gm. per 24 hours.

<u>The Relationship of Hypercalcuria to Recurrence.</u>

The extreme right hand column of Table 57 attempts to show the relationship of the urinary calcium output to recurrence. The results are condensed in Table LIX which incorporates the six cases of hyperparathyroidism, as well as the 19 patients who had Sulkowitch tests.

Of the series of 92, (Table LIX), 85 had received operative treatment, roughly half developing recurrence. Consideration of the top set of figures in the Table shows that in those patients whose calcium excretion was measured on a low intake only 13 of the34 who were free from recurrence had hypercalcuria (40 per

per cent.), compared with 20 of the 34 who had developed recurrence (60 per cent.). It is probable, therefore that hypercalcuria plays a significant part in the aetiology of primary and recurrent upper urinary tract stone. The combined figures at the foot of Table LIX confirm these results. The fact that operation was necessary in a high proportion of the patients might appear to bias the figures in the direction of hypercalcuria, but it will be noted from the right hand column that three of the seven patients who did not require operation had hypercalcuria (42 per cent.).

Case History : Rapid Recurrence in a Patient with Idiopathic Hypercalcuria.

The sequence of events in a young stone patient who showed rapid recurrence is indicated in the serial radiographs in Fig.68.

| | |
|---|---|
| | Male, aged 25. |
| 30. 8.55. | Left renal colic, two attacks in three years with aching lumbar pain in the intervening period. Passed one small stone five weeks previously. X-ray showed a single large stone in the left renal pelvis with no evidence of hydronephrosis. |
| 1. 9.55. | Left pyelolithotomy was performed. No leak; smooth convalescence. |
| 13. 9.55. | Routine post-operative plain film showed no opaque calculus. The urine was sterile. Blood chemistry was normal. Urinary calcium output on a low calcium intake was 300 mgm. per day. |
| 7.11.55. | Left renal colic. Passed stone. Analysis of this and of the one removed at operation showed a mixture of calcium oxalate and phosphate. Plain film showed three opacities in the left renal area. Fresh stone-formation had therefore taken place within two months of operation. Once again the urine was sterile but the Sulkowitch test showed a marked increase of urinary calcium excretion on a normal diet. |
| 11. 2.56. | In the interval had passed seven stones, one per fortnight, with clocklike regularity. |

11. 2.56. (Contd.) Intravenous urography showed two medium sized stones in the left renal pelvis, and another of the same size at the junction of the upper and middle thirds of the left ureter. Kidney function was only fair, there being evidence of hydronephrosis.

23. 4.56. Plain film showed a single stone in the left renal pelvis now much too large to have any chance of passing naturally.

24. 4.56. Left pyelolithotomy. No leak and smooth convalescence. Blood chemistry was repeated and found to be normal. The urinary calcium output on a fixed low intake was now 0.26 gm. per 24 hours.
Stone analysis: almost pure calcium phosphate.

8. 5.56. Plain post-operative film - clear.

5. 7.56. Further left colic. Plain film showed small stone in left kidney.

7. 9.56. Passed a stone and the last x-ray shows that he is now clear.

Comment: Apart from the finding of idiopathic hypercalcuria there is no obvious aetiological factor to explain the excessive speed of recurrence. He also illustrates vividly our present state of impotence in respect of prevention of recurrence, because he has been tried on aluminium hydroxide gel, salicylates, forced fluids, and an acid-ash diet without benefit. Albright and Reifenstein (1948) recommend vitamin D and calcium for idiopathic hypercalcuria but these measures are contra-indicated here on account of the persistent lithiasis.

Significance of Low Calcium Output in Urine.

If patients with hypercalcuria are more prone to recurrence, do those with a low urinary calcium excretion enjoy immunity from this complication? Pyrah (1955) gained this impression from his extensive study of stone patients, and he used the urinary calcium excretion as a guide to the advisability of operating on patients with stone in a solitary kidney. If the urinary calcium was low he felt that the risk of operation was justified. He also commented on the fact that stone patients seemed to have a wider range of urinary calcium output than healthy patients on a similar normal hospital diet; in other words some were higher than normal, while others were well below the normal figure.

Table 57 of the Appendix shows that 16 of the 67 patients examined had a urinary calcium output of less than 0.10 gm. in 24 hours. Three of them had not undergone operation, one of them being the patient with huge bilateral staghorn calculi treated conservatively for 16 years, whose serial radiographs are shown in Fig.26. The remaining 13 had received operative treatment, six of them showing evidence of recurrence, three mild and three severe. The proportion affected by recurrence was therefore almost exactly the same as in those who had hypercalcuria. Pyrah's impression is not confirmed.

Here, then, is an intriguing state of affairs, and an obvious starting point for further investigation. If those who had a low urinary calcium output all had large rapidly progressing calculi it might be reasonable to postulate that the initial excess of calcium excreted was absorbed in the process of forming the stones; but such is not the case for some of them have quite small stones, while others whose stones are large do not show evidence of rapid growth.

Relationship of Hypercalcuria to Hyperphosphaturia.

If 0.50 gm. per 24 hours be regarded as the upper limit of the urinary phosphorus excretion on a fixed low intake of 0.50 gm.

per day, 24 patients had evidence of hyperphosphaturia, the phosphorus output being over 0.60 gm. per 24 hours in 22; over 0.70 gm. in eleven; over 0.80 gm. in nine; over 1.0 gm. in five patients; and over 2.0 gm. per 24 hours in one.

In the 28 patients who had a daily urinary calcium excretion above 0.20 gm., 16 (57 per cent.) had hyperphosphaturia: while in those whose 24 urinary calcium excretion was under 0.20 gm., only 9 of the 39, (or 23 per cent.) had hyperphosphaturia. Hence, where the urinary calcium is not in excess of normal, the urinary phosphorus excretion in most cases was within normal limits, but in patients with hypercalcuria, 57 per cent. had evidence of hyperphosphaturia. Where the calcium output was more than 50 per cent. in excess of normal, i.e. over 0.30 gm. per 24 hours, seven of the eleven patients affected, (or over 60 per cent.), had a urinary phosphorus excretion greater than 0.50 gms. per 24 hours. Albright claimed that the excessive loss of calcium to the body in idiopathic hypercalcuria caused compensatory parathyroid over-activity, leading to an increased urinary excretion of phosphorus, and a low blood phosphorus level. The serum inorganic phosphorus was normal in all but seven of the 67 patients of the present series, and none of those in whom it was normal had any elevation of the blood urea to suggest that renal insufficiency was raising the serum phosphorus. Under these circumstances it seems unnecessary to invoke parathyroid over-activity to explain the hyperphosphaturia. Calcium ions are not excreted in the urine on their own, as it were, but since they are basic are balanced by the appropriate number of anions, such as phosphate, carbonate, or oxalate. It is possible that the increase in urinary phosphorus merely represents the anion balance to the increased number of calcium ions present in the urine. (Anderson, 1954).

Causes of Hypercalcuria.

The subject has already received fairly lengthy consideration elsewhere, and there is little that need be added to it here. According to Albright and Reifenstein (1948) the conditions leading to increased urinary calcium output are:-

1. Hyperparathyroidism. Six examples were detected in the present series.
2. Renal tubular acidosis, or tubular-insufficiency-without-glomerular-insufficiency. No example occurred.
3. Rapidly progressing osteoporosis. No example occurred.
4. Other forms of bone disease e.g., multiple myelomatosis, sarcoidosis, etc.
5. Idiopathic hypercalcuria. The 67 examples quoted in Table 57 in the Appendix were of this type. Albright thought that a preceding staphylococcal pyelonephritis might have been responsible in certain cases, but it is hard to believe that an infection can be sufficiently specific in its action that it selects only one of the tubular reabsorptive functions, (that of calcium), while sparing the others.

Effects of Hypercalcuria.

Long continued hypercalcuria may give rise to osteomalacia of the biochemical type. It is usually of first degree in which the low calcium has been elevated to normal by parathyroid over-activity, leading to a corresponding lowering of the serum inorganic phosphorus. The serum alkaline phosphatase is usually not elevated, as it would be in second stage biochemical osteo-malacia. In neither type are skeletal changes manifested.

The blood chemistry has been examined in all of the 67 patients (cases of hyperparathyroidism being omitted), and biochemical osteomalacia was detected in seven. The urinary calcium output in gms. per 24 hours in these seven was:- 0.313; 0.093; 0.21; 0.122; 0.11; 0.034; and 0.56. Three therefore showed the anticipated hypercalcuria, but two were actually under 0.10 gm. per 24 hours, and the remaining two were well within normal limits. No other cause for the first stage biochemical osteomalacia was apparent. Here is another mystery to add to the growing collection encountered in association with this nebulous condition called idiopathic hypercalcuria.

Treatment of Hypercalcuria.

The treatment is quite easy when the cause is known, and this applies to hyperparathyroidism, renal tubular acidosis, and rapidly progressing osteoporosis. When we come to consider idiopathic hypercalcuria, especially in stone patients, the matter is much more complex, as the vitamin D and calcium therapy recommended by Albright and Reifenstein is advisable. Treatment of urinary infection seems an inadequate answer when none is present, as was noted in the patient in Fig. 68, who developed rapid recurrence in association with idiopathic hypercalcuria.

The Practical Value of Studies of Urinary Calcium Output.

When all is said and done the main value of these particular studies is the contributory evidence it produces in "screening" or detecting cases of hyperparathyroidism, in which in addition to the raised serum calcium and low serum phosphorus there is hypercalcuria and hyperphosphaturia. Albright felt that the urinary phosphorus was raised in most cases of idiopathic hypercalcuria and the serum phosphorus lowered, so that only the hypercalcaemia distinguished the condition from one of hyperparathyroidism. So far as this series is concerned the blood chemistry in the main has been normal and there has been no evidence of metabolic bone disease.

The finding of idiopathic hypercalcuria is of little value to the patient, since treatment is impossible at present.

The condition has to a great extent been overlooked in the past. Future investigation might attempt to explain some of the anomalies encountered in idiopathic hypercalcuria, as well as its role in the formation of urinary stone.

Section 111: Blood Chemistry.

The blood chemistry has been studied in 210 of the total of 1114 stone patients. It was considered necessary in all those admitted to hospital for operation or investigation of calculous disease, as well as in cases of bilateral stone or post-operative recurrence seen in the Outpatient Department.

It is natural that the finding which aroused most interest and which was sought most eagerly should be hyperparathyroidism, a rare but important condition which receives separate consideration in the following section. The remaining abnormalities revealed by blood chemical examinations have proved to be an ill-defined assortment, and it has become increasingly clear that the boundary line between the "normal" and the "abnormal" is indistinct.

Methods.

The standard investigations carried out were the serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, plasma proteins, and blood urea. The methods of analysis are indicated briefly in the Appendix, page 77.

When the results of these investigations suggested any abnormality they were repeated (twice if need be) for confirmation, particularly when hyperparathyroidism was suspected. If any other form of metabolic bone disease was thought to be likely, the blood electrolytes were also determined, and the skeleton examined radiologically.

The "Normal" Range.

Cases of hyperparathyroidism having been excluded, the range of the serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, and plasma proteins was estimated in the remainder and regarded in the broadest possible sense as the "range of normal". Since this includes examples of biochemical osteomalacia, renal osteodystrophy, and other deviations from normal, it hardly seems fair to use the term "normal" in connection with it; but the distinctions will be made as the theme develops.

The results are indicated in some detail in the Appendix, Table 58, page 70, and they are summarised in histogram form in Fig. 69.

Serum Calcium.

The normal range of the serum calcium is usually regarded as 10 mgms. per 100 ml. plus or minus 1 mgm., i.e. 9 to 11 mgms. It is, however, the ionized calcium that claims our special interest and the total calcium level gives no true indication of this unless the plasma protein is taken into consideration. The non-diffusible portion of calcium amounting to 4 or 5 mgms. per 100 ml. (45 per cent. of the total) is bound to the plasma proteins, particularly the albumin, and is inactive. The diffusible part consists largely of ionized calcium (as carbonate and phosphate), 4.75 to 6.25 mgms. per 100 ml., with a very small quantity which is weakly ionized or non-ionized as a citrate complex. If the total calcium and the plasma protein level are known it is possible to determine the ionized calcium very quickly and simply from McLean and Hastings nomogram (Fig.70). The importance of this point lies in the fact that a serum calcium of, say, 10.5 mgms. per 100 ml. does not normally raise any suspicion of hyperparathyroidism, and this would be accurate if it were associated with a plasma protein level of 7.4 gms. per 100 ml; but if the plasma proteins were only 5.6 gms. per cent. this would indicate that the amount of ionized calcium was now approaching the hyperparathyroidism level. In 286 examinations the serum calcium was found to be lower than 9 mgms. per 100 ml. in 17 instances, and higher than 11 mgms. per 100 ml. in 40 cases. The average was 10 mgm. per 100 ml.

Serum Inorganic Phosphorus.

The normally accepted figure for the serum inorganic phosphorus is 3.2 mgms. plus or minus 0.5 mgms. giving a range of 2.7 to 3.7 mgms. per 100 ml. The figure is higher by 1 to 2 mgms. per 100 ml. in growing children, and it is raised at once at all ages by impaired renal function.

In 289 examinations the serum inorganic phosphorus level was under 2.6 mg. per 100 ml. in 38 cases and over 4 mgm. per 100 ml. in 45 instances. The average for the series was 3.4 mgm. per 100 ml.

Plasma Proteins.

Considerable variation may be expected in the plasma protein level. Its principal importance stems from the influence its content has on the ionized calcium. The average found in this series was 7.4 gms. per 100 ml.

A fact which was noted with some surprise was the high incidence of hyperglobulinaemia (Appendix, Table 59, page 71). If 3.2 gms. per 100 ml. be regarded as the upper limit of normal for globulin, 31 out of 79, or 40 per cent. had a level higher than that, and if the upper limit is regarded as 3.5 gms. per cent., 22 were affected, or roughly 28 per cent. Hyperglobulinanaemia was associated with urinary infection very commonly.

Serum Alkaline Phosphatase.

The normal range is 3 to 13 King-Armstrong units per 100 mls., the upper limit being reached by children during the stage when osteoblastic activity is most marked. The average level found in this investigation was 9.5 K.A.Units per 100 ml., but this figure was probably elevated considerably by the 33 patients who had levels above 14 K.A.Units.

Some Examples of the Normal Variations of Blood Chemistry.

The patients described in the Appendix, Table 60, page 72, all have blood chemical findings which at one time appear normal, and at another abnormal. This applies in particular to their serum calcium and phosphorus levels. Patient "J.McN." who is the last example at the foot of the Table has a serum calcium which fluctuates from 9.4 to 12.3 mgms. per cent. within the course of three years without any marked change in the level of the plasma proteins. The figure 12.2 mgms. per 100 ml. of calcium in association with a plasma protein of 7.4 gms. per 100 ml. actually falls within the hyperparathyroidism range, if reference is made to McLean and Hastings' nomogram (Fig.70). Patient "W.Br." who is five up from the foot of the Table provides an even better illustration of the range of normal since his serum calcium varies from 9.5 to 12.2 mgms. per 100 ml., and his serum inorganic phosphorus from 2.9 to 4.9 mgms. per 100 ml. during a period of seven years. There is no name which can be put to his biochemical behaviour except to say that he provides a most interesting example of the wide variation of the normal range. Immediately underneath is patient "D.B." whose serum inorganic phosphorus fluctuates from 2.12 to 3.6 mgms. per 100 ml. during two years, without any appreciable change in blood urea, or any suggestion that haemolysis had affected either of the specimens. The lower of these two figures merits consideration as biochemical osteomalacia with parathyroid compensation.

Two conclusions emerge from these studies:-

(1) There is no stability of the level of calcium and phosphorus in the serum. Over the years fluctuations may well occur which appear to be "within normal limits" even though the range is as wide as 3 mgms. per 100 ml. for calcium.

(2) The practical importance of this broad spectrum of the normal values lies in the great ease with which non-existent hyperparathyroidism may be diagnosed, or the real thing overlooked. Repetition of the tests, and constant relation of the serum calcium level to the plasma protein value will do much to avoid mistakes of either kind. This is absolutely essential when the clinician depends entirely on blood chemistry for the diagnosis of hyperparathyroidism.

Summary of the Results of Blood Chemistry.

By this stage it will be appreciated that the distinction between the normal and abnormal in terms of blood chemistry is no easy matter. Equivocal results are common, and call for repetition of the tests; even then the issue may remain confused.

This may help to explain the rather lengthy "summary" of the blood chemistry in 210 stone patients which appears in the Appendix, Table 61, page 73. The series includes 177 treated by operation and 33 treated conservatively, and the cases have been divided (with some difficulty it must be admitted) into the "normal" and the "abnormal".

1. The "Normal". Patients with normal blood chemistry constituted 174 of the total, or slightly more than 80 per cent. In 118 the findings were unequivocally within normal limits, and it is significant that, of the 96 who came to operation, only 36 had recurrence thereafter. In 28 the normal blood chemistry was associated with a urinary calcium output in excess of average, an indication that hypercalcuria is not often a cause of biochemical osteomalacia. The remaining four groups under the heading of "normal" indicate the difficulty of placing them in any particular category. Those with wide variations of the normal have already been discussed, but there are others in whom either the calcium or the phosphorus, or both, may be at, or slightly beneath, the lower limit of normal.

Of the 174 patients with normal blood chemistry, 144 came to operation and of these 56 had recurrence (40 per cent.).

The "Abnormal". Patients with abnormal blood chemistry numbered 36, or less than 20 per cent. of the total examined. Here we are on firmer ground because the deviations from normal are more marked.

Hyperparathyroidism was diagnosed in six patients, all of whom had post-operative recurrence.

Biochemical Osteomalacia indicates that the blood chemistry reflects the fact that, for some reason the body is short of calcium, whether it be by deficient intake or by excessive loss. In the early stages the serum calcium is low, and the serum inorganic phosphorus normal. If the parathyroids are stimulated by this to compensatory overactivity the serum calcium rises to within normal limits and there is a reciprocal fall in serum inorganic phosphorus. If the parathyroid compensatory over-activity is present but is inadequate, both the calcium and phosphorus will be low (Albright and Reifenstein, 1948). These findings are termed "First stage biochemical osteomalacia", and it was detected in nine of the 36 with abnormal blood chemistry. When, in addition to the blood changes already described the serum alkaline phosphatase is also raised the condition is termed "Second stage biochemical osteomalacia", and four patients showed evidence of this. It is stressed that neither of these stages manifests itself by radiological evidence of the disease, which only appears in the third and fourth stages as Milkman's pseudo-fractures, and finally generalised demineral-isation of the skeleton.

Biochemical osteomalacia is shown most commonly by a low serum inorganic phosphorus level. The critical point was taken as less than 2.5 mgms. per 100 ml. for this series. Less often the serum calcium level falls, and care must be taken to relate the calcium level to the plasma protein content by using the nomogram.

It will be readily be appreciated that there were many borderline cases but doubtful examples have been excluded, and are found in the last four groups of the "normal" above.

A total of 13 patients had first or second stage biochemical osteomalacia and of the 11 who came to operation eight had recurrence, (over 70 per cent.).

Idiopathic hypercalcuria occurred in only four of the cases of biochemical osteomalacia. Calcium loss in the urine is not the complete explanation of this blood abnormality; in fact some of the cases of biochemical osteomalacia have a much lower urinary calcium output than normal, as has already been shown.

Renal Osteodystrophy was present in nine patients, as shown by elevation of the blood urea and serum phosphorus, leading to a reciprocal fall in serum calcium. Post-operative recurrence was less common in this group only two out of nine being affected, 22 per cent.

Increased serum alkaline phosphatase as an isolated finding was noted in eight patients, but its significance was not always clear. It did not represent a second stage biochemical osteomalacia since the serum calcium and phosphorus levels were within normal limits; nor was it associated with outspoken skeletal disease since radiological examination of the skeleton was normal.

The biochemical findings in 177 operation cases are summarised in Table LX, from which it is clear that recurrence follows roughly 40 per cent. with normal blood chemistry, compared with 60 per cent. of those with abnormal blood chemistry. Conclusion. From the practical point of view studies of blood chemistry are of value mainly in respect of their assistance in detecting cases of hyperparathyroidism. The wide variations of normal necessitate repeated investigations if results are in any way equivocal, and advantage should be taken of the various complementary methods of confirming the diagnosis of parathyroid adenoma . Much that has been discussed in this section remains obscure, even to the biochemists themselves. Like idiopathic hypercalcuria, further research is required to place the interpretation of the results of serum calcium and phosphorus estimations on a secure footing.

## Section IV: Hyperparathyroidism.

Systematic and careful biochemical examination of all upper urinary tract stone cases attending urological clinics has revealed an increasing incidence of hyperparathyroidism as one of the causes of primary and recurrent stone. Until 1947 the world series of recorded cases stood at 314; since that time a similar number has been added, due to increasing awareness of the condition, and it is now possible for individual clinicians to publish series of remarkable size e.g. Pyrah (1955) had seen 32 cases over a period of 21 years, and Hellstrom (1955) was able to produce a series of 70 personal cases. In the last decade more than half the cases have been diagnosed on the strength of renal calculi alone, and according to those great authorities on the subject, Albright and Reifenstein (1948), five per cent. or more of urinary calculi are associated with hyperparathyroidism.

These facts have been repeated in miniature in the Victoria Infirmary. The total number of cases diagnosed is twelve, and six of these have been revealed by the present stone follow-up, all in patients with recurrent stone. In the course of the last year alone, three cases have been discovered from routine biochemical investigation of stone patients, and if this trend is maintained it seems certain that in future the majority of cases of hyperparathyroidism will be brought to light in this way.

The incidence of hyperparathyroidism in the 210 stone patients who have had full blood chemical studies is 3 per cent., the figure claimed by Hellstrom (1955). For the total series of 1114 stone patients the incidence is 0.5 per cent., and it seems fairly certain that amongst the remaining 900 patients there are other cases not diagnosed. It might well be asked if there is any point in looking for a few needles in such a large haystack, particularly as they do not appear to be causing any harm. The answer lies in a simple statement of the known late effects of the disease:

(1) Almost certain recurrence of the renal stones unless the adenoma is removed;

(2) Renal parenchymal damage producing nephrosclerosis with widespread intrarenal calcification (nephrocalcinosis). These changes are permanent though not necessarily

progressive, and many cases gradually develop hypertension. (Pyrah, 1955).

Treatment is therefore indicated whether or not the patient is troubled by his urinary tract condition, since not only does it prevent recurrence of stones, but it protects the kidney from further damage.

So many series of cases of hyperparathyroidism have by this time appeared in print that there seems very little point in indulging in great detail about the very small number encountered in this particular study. The justification for further discussion lies in the method of "screening" which has been evolved in collaboration with the Biochemistry Department staff. This aims to achieve accurate diagnosis with the least possible investigation, since the calcium balance tests which were once the rule have proved to be time-consuming, and not especially valuable.

## Biochemical Methods of Diagnosis.

1. Blood Chemistry. This has already been described in great detail. Probably the most important single biochemical examination is the serum calcium. Two or three consecutive readings over 12 mg. in a fasting blood specimen and in the presence of a normal plasma protein level, are highly suspicious. The serum inorganic phosphorus level is lower than normal, and a figure under 2.5 mg. helps to add significance to a high calcium reading. It may, however, be normal until they are placed on a low phosphorus duet. The serum alkaline phosphatase is raised only if skeletal changes are present, and any increase indicates

the need for radiological examination of the skull, hands, and jaws in particular.

2. Calcium Balance Tests. These are founded on the understanding that the typical case of hyperparathyroidism produces hypercalcuria and hyperphosphaturia.

(a) Urinary Calcium Excretion has already been studied. The 24 hour specimens are collected on the seventh, eighth, and ninth days of a low calcium and phosphorus diet (150 mg. calcium; 500 mg. phosphorus/24 hours). On this diet the 24 hour urinary excretion should not exceed 200 mg. calcium and 500 mg. phosphorus in normal persons. The values obtained in hyperparathyroidism are very much higher.

(b) Negative Calcium Balance: this is a much more complicated test in which the total calcium excretion in urine and faeces is measured against a fixed low calcium intake (150 mg. per day). A strict ward routine is enforced. Diet is provided from the food kitchen, one-quarter of each sample being preserved for chemical analysis. Uneaten food is collected and analysed. The excreta, urine and faeces, are collected in six-day periods, the latter being identified by carmine markings. Distilled water only is provided for drinking. Toothpaste and medicines are forbidden. It is obvious that a regime of this nature can only be conducted satisfactorily in a Metabolic Ward. In a General Surgical or Urological Ward the possibilities of flaws in technique are endless, and the length of time for which the balance continues (18 days) does not help to minimise these.

Normally the negative calcium balance does not exceed 130 mg./ 24 hours. In hyperparathyroidism the negative balance is very much greater.

The Renal Phosphorus Clearance Test is akin to these in that it demonstrates the marked hyperphosphaturia which accompanies the typical case of hyperparathyroidism. Normal values vary from 4 to 14, and higher readings would be expected in hyperparathyroidism.

3. The Induced Hypercalcaemia Test. Howard and his associates (1953) at the Johns Hopkins Hospital in Baltimore noted that intravenous administration of calcium salts to normal persons in the dosage, 15 mg. per kilogram over 4 hours, resulted in a rise in serum phosphorus and a reduction in the urinary excretion of phosphorus. They considered that the latter was due to the "shutting-off" effect of the induced hypercalcaemia on parathyroid activity. In patients with hyperparathyroidism they noted that the response to the induced hypercalcaemia was less marked in respect of the serum phosphorus elevation than it was in normal subjects; and similarly the urinary phosphorus excretion was not reduced to the same extent or was even increased. If such a test proved to be reliable it would obviously be of great benefit in the diagnosis of hyperparathyroidism since it would save a great deal of time. The figures quoted for the normal increase of the serum phosphorus are 0.4 to 2.4 mg. per cent. with an average of 1.6 per cent. Likewise the figures in the normal subject for reduction of urinary phosphorus excretion are 18 to 66 per cent. the average being 35 per cent.

The four-hour skeletal calcium retention in the induced hypercalcaemia test has recently been reported by Nordin and his colleagues (1956) at the Postgraduate Medical School. Normally 50 to 62 per cent. of the infusion dose is retained. The figures for hyperparathyroidism in this series have been lower.

4. Other Tests. The urea clearance is performed in each case to assess the amount of renal damage. The T.R.P./G.F.P. ratio is also determined.

The description of these diagnostic measures has been a necessary prelude to the six case histories which follow. Histological confirmation has been obtained in the first four, biochemical confirmation in the fifth, while the sixth who presents the classical picture of bilateral recurrent lithiasis awaits confirmation of the diagnosis.

## Case Histories of Patients with Hyperparathyroidism.

CASE I. Male, aged 57.

Urological History:- A bladder stone was crushed in 1951, and three stones of moderate size were removed from the left kidney and upper ureter. Within two years he had recurrent calculi in the left kidney and upper ureter (Fig.71a) with evidence of hydronephrosis (Fig.71b).

Skeletal Radiography:- Minimal lesions were present in skull and long bones.

Blood Chemistry: Serum calcium 14.4 to 16.8 mg. per 100 ml. Serum phosphorus:- 2.0 to 2.8 mg./100 ml. Serum alkaline phosphatase:- 21 to 22 K.A. Units. (Confirming the minimal skeletal changes).

Calcium Balance: The intake was excessively high (over 1.0 grams). The urinary output averaged 1.219 grams/24 hours and the faecal output was normal. The negative calcium balance was 0.417 (three times normal). The negative phosphorus balance was twice normal.

Renal Phosphorus Clearance:- 38 (or eight times normal).

Urea Clearance: 58 per cent. of normal, which explains why his serum phosphorus was 2.8 mg./100 ml. at first and only settled to 2.0 on a low P. diet.

Operation Note: An adenoma of the right lower parathyroid was discovered with some difficulty, attached to a thyroid cyst. The sternum had been split earlier in the search for the gland. Operation by Mr. J. Hinton Robertson.

Post-operative Progress: As bone disease was more or less absent tetany from "hungry bones" was not anticipated. The calcium and phosphatase fell and the phosphorus rose to normal, so that all were normal within one week.

Histology: Figure 72 (a) and (b) indicate that the adenoma was composed of chief cells with a reticular arrangement.

Follow-up: He refused to have operative treatment of the recurrent stones. They are still present in fact, (Fig.71c and 71d), and there has been no marked increase in their size or in the degree of hydronephrosis two years later.

Comment: The cessation of growth of the stones as soon as the adenoma was removed was most striking.

CASE 2. Female, aged 41.

Urological History:-1948 - Right pyelolithotomy for single stone in renal pelvis.
1949 - Reviewed - no recurrence.
1955 - Passed stone after right renal colic. Small stone in left lower calyx.

Skeleton: Normal.

Blood Chemistry: Serum calcium:- 11.0 to 13.6 mg./100 ml.
Serum Phosphorus:- 1.8 to 2.8 mg./100 ml.
Serum alkaline phosphatase:- 4 to 7 K.A.Units.

Calcium Balance: Urinary calcium excretion was 386 mg./100 ml.
Negative calcium balance was 191 mg./100 ml.

Phosphorus Balance: Urine 0.673 gm. in 24 hours.
Negative balance was present.

Renal Phosphorus Clearance: 28 (seven times normal).

Induced Hypercalcaemia Test: (infusion of 15 mg. per kilo for 4 hours).
Rise in Serum P:- 1.6 mg./100 ml.
Fall in Urinary Phosph:- 19 per cent.
N.B. Both these figures are within the normal range.

Urea Clearance: 64 per cent. of normal.

Operation Note: Operation by Mr. J. Hinton Robertston. Adenoma weighing 0.37 gm. removed from left lower parathyroid.

Post-operative Progress: Uneventful.

Histology: The photomicrograph appears in Figure 73.

Comment: The operation in this case was a preventive one, the main object being to stop further deterioration of renal function. The case is one of mild hyperparathyroidism in that the stone shows no tendency to grow rapidly. It also illustrates the fact that unilateral small stones may be associated with hyperparathyroidism.
The induced hypercalcaemia test gave results within the normal range, and was therefore of no assistance in diagnosis.

CASE 3. Female, aged 43.

Urological History:- 1954 - Right pyelolithotomy.
1956 - Reviewed - moderate right lumbar pain.
Scattered calcification in both renal areas. Passed small stone after endoscopic manoeuvre.

Skeleton: Minimal changes in skull and long bones radiologically.

Blood Chemistry: Serum Calcium: 13.3 - 14.1 mg. per 100 ml.
Serum Inorg. P: 2.1 - 2.7 mg. per 100 ml.
Serum Alkaline Phosphatase: 13 - 17 K.A.Units.
Plasma Proteins: 6.5 gm. per 100 ml.

Calcium Balance: Urinary Calcium Excretion 0.241 gm. per 24 hours.
Negative Calcium Balance 0.174 gm. per 24 hours.
(Both well above normal.)

Phosphorus Balance: Urinary Phosphorus excretion was 0.390 gm. in 24 hours (within normal limits).
Minimal negative phosphorus balance.

Renal Phosphorus Clearance: 22 (or five times normal)

Urea Clearance: 73 per cent. of normal.

Induced Hyper-calcaemia Test: Rise in Serum Phosphorus - 0.7 mg. per 100 ml. There was no change in the urinary P.

Operation Note: Operation by Mr. J. Hinton Robertson. An adenoma weighing 2.5 gm. was removed with ease from the right lower parathyroid.

Post-operative Progress: Unexplained pyrexia in the early days. Intravenous calcium gluconate in normal saline lest tetany develop. Uneventful thereafter.

Histology: The photomicrographs in Figures 74a and 74b show a highly cellular diffuse tumour composed of chief cells.

Comment: In respect of the normal phosphorus 24-hour excretion this case was atypical. The induced hypercalcaemia test was positive on this occasion.
A further point of interest is the presence of the bilateral scattered calcification (unfortunately not clear enough to show on an x-ray reduction).
Hyperparathyroidism has therefore been associated with mild bilateral recurrence.

CASE 4. Male, aged 62.

Urological History:- In Jan.1956 a stone was removed from the lower end of the left ureter. Convalescence was complicated by deep vein thrombosis and pulmonary embolism.
Sept.1956. Painful micturition and haematuria. Stone in the bladder, size of florin.
Dendritic stone in left upper calyx (symptomless).
Lithotrity, followed by calcium and phosphorus metabolic studies. Prostatic calcification of massive degree also present.

Skeleton: Early "ground-glass" changes in skull, with some vertical striation of the vertebrae, signifying early decalcification.
Fingers and jaws not affected.

**Blood Chemistry:** Serum calcium: 12.2 - 12.8 mg. per 100 ml.
Serum Phosphorus: 1.8 - 3.5 mg. per 100 ml.
Serum Alkaline Phosphatase: 10 - 13 K.A. Units.
Plasma Proteins: 7.6 gms. per 100 ml.

**Calcium Balance:** Urinary Calcium Excretion in 24 hours - 0.354 gm.
Negative calcium balance 0.327 gm./24 hours.
(Both figures twice the normal value).

**Phosphorus Balance:** The patient was in negative nitrogen balance during the test, and the high negative balance had no diagnostic significance.
The urinary phosphorus was at the upper limit of normal, viz. 0.600 gm./24 hours.

**Renal Phosphorus Clearance:** 33 (or eight times the normal value).

**Induced Hyper-calcaemia Test:** (Infusion of 15 mg. per kilo for 4 hours).
1. Rise in Serum Phosphorus 1.3 mg. per 100 ml.
2. Urinary P. output fell by 13 per cent.
3. Four-hour skeletal calcium retention was 29 per cent. of the infused dose, the normal being 50 - 62.

**Comment on the Induced Hyper-calcaemia Test:** The rise in the serum phosphorus is within normal limits, but the fall in urinary phosphorus output is less than would be expected in a normal person, and this is supported by the diminished four-hour skeletal calcium retention. The results are equivocal but tend, on the whole, to support the diagnosis of hyperparathyroidism.

**Urea Clearance:** 67 per cent. of normal.

**Operation Note:** A large adenoma was found with great ease nestling under the lower pole of the right half of the thyroid. It was at least the size of a large grape. (Fig.76 at the arrow). (Operation by Mr. J. S. Mackay.)

**Post-operative Course:** On account of the mild skeletal changes, and slight elevation of the serum alkaline phosphatase a drip containing calcium gluconate was set up to forestall the onset of tetany. Convalescence was quite uneventful.

**Histology:** Photomicrographs at different magnifications are shown in Figs. 75 a, c, and c.

**Comment:** This is a good example of severe and rapid recurrence due to hyperparathyroidism, for his urinary tract was known to be free from stone when he left hospital earlier this year. It is as though the performance of the first operation had set off some trigger mechanism responsible for stone formation.
Even at his age and in his condition the operation was justifiable since it will give him a measure of protection against rapid recurrence.
No action is intended for the calyceal symptomless stone, and it will be interesting to see if there is any evidence of natural dissolution in due course.

**CASE 5.** Female, aged 62.

**Urological History:** In 1939 a right nephrolithotomy was performed.
1951 - reviewed in this follow-up. No symptoms. I.V.P. showed several opacities in a non-functioning right kidney.

**Skeleton:** Early changes were present in the skull and in some of the long bones.

**Blood Chemistry:** Serum Calcium: 12.2 - 13.0 mg. per 100 ml.
Serum Phosphorus: 2.1 - 2.6 mg. per 100 ml.
Serum Alkaline Phosphatase: 16 to 21 K.A.Units.

**Calcium Balance:** Urinary calcium Excretion: 0.326 gm.per 100 ml.
Negative Calcium Balance: 0.283 gm./24 hours.

**Phosphorus Balance:** Urinary Phosphorus output: 1.130 gm./24 hours.
Negative Phosphorus Balance: 0.208 gm./24 hours.

**Renal Phosphorus Clearance:** 18 (or three times the normal).

**Induced Hyper-calcaemia Test:** Rise in Serum Phosphorus: 0.9 mg. per 100 ml.
Fall in Urinary P. Output: 7 per cent.
The first is within normal limits, the second is outside the range of normal.

**Urea Clearance:** 37 per cent. of normal.

**Progress:** Her name was placed on the waiting-list for

**Progress: (Contd.)** operation but she moved to the Edinburgh area before this could be carried out. The last information concerning her was that operation had still not been performed. She was in good health.

**Comment:** It is in cases of this sort that the doubt creeps into the mind of the surgeon; is there anything to be gained for such a patient by removal of a parathyroid adenoma which does not appear to be responsible for rapid stone-formation? Kidney function has been damaged to some extent, judging by the urea clearance value, and the damage may continue unless the process of widespread calcification can be halted. If she is fit enough she should certainly have operative treatment for the parathyroid disorder.

## CASE 6.

The last of the six cases was also unproven for the very good reason that he is at present waiting to come in for thorough biochemical survey. He has undergone five kidney operations and now has only one kidney. His blood chemistry is quite characteristic - Calcium 12.6 mg. per 100 ml; Phosphorus 2.2 mg. per 100 ml.; Phosphatase: 15 K.A.Units. Estimation of the urinary calcium output by the ordinary Sulkowitch has shown on two or three occasions that there is a great increase present. There is therefore every reason to expect that he will prove to be a case of hyperparathyroidism.

## Conclusions.

1. Sex - the numbers were exactly equal.
2. Skeletal involvement, of minor degree admittedly, was present in four of the six. Just as in the case of hyperparathyroidism itself, the more closely one searches for skeletal x-ray changes the more likely one is to find them; and this is particularly so when the serum alkaline phosphatase is elevated until it approaches the upper limit of normal.
3. The blood chemistry is summarised for the series of six in the Appendix Table 62 , page 78 . (Which also gives

information about the balance tests, induced hypercalcaemia, renal phosphorus clearance, and urea clearance.) The serum calcium level has unfailingly been raised above 11.0 mg. per 100 ml., and most often it is actually above 12.0 mg. per 100 ml. The serum phosphorus may have started as a normal level, but has fallen to the expected low level once they have been placed on a diet.

4. The results of the balance tests in the same Table in the Appendix show that all five had positive results in respect of an increased urinary output and a negative calcium balance.
5. The induced hypercalcaemia test has not been completely successful. The range of normal is so wide that it is hardly surprising that some of the results of the hyperparathyroidism cases fall within it. This has made the rise in the serum phosphorus difficult to interpret in the four in whom it was carried out. All fell within normal limits. On the other hand the percentage change in the urinary phosphorus after induced hypercalcaemia gave positive results (lower than in normal persons) in three out of four (75 per cent.).
6. The renal phosphorus clearance tests showed the anticipated increase in 100 per cent. of cases.

Dr. Anderson, Biochemist to the Victoria Infirmary has worked out corresponding figures for the complete series of eleven cases, and has found that positive results are obtained in only 50 per cent. with the induced hypercalcaemia test, in 70 per cent. with urinary calcium excretion test, in 80 per cent. with the full calcium balance test, and in 78 with the renal phosphorus clearance test.

Method of "Screening" Stone Patients to Isolate Examples of Hyperparathyroidism.

1. Serum calcium, serum phosphorus, serum alkaline phosphatase, and plasma proteins are estimated in fasting blood, and if there is any doubt about the validity of the result or if hyperparathyroidism appears likely they are repeated until a clearer picture emerges.
2. A raised serum alkaline indicates the need for an x-ray of the skeleton.
3. A rough impression of the urinary calcium output is gained in the Outpatient Department from the Sulkowitch test.
4. If these findings still indicate the possibility of hyperparathyroidism the patient is admitted for estimation of the urinary calcium output on a fixed low intake and at some time during the test the renal phosphorus clearance is estimated. It is felt that these two simple and relatively rapid methods give just as reliable results as the more complex calcium balance and induced hypercalcaemia methods.

If a common policy were agreed amongst clinicians, a simple method of screening stone patients such as that suggested would quickly give an accurate account of the true incidence of hyperparathyroidism. It can never be claimed that hyperparathyroidism is a large part of the answer to the cause of stone. It is, however, one of the few known aetiological factors, for which, fortunately, treatment is possible.

## SUMMARY (of Part VI.)

Analysis of calculi by the older biochemical methods has been compared with the results of the highly refined modern biophysical techniques, and it has been noted that, from the viewpoint of the clinician, each provides equally valuable assistance in determining the best preventive regime.

It has been shown that phosphate stones are more commonly associated with infection and recurrence.

Studies of urinary calcium output have indicated that over 40 per cent. of the stone patients examined had evidence of idiopathic hypercalcuria for which, in our present state of knowledge, no treatment is possible. The principal merit of these studies at present, lies in their contribution to the diagnosis of hyperparathyroidism.

Wide variations have been shown to exist within the normal range of serum calcium and phosphorus. The calcium level should be related always to the plasma protein level.

Hyperparathyroidism has been noted in six patients out of 210 in whom it had been possible to carry out full biochemical blood examination. The incidence is therefore 3 per cent., but it is almost certain that other cases of hyperparathyroidism remain undiagnosed amongst the other 900 whose blood chemistry has not yet been examined. A scheme of "screening" has been presented after consideration of the effectiveness of the various diagnostic methods as applied to the patients in this series.

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## GENERAL SUMMARY.

Clinical, biochemical and experimental studies in upper urinary tract stone have been carried out in more than one thousand patients. The investigation has been conducted during the last eight years in the Urological Department of the Victoria Infirmary.

A broad picture of the general incidence and diagnostic findings has been presented with reference to the complete series, the numbers receiving operative and expectant treatment proving to be almost equal. A general increase in the incidence of the disease over the last thirty years has been noted.

The purely clinical approach to aetiology has been disappointing, and a satisfactory cause has been shown in a very small proportion of all patients. The factors of possible and doubtful significance have been stated. Lack of information about aetiology has been felt at all times to be the main obstacle to progress in prevention and treatment.

The natural history of upper urinary tract stone has been studied to provide a standard or "control" series by which the results of operation may be judged, and to fill a gap which clearly exists in our understanding of the disease. The clinical progress of all stones originating in the kidney has been followed to its termination, either in operative removal or natural expulsion. Obstructive potential has been shown to be more important than size per se. Early removal of the obstructive stone has been considered to be its most conservative treatment. A plea, however, has been made for an expectant attitude, with careful supervision in a Stone Clinic in the case of (1) small symptom-free, calyceal stones with normal pyelograms, (2) large symptomless bilateral branched stones, and (3) small ureteric calculi which are making satisfactory progress in the absence of hydronephrosis.

It has been shown that more than 80 per cent. of all stones which enter the ureter eventually pass, and that there is therefore no particular virtue in claiming similar results from treatment by endoscopic or open surgical procedures (if these are applied to every case encountered).

The late results of operative treatment indicate a depressingly high recurrence rate. Recurrences have been graded as "mild" and "severe", depending on whether or not secondary operation has been necessary. In round figures, one out of every four patients undergoing operative treatment has developed severe recurrence, and the total figure for recurrence has been shown to be somewhere between thirty and fifty per cent. False recurrence, which has not been included in these figures, has been detected in one out of eight patients examined.

The factors responsible for, or related to, recurrence have been studied at some length. Nephrolithotomy has been shown to be undesirable on account of its higher mortality rate, the incidence of pseudo- and true recurrence associated with it, and its harmful effect on renal function. Ablation of the kidney has proved to be no guarantee of immunity from recurrence on the opposite side, since the incidence of contralateral recurrence has been the same after nephrectomy and conservative procedures. There has been a steady decrease in recurrence rates in the last three decades. Urinary infection, hyperparathyroidism, hypercalcuria and uncorrected pelvi-ureteric obstruction all have much in common with recurrence, and attention to their treatment, together with complete removal of the stones, give the patient the best early chance of escaping this complication.

Long-term preventive measures have been shown to depend, in our present incomplete state of knowledge, on the chemical analysis of the stone, the aim being the production of the maximum solubility of the main crystalloid present.

Clinical trials on stone patients and experimental work in animals have failed to confirm that hyaluronidase is valuable in preventing recurrent stone or in reducing the size of those already present in the urinary tract.

The place of oestrogens, aluminium hydroxide gel, and salicylates in the prevention of recurrence has been discussed.

Comparative studies have indicated that bilateral stone is more serious than the unilateral condition, principally in respect of the post-operative mortality and the late results.

A policy of management for bilateral calculi has been proposed on the basis that surgery is indicated in the majority of obstructive stones, whereas the non-obstructive are better treated conservatively (except in the case of unilateral infection or severe and disabling pain).

The principal value of biochemical study of these patients has been the assistance given in deciding on a prophylactic regime from quantitative chemical analysis of the calculi. Hyperparathyroidism has proved to be rare, but should be excluded in every case by the method of "screening" described.

The present investigation has left many questions unanswered. Far from resolving the various issues connected with upper urinary tract stone, it has indicated the need for many other lines of research, for which it may be regarded as merely the launching ground.

Further study of racial, topographical and sexual differences is clearly required. Refinements in radiographic techniques to permit visualisation of the earliest stages of calculogenesis might lead to profitable research on aetiology. Very little research work has been done on the idiopathic hypercalcuria which accompanies so many stones and which must be of great significance since more than 90 per cent. of stones contain calcium. The urinary bicolloids are an essential part of any calculus. Although their exact nature remains obscure, it is probable that they are akin to the acid mucopolysaccharides, and therefore may be separated into their various components by partition chromatography. Research to this end will shortly be undertaken.

Purely surgical methods at present have little more to offer. The most useful field of surgical research lies in renal transplantation, which should be possible once the adverse tissue reactions have been explained. The ability to provide a kidney graft for any patient (stone or otherwise) dying from pure renal failure, would represent a great advance in restorative surgery. Even so, the indications for its use in stone cases will steadily diminish as our knowledge of aetiology increases.

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## BIBLIOGRAPHY


Albright, F., and Reifenstein, E.C. (1948) — "The Parathyroid Glands and Metabolic Bone Disease." Baltimore: Williams and Wilkins.

Albright, F., Sulkowitch, H., and Bloomberg, E. (1937) — Amer.J.med.Sci. 193, 800.

Anderson, I.A. (1954) — "The Diagnosis and Treatment of Metabolic Bone Disease." (Unpublished).

Anderson, I.A. (1955) — "The Significance of Hypercalcuria in the Aetiology of Urinary Calcium Stones." (Unpublished).

Anderson, L., and McDonald, J.R. (1946) — Surg., Gynec., and Obstet. 82, 275.

Anderson, W.A.D. (1940) — J.Urol. 44, 29.

Andrews, J.C., et al. (1955) — J.Urol. 73, 930.

Baker, R., et al. (1954) — J.Urol. 71, 511.

Baker, R., and Sison, F. (1954) — J.Urol. 72, 1032.

Baker, R., and Connelly, J.P. (1956) — J.Amer.med.Ass. 160, 13, 1106.

Barney, J.D. (1922 a) — Surg.Gynec.Obstet. 35, 743.

Barney, J.D. (1922 b) — Boston med.surg.J. 186, 1, 9.

Barney, J.D., and Chute, R. (1931) — J.Urol. 25, 173.

Barney, J.D., and Mintz, E.R. (1936) — Brit.J.Urol. 8, 36.

Barney, J.D., and Sulkowitch, H.W. (1937) — J.Urol. 37, 764.

Barrett, G.S. (1951) — J.Urol. 66, 315.

Barrett, J.F. (1942) — Lancet. 2, 574.

Beard, D.E., and Goodyear, W.E. (1950) — J.Urol. 64, 638.

Beischer, D.E. (1955 — J.Urol. 73, 653.

Benjamin, E.W. (1931) — J.Urol. 25, 165.

Birdssall, J.C. (1939) — J.Urol. 42, 917.

Black, B.M. (1954) — Amer.Surg. 20, 1044.

Bogash, M., and Dowbden, R.M. (1954) — J.Urol. 72, 1957.

Boyce, W.H., et al. (1954) — J.Clin.Invest. 33, 1287.

Boyce, W.H., et al. (1954) — J.Urol. 72, 1019.

Boyce, W.H., and Garvey, F.K. (1956) — J.Urol. 76, 213.

Braasch, W.F., and Moore, T. (1915) — J.Amer.med.Ass. 65, 1234.

Braasch, W.F. (1917) — Surg.Gynec.Obstet. 24, 8.

Braasch, W.F., and Foulds, G.S. (1923) — Trans.Amer.Ass.gen-urin Surg. 16, 155.

Brongersma, H. (1924) — J.d'Urol. 18, 157.

Burkland, C.E. and Rosenberg, M. (1955) — J.Urol. 73, 198.

Butt, A.J. (1952) — J.Urol. 67, 4, 450.

Butt, A.J., et al. (1952) — J.Amer.med.Ass. 150, 1096.

Butt, A.J., et al. (1953) — Arch.Surg. 66, 730.

Butt, A.J. (1954) — J.Urol. 72, 337.

Cabot, H., and Crabtree, E.G. (1915) — Surg.Gynec.Obstet. 21, 223.

Cahill, G.S. (1935) — J.Amer.med.Ass. 104, 15, 1306.

Carr, J.A. (1953) — Brit.J.Urol. 25, 26.

Carr, R.J. (1954) — Brit.J.Urol. 26, 105.

Carroll, G., and Brennan, R.V. (1952) — J.Urol. 68, 88.

Cary, M.K. (1937) — J.Urol. 37, 651.

Catiglioni, A. (1943) J.Urol. 50, 632.

Chapman, T.L. (1946) Glas.med.J. 27, 391.

Chapman, T.L. (1949) Brit.J.Urol. 21, 42.

Chute, R., and Suby, H.I. (1940) J.Urol. 44, 590.

Cifuentes, P. (1924) Rep.2nd Congr.Int.Soc.Urol., Rome. 1, 266.

Collings, M. (1950) Amer.J.Surg. 80, 323.

Conway, N.S. et al. (1949) Brit.J.Urol. 21, 1, 30.

Cook, E.N. and Keating, F.R. (1945) J.Urol. 54, 525.

Cope, O. (1942) J.Mo.med.Ass. 39, 273.

Counseller, V.S., and Hoerner, M.T. (1936) J.Urol. 35, 21.

Davidson, C.N. et al. (1954) Radiology. 62, 203.

Davalos, A. (1943) J.Urol. 49, 639.

Davalos, A. (1945) J.Urol. 54, 182.

Denos, (1914) Article on the History of Urology, Encyclopédie française d'Urologie. Vol.1, 1914, pp. 1 - 294.

Dent, C.E., and Philpot, C.R. (1954) Lancet, 1, 182.

Dent, C.E., et al. (1954) J.Clin.Invest. 33, 1210.

Dent, C.E., and Senior, B. (1955) Brit.J.Urol. 27, 317.

Dix, V.W. (1951) Proc.R.Soc.Med. 44, 933.

Dobson, J.F. (1928) Brit.med.J. No.3507, 486.

Dodson, A.J., and Clark, J.R. (1946) J.Amer.med.Ass. 132, 1063.

Douillet, M. (1933) Arch.d.mal.reins d.organes gén-urin. 7, 307.

Dourmashkin, R.L. (1945) J.Urol. 54, 245.

Dourmashkin, R.L., and Solomon, A.A. (1942) J.Urol. 48, 196.

| | |
|---|---|
| Dulce, H.J. (1955) | Ztschr.f.physiolog.Chem. 302, 49. |
| Ebstein, W., and Nicolaier, A. (1891) | "Uber die experimentelle Erzeugung von Harnsteinen." Wiesbaden: Bergmann. |
| Eliot, H. (1910) | "Étiologie, Pathogénie, Traitement, de l'Anurie au Cours de la Lithiase." (Paris). |
| Engel, J.W. (1952) | J.Urol. 57, 619. |
| Engel, J.W. (1952) | J.Urol. 68, 105. |
| Flocks, R.H. (1939) | J.Amer.med.Ass. 130, 1466. |
| Flocks, R.H. (1946) | J.Amer.med.Ass. 113, 913. |
| Flocks, R.H. (1950) | J.Urol. 64, 633. |
| Foley, F.E.B. (1935) | J.Amer.med.Ass. 104, 1314. |
| Grossmann, W. (1938) | Brit.J.Urol. 10, 46. |
| Grove, W.J. et al. (1950) | J.Urol. 64, 549. |
| Hammarsten, G. (1938) | Skand Arch.f.Physiol. 80, 165. |
| Hammarsten, G. (1937) | "Calciumoxalat als Steinbildner in den Harnwegen." Lund: Gleerup and Harrassowitz. |
| Hammarsten, G., (1945) | J.Path.Bact. 57, 3, 375. |
| Harlin, H.C., and Wiesel, L. (1954) | J.Urol. 72, 1046. |
| Harrington, H.L. (1940) | J.Urol. 44, 507. |
| Hauser, E.A., and le Beau, D.S. (1953) | Kolloid. Ztschr. 132, 78. |
| Hedenberg, I., et al. (1953) | Brit.J.Urol. 25, 33. |
| Hellström, J. (1933) | Z.urol.Chir. 37, 83. |
| Hellström, J. (1938) | Brit.J.Urol. 10, 348. |
| Hellström, J. (1949) | Brit.J.Urol. 21, 1, 9. |
| Hellström, J. (1955) | Brit.J.Urol. 27, 387. |

Higgins, C.C., and Mindenhall E.E. (1940) — J.Urol. 42, 3, 436.

Higgins, C.C. (1932) — J.Urol. 29, 157.

Higgins, C.C. (1936) — Surg.Gynec.Obstet. 63, 23.

Higgins, C.C. (1938) — J.Urol. 40, 1, 184.

Higgins, C.C. (1939 a) — J.Amer.med.Ass. 113, 1460.

Higgins, C.C. (1939 b) — Int.Abstr.Surg. 392, in Surg.Gynec.Obstet. 68.

Higgins, C.C. (1952) — J.Urol. 68, 117.

Hill, A. Bradford, (1955) — "Principles of Medical Statistics." London: The Lancet.

Holmes, R.J., and Coplan, M.M. (1930) — J.Urol. 23, 477.

Holmes, R.J. (1937) — J.Amer.med.Ass. 113, 1460. Discussion after Higgins' paper.

Howard, J.E. (1954) — J.Urol. 72, 999.

Hunner, G.L. (1928) — J.Urol. 20, 1, 61.

Illingworth, C.F.W., and Dick, B.M. (1945) — "Textbook of Surgical Pathology." p.635. Churchill, London.

Illyes, G.D. (1934) — J. d'Urol. 38, 57.

Jacobs, A. (1932) — Brit.med.J. 1, 513.

Jeanbrau, E. (1914) — Encyclopédie française d'Urologie. Vol.111. Paris; Doin.

Joly, J.S. (1929) — "Stone and Calculous Disease of the Urinary Organs." Heinemann; London.

Joly, J.S. (1932) — J.Urol. 32, 541.

Kairis, Z. (1955) — Rep. 10th Congr.Int.Soc.Urol., Athens, 1955.

Keating, F.R., and Cook, E.N. (1945) — J.Amer.med.Ass. 129, 994.

Keyser, L.D. (1923) — Ann.Surg. 77, 210.

| | |
|---|---|
| Keyser, L.D. (1934) | J.Urol. 31, 219. |
| Keyser, L.D. (1935) | J.Amer.med.Ass. 104, 15, 1299. |
| Keyser, L.D. (1943) | J.Urol. 50, 169. |
| Kittredge, W.E., and James, D.W. (1954) | J.Urol. 72, 3, 342. |
| Kretschmer, H.L., and Brown, R.C. (1939) | J.Amer.med.Ass. 113, 1471. |
| Kretschmer, H.L. (1942) | Surg.Gynec.Obstet. 74, 1065. |
| Lagergren, C. (1956) | Acta Radiologica Supplement.133. |
| Lamson, O.F. (1920) | Ann.Surg. 71, 1, 16. |
| Lau, F.T. (1925) | J.Amer.med.Ass. 84, 4, 272. |
| Lett, H. (1936) | Brit.J.Urol. 8, 205. |
| Levy, C.S. (1954) | J.Urol. 71, 530. |
| Lichtwitz, L. (1919) | "Uber die Bildung von Niederschlagen und Konkrementen im Harn in den Harnwegen." Kraus and Brugsch, Vol.1. 1919. |
| Long, H., and Pyrah, L.N. (1939) | Brit.J.Urol. 11, 216. |
| McCarrison, R. (1927) | Brit.med.J. 1, 717. |
| McCarrison, R. (1931) | Brit.med.J. 1, 1009. |
| McDonald, S.G. (1936) | Lancet, 1, 1311. |
| McIntyre, J. (1896) | Lancet, 2, 118. |
| McKenzie, D.W., and Seng, M.I. (1933) | J.Urol. 29, 321. |
| Marion, G. (1922) | J.Urol.med.chir. 13, 1. |
| Meyer, J. (1929) | Ztschr.f.klin.Med. 111, 613. |
| Moore, T.D. (1937) | J.Urol. 37, 1. |
| Morrissey, J.H. (1947) | J.Urol. 57, 635. |
| Mortensen, J.D., and Baggenstoss, A.H. (1954) | Am.J.Clin.Path. 24, 45. |

| | |
|---|---|
| Mulvaney, W.P. (1953) | J.Urol. 70, 704. |
| Naoumidis, S.P. (1949) | "Sur la récidive de la lithiase rénale." M.D.Thesis, Evangelismos Hospital, Athens. |
| Nay, E.O. (1928) | J.Urol. 20, 5, 533. |
| Nielsen, I.M. (1956) | J.Urol. 75, 602. |
| Oppenheimer, G.D. (1937) | Surg.Gynec.Obstet. 65, 829. |
| Ormond, J.K. (1940) | Surg.Gynec.Obstet. 70, 584. |
| Osborne, T.B., and Mendel, L.B. (1917) | J.Amer.Med.Ass. 69, 32. |
| Pavlakis, F. (1949) | "Frequency and Distribution of Nephrolithiasis in Greece." Evangelismos Hospital, Athens. |
| Pepys, S. 1632 - 1703. | "The Diary of Samuel Pepys." London and Glasgow; Collins. |
| Petkovic, S. (1953) | J.Internat.Coll.Surg. 20, 709. |
| Prien, E.L., and Frondel, C.(1947) | J.Urol. 57, 949. |
| Prien, E.L. (1949) | J.Urol. 61, 821. |
| Prien, E.L. (1954 a). | J.Amer.med.Ass. 154, 744. |
| Prien, E.L. (1954 b). | J.Louis.med.Soc. 106, 123. |
| Prien, E.L. (1955) | J.Urol. 73, 627. |
| Prien, E.L., and Walker, B.S. (1955) | J.Urol, 74, 4, 440. |
| Priestley, J.T., and Braasch, W.F. (1937) | J.Amer.med.Ass. 109, 1703. |
| Priestley, J.T. (1939) | J.Urol. 42, 933. |
| Priestley, J.T., and Dunn, J.H. (1949) | J.Urol. 61, 2, 194. |
| Prince, C.L. (1945) | J.Urol. 54, 368. |
| Pyrah, L.N., and Fowweather, F.S. (1938) | Proc.R.Soc.Med. 31, 593. |
| Pyrah, L.N., (1954) | Brit.med.J. 2, 963. |

Pyrah, L.N., and Raper, F.P. (1955) Brit.J.Urol. 27, 333.

Quinby, W.C. (1933) Trans.Amer.Ass.gen-urin.Surg. 16, 285.

Randall, A. (1927) Surg.Gynec.Obstet. 64, 317.

Randall, A. (1932) Amer.J.Surg. 18, 482.

Randall, A., and Melvin, P.D. (1937) J.Urol. 37, 737.

Randall, A., Eiman, J.E., and Leberman, P.R. (1937) J.Amer.med .Ass. 109, 1698.

Randall, A. (1940 a) Internat.Abstr.Surg. 209, in Surg.Gynec.Obstet. 71.

Randall, A. (1940 b) J.Urol. 44, 580.

Ravich, A. (1932) J.Urol. 29, 171.

Ravich, R.A., and Ravich, A. (1954) J.Urol. 72, 1050.

Reaser, E.F. (1935) J.Urol. 34, 148.

Reynolds, T.B. (1955) J.Urol. 74, 257.

Robinson, R.H.O.B. (1947) Proc.R.Soc.Med. 15, 2, 201.

Rosenow, E.C., and Meisser, J.G. (1922) J.Amer.med.Ass. 78, 266.

Rosenow, E.C. (1926) J.Illinois.Med.Soc. 49, 1, 28.

Rosenow, E.C., (Jnr.) (1940) J.Urol. 44, 19.

Rovsing, C.M. (1924) Acta.chir.Scand. 57, 5, 387.

Sanford, J.H., and Barnhart, W.T. (1941) J.Urol. 46, 1061.

Schenck, G.F., and Lane, C.R. (1937) J.Urol. 37, 79.

Shattock (1905) Trans.Path.Soc.Lond. 66, 275.

Shorr, E. (1945) J.Urol. 53, 507.

Shorr, E., and Carter, A.C. (1950) J.Amer.med.Ass. 144, 1549.

| | |
|---|---|
| Sinha, R.V.P. (1956) | Personal Communication re Incidence in India. |
| Smiddy, F.G. (1954 a) | Proc.R.Soc.Med. 47, 807. |
| Smiddy, F.G. (1954 b) | Brit.J.Urol. 26, 266. |
| Smiddy, F.G. (1954 c) | Brit.J.Urol. 26, 270. |
| Smith, G.G. (1939) | Surg.Gynec.Obstet. 68, 527. |
| Spellmann, R.M., and Marshall, V.F. (1955) | J.Urol. 73, 660. |
| Spence, H.M., and Baird, S.S. (1939) | Amer.J.Surg. 44, 348. |
| Squires, C.B. (1930) | J.Urol. 24, 461. |
| Stevens, A.R. (1934) | Trans.Am.Ass.gen-urin.Surg. 26, 267. |
| Stewart, H.H. (1952) | Ann.R.Coll.Surg.Engl. 11, 1, 32. |
| Stewart, H.H. (1955) | Brit.J.Urol. 27, 352. |
| Stirling, W.C. (1927) | J.Urol. 18, 259. |
| Stout, H.A., et al. (1955) | J.Urol. 74, 8. |
| Suby, H.I. (1944) | Proc.R.Soc.Med. 37, 609. |
| Suby, H.I., and Suby, R.M. (1947) | J.Urol. 57, 995. |
| Suby, H.I., et al. (1951) | J.Urol. 66, 527. |
| Suby, H.I. (1952) | J.Urol. 68, 96. |
| Sutherland, J.W. (1954) | Brit.J.Urol. 26, 22. |
| Twinem, F.P. (1937) | J.Urol. 37, 2, 259. |
| Twinem, F.P. (1939) | J.Urol. 42, 3, 420. |
| Twinem, F.P. (1940 a) | Surg.Clin.N.Amer. 37, 2, 259. |
| Twinem, F.P. (1940 b) | J.Urol. 44, 596. |
| Vermeulen, C.W., et al. (1950 a) | J.Urol. 64, 541. |
| Vermeulen, C.W., et al. (1950 b) | J.Urol. 66, 1. |
| Vermeulen, C.W., et al. (1950 c) | J.Urol. 66, 6. |

Vermeulen, C.W., and Goetz, R. (1954 a) J.Urol. 72, 761.

Vermeulen, C.W., and Goetz, R. (1954 b) J.Urol. 72, 93.

Vermeulen, C.W., and Goetz, R. (1954 c) J.Urol. 72, 99.

Vermeulen, C.W., et al. (1956) J.Urol. 75, 592.

Vermooten, V. (1941) J.Urol. 46, 193.

Walters, W., and Counsellor, V.S. (1932) J.Urol. 31, 649.

Williams, R.T., and Synge, R.L.M. (1949) "Partition Chromatography." Biochemical Soc.Symp. No.3. Cambridge.

Winsbury-White, H.P. (1936) J.Urol. 36, 5, 469.

Winsbury-White, H.P. (1946) Brit.J.Urol. 18, 3.

Winsbury,White, H.P. (1954) "Stone in the Urinary Tract." London: Butterworth.

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# C O N T E N T S



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## Index of Photographed Tables and Figures.

### PART I.

### General Incidence, etc.



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## PART 2.

## The Results of Conservative Management.



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## PART 3.

## The Results of Operative Treatment.

PART 3. (Continued).



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## PART 4.

### The Prevention of Recurrence.



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## PART 5.

## Bilateral Calculi.



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PART 6.

Biochemical Studies.

# FIGURES and TABLES

relating to

# PART I

## TABLE I.

### Source of 1114 Stone Patients.

Source of Cases.

| | Urological Department | | Victoria Infy. Surgeons | | Others | | Total | |
|---|---|---|---|---|---|---|---|---|
| | Number | % | Number | % | Number | % | Number | % |
| All Cases | 891 | 80.0 | 161 | 14.5 | 62 | 5.5 | 1,114 | 100.0 |
| Operation Cases | 323 | 60.0 | 161 | 30.0 | 62 | 10.0 | 546 | 100.0 |

## TABLE II.

### Follow-up of 1114 Stone Patients.

**Series of 1,114 Cases of Upper Urinary Tract Stone.**

**Disposal in terms of Follow-up**

| Method | Number | Per Cent. | Died (135 cases) |
|---|---|---|---|
| 1. Interviewed | 778 | 70.0 | 1. Post-operative 23 |
| 2. Questionnaire | 213 | 20.0 | 2. Urological causes 16 |
| 3. Untraced | 123 | 10.0 | 3. Other causes 96 |
| | | | Total = 135 |
| Total | 1,114 | 100.0 | |

## TABLE III.

The "operation" and "no operation" Series Contrasted.

**A Study of Operation and No Operation Series - 1,114 Cases**

No Operation (568 Cases)

415 Passed stone.
153 Retained stone or were untraced.

Operation (546 Cases)

All had operations - 546

400 Renal Primary.
146 Ureteric Primary.

In addition:-

106 Passed stones.
26 Had large untreated stones, primary or recurrent.
71 Had small untreated stones, primary or recurrent.

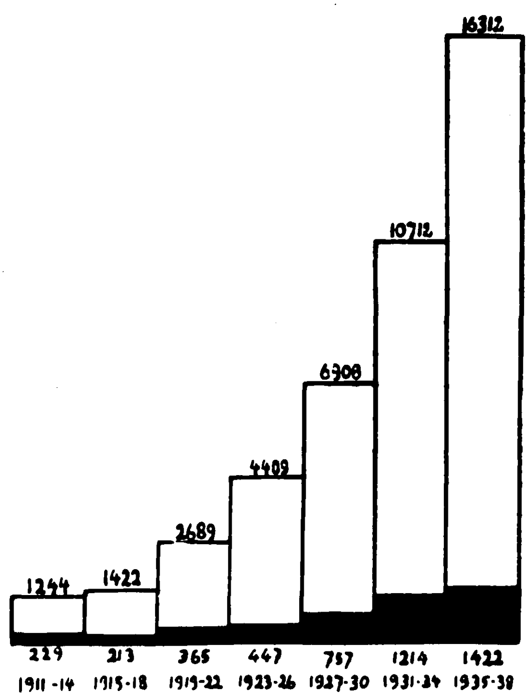



FIG. I.

Incidence of kidney stone in Sweden 1911-1938.
Black = operation cases. White = total.

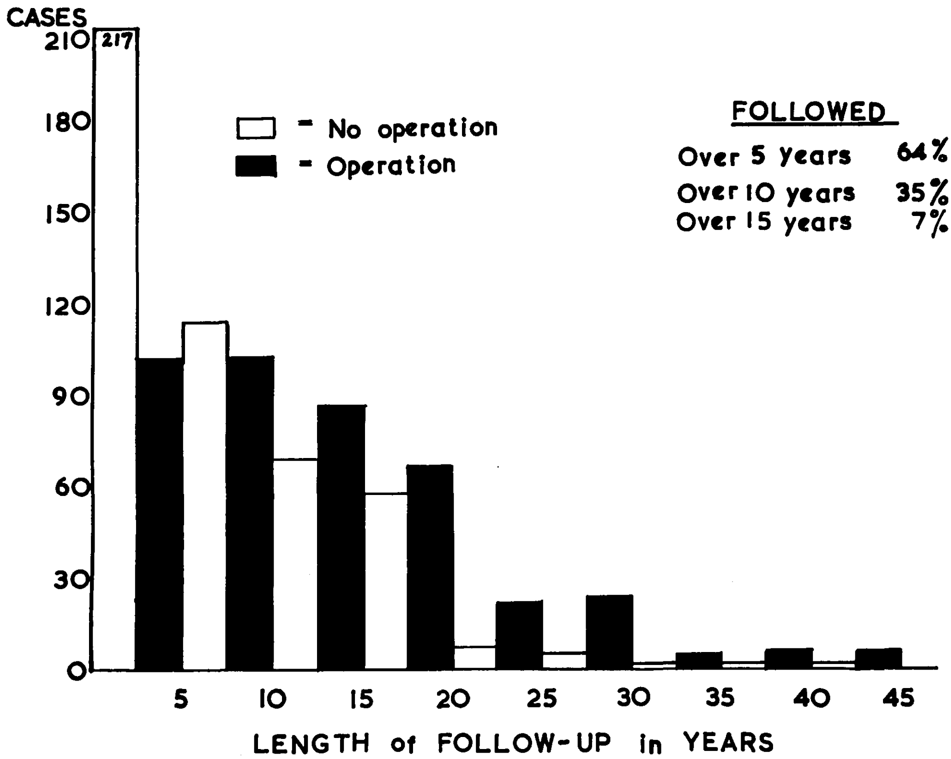



FIG. 2.

Length of Follow-up.

# TABLE IV.

## Sex Incidence.

Series of 1,114 Cases of Upper Urinary Tract Stone.

Sex

| | Male | Female | Total | Male/Female |
|---|---|---|---|---|
| Operation | 306 | 240 | 546 | 1.25 : 1 |
| No Operation | 423 | 145 | 568 | 3 : 1 |
| Total | 729 | 385 | 1,114 | 1.9 : 1 |

# TABLE V.

## Side Incidence.

Side

| | Number | Per Cent. | |
|---|---|---|---|
| Right | 487 | 43.7 | Bilateral = 149 |
| Left | 478 | 42.9 | Operation $\frac{96}{546}$ = 17.6% |
| Bilateral | 149 | 13.4 | No Op. $\frac{53}{568}$ = 9.0% |
| Total | 1,114 | 100.0 | |

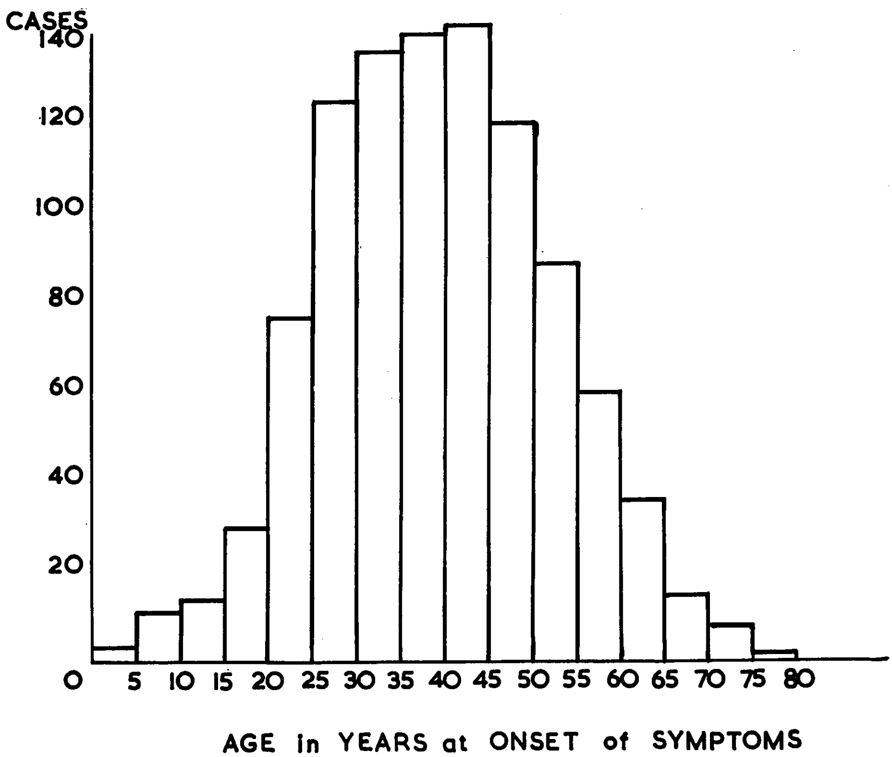



FIG. 3.

Age Incidence at Onset of Symptoms.

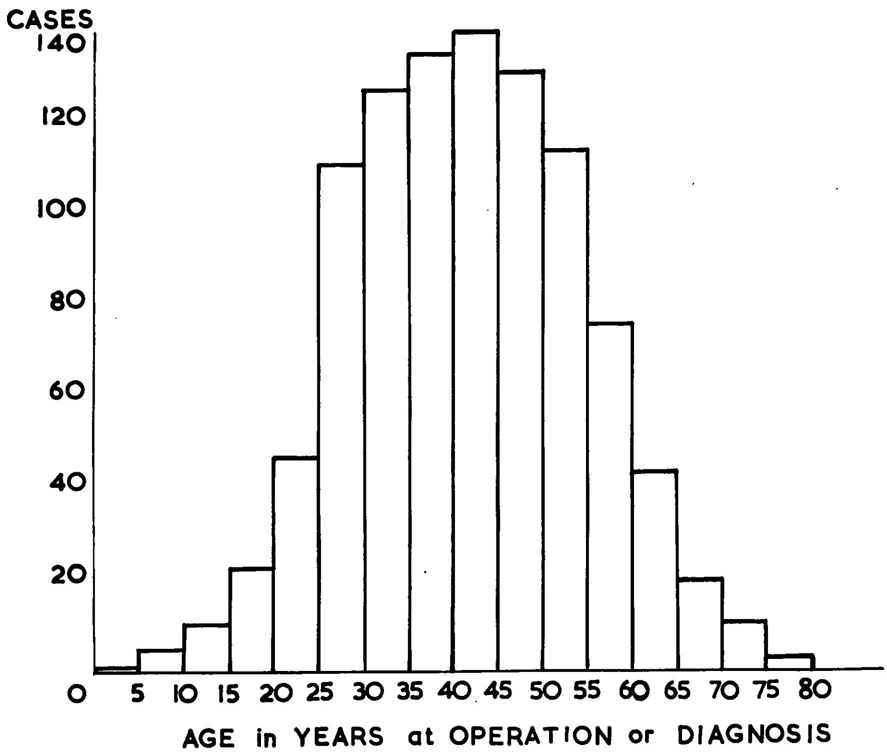

CASES
140
120
100
80
60
40
20
0
5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80
AGE in YEARS at OPERATION or DIAGNOSIS

FIG. 4.

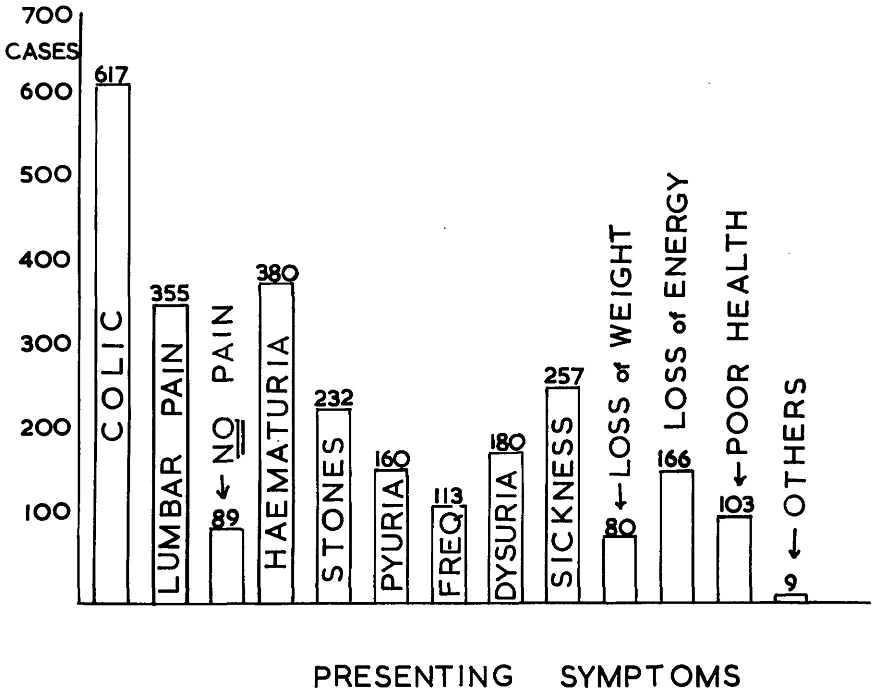
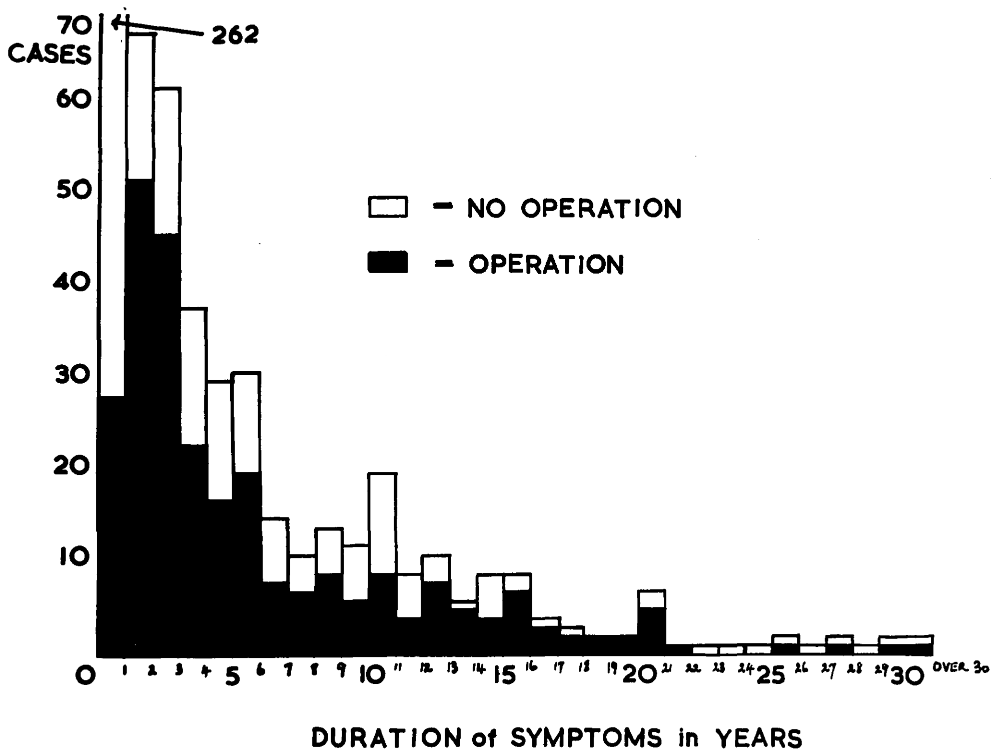

700
CASES
600
500
400
300
200
100
617
COLIC
355
LUMBAR PAIN
89
← NO PAIN
380
HAEMATURIA
232
STONES
160
PYURIA
113
FREQ
180
DYSURIA
257
SICKNESS
80
← LOSS of WEIGHT
166
LOSS of ENERGY
103
← POOR HEALTH
9
← OTHERS
PRESENTING SYMPTOMS

FIG. 5.



70
CASES
262
60
50
40
30
20
10
0
5
10
15
20
25
30
OVER 30
NO OPERATION
OPERATION
DURATION of SYMPTOMS in YEARS


FIG. 6.

# TABLE VI.

## Incidence of Urinary Infection at First Examination.

**Summary of Urine Examinations at First Visit (665 Cases)**

| Reaction (481 Cases) | | | |
|---|---|---|---|
| | Operation | No Op. | Total |
| Acid | 101 | 169 | 270 |
| Alkaline | 43 | 82 | 125 |
| Amphoteric | 26 | 60 | 86 |
| Total | 170 | 311 | 481 |

**Incidence of Infection**

| | |
|---|---|
| Total Cases | 665 (100 per cent.) |
| Sterile | 334 ( 50 per cent.) |
| Infected | 331 ( 50 per cent.) |

(Pyuria alone) 173
Infecting Organism 158

| | |
|---|---|
| B.coli | 93 |
| B.coli + Strep.Faec. | 11 |
| B.coli + Proteus | 4 |
| B.coli + Staph.Albus | 2 |
| B.coli + Staph.Aur. | 2 |
| B.coli + Pyocyanea | 1 |
| Staph. Aur. | 7 |
| Staph. Aur + Proteus | 1 |
| Staph. Albus | 6 |
| Strep. Faecalis | 15 |
| Strep. Faec + Pyocyanea | 1 |
| Ps. Pyocyanea | 2 |
| Proteus Vulgáris | 13 |
| **Total** | **158** |

# TABLE VII.

Incidence of Urinary Infection in "No Operation" and "Operation" Series at Diagnosis.

No Operation (347 Cases)

| | Number | Per cent. |
|---|---|---|
| Sterile | 211 | 60.8 |
| Infected | 136 | 39.2 |

Operation (318 Cases)

| | No Recurrence | Recurrence | Total | Percentage Recurrence |
|---|---|---|---|---|
| Sterile | 98 | 25 | 123 | 20.3 |
| Infected | 107 | 88 | 195 | 45.1 |
| Total | 205 | 113 | 318 | 35.5 |
| Percentage Infected | 52.2 | 78.0 | 61.3 | |

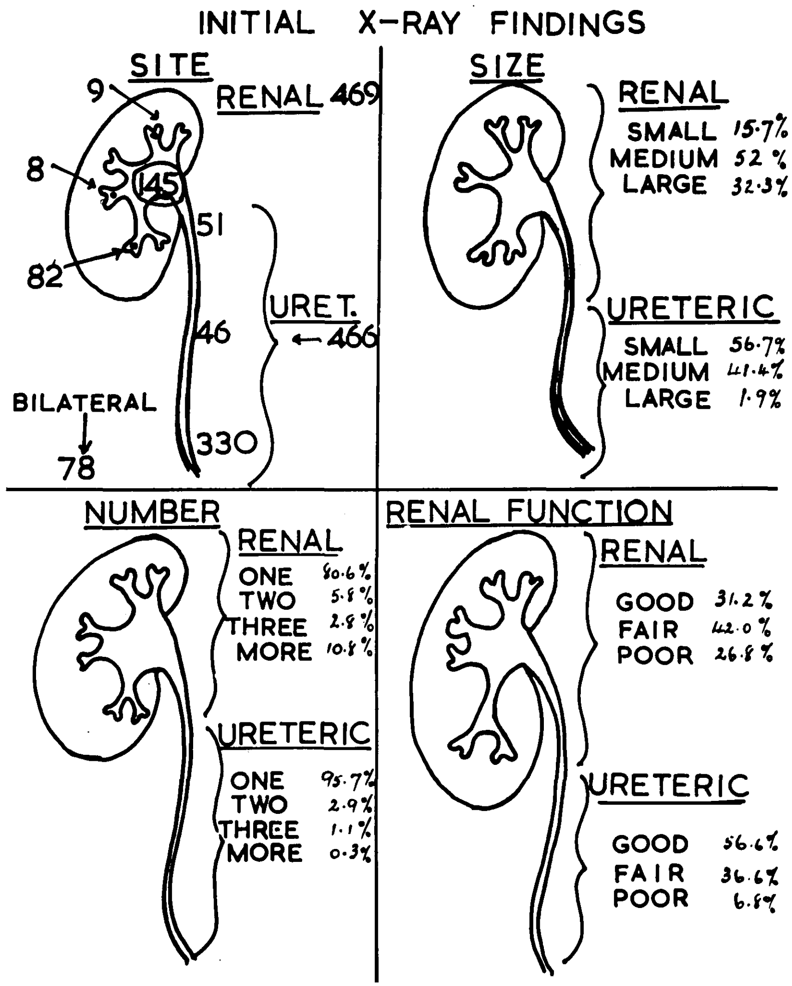



FIG. 7.

Summary of Initial X-ray Findings.

# TABLE VIII.

## Site of the Stones.

Summary of Original Radiological Findings in 1,027 Cases

| | Number | Per cent. |
|---|---|---|
| Renal | 469 | 45.6 |
| Ureteric | 466 | 45.4 |
| Renal and Ureteric | 14 | 1.4 |
| Bilateral | 78 | 7.6 |
| Total | 1,027 | 100.0 |

# TABLE IX.

Number of Stones - 1,027 Cases.

| | Total | | 1 | | 2 | | 3 | | More | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | Per cent. | No. | Per cent. | No. | Per cent. | No. | Per cent. | No. | Per cent. |
| Renal | 469 | 100.0 | 378 | 80.6 | 27 | 5.8 | 13 | 2.8 | 51 | 10.8 |
| Ureteric | 466 | 100.0 | 446 | 95.7 | 13 | 2.9 | 5 | 1.1 | 2 | 0.3 |
| Renal & Ureteric | 14 | 100.0 | 6 | 42.9 | 3 | 21.4 | 1 | 7.1 | 4 | 28.6 |
| Bilateral | 78 | 100.0 | - | - | 38 | 48.7 | 3 | 3.8 | 37 | 47.5 |
| Total | 1,027 | 100.0 | 830 | 80.8 | 81 | 7.9 | 22 | 2.1 | 94 | 9.2 |

## TABLE X.

## The Size of the Stones.

SIZE of Stone

| | Total | Small | | Medium | | Large | |
|---|---|---|---|---|---|---|---|
| | | No. | Per cent. | No. | Per cent. | No. | Per cent. |
| Renal | 469 | 73 | 15.7 | 244 | 52.0 | 152 | 32.3 |
| Ureteric | 466 | 264 | 56.7 | 193 | 41.4 | 9 | 1.9 |
| Renal & Ureteric | 14 | 5 | 35.7 | 7 | 50.0 | 2 | 14.3 |
| Bilateral | 78 | 15 | 19.2 | 36 | 46.2 | 27 | 34.6 |
| Total | 1,027 | 357 | 34.8 | 480 | 46.7 | 190 | 18.5 |

## TABLE XI.

## Renal Function at Diagnosis.

Renal Function - 932 Cases

| | Total | | Normal | | Early or moderate Hydro-nephrosis | | Advanced Hydro-nephrosis | |
|---|---|---|---|---|---|---|---|---|
| | No. | Per cent. | No. | Per cent. | No. | Per cent. | No. | Per cent. |
| Renal | 388 | 100.0 | 121 | 31.2 | 163 | 42.0 | 104 | 26.8 |
| Ureteric | 454 | 100.0 | 257 | 56.6 | 166 | 36.6 | 31 | 6.8 |
| Renal & Ureteric | 14 | 100.0 | 3 | 21.4 | 5 | 35.7 | 6 | 42.9 |
| Bilateral | 76 | 100.0 | 18 | 23.7 | 33 | 43.4 | 25 | 32.9 |
| Total | 932 | 100.0 | 399 | 42.8 | 367 | 39.4 | 166 | 17.8 |

SIMULTANEOUS OCCURRENCE OF STONES IN BROTHERS

FIG. 8.

Plain film. Multiple calculi in non-functioning kidney.

FIG. 9.

Stone in bladder having descended from left kidney.
Brother of patient shown in Fig.8.

FIG. 10 (a).
Plain film. Multiple small stones in right kidney.

FIG. 10 (b).
Intravenous pyelogram. Intrarenal hydronephrosis to which the stones are secondary.

STONES IN HORSESHOE KIDNEYS

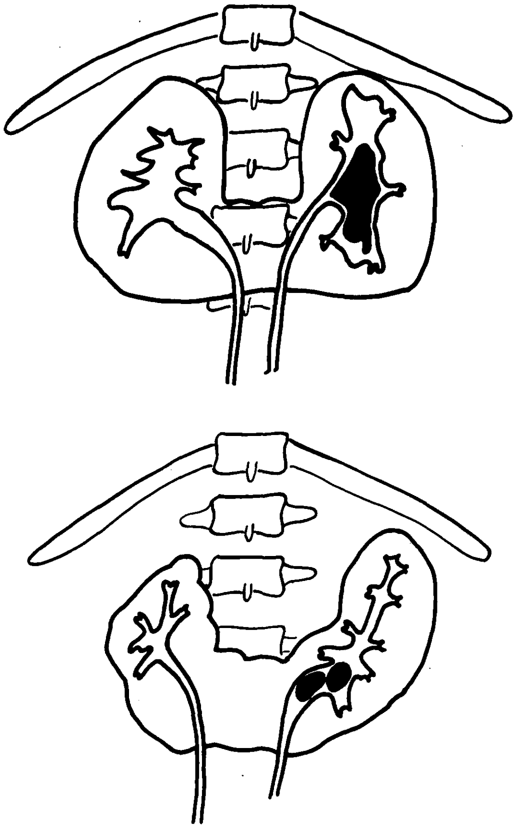


FIG. 11.

FIG. 12 (a). Plain film.

FIG. 12 (b).

Intravenous pyelogram. Five stones in pelvis of left half of horseshoe kidney.

FIG. 13 (a).

Plain film. Opacity in left renal area.

FIG. 13 (b).

Intravenous pyelogram. Stone in left half of horseshoe kidney.

# FIGURES and TABLES

relating to

# PART II

# TABLE III.

(Repeated here for convenience)

**A Study of Operation and No Operation Series - 1,114 Cases**

| | |
|---|---|
| No Operation (568 Cases) | 415 Passed stone.<br>153 Retained stone or were untraced. |
| Operation (546 Cases) | |
| All had operations - 546 | 400 Renal Primary.<br>146 Ureteric Primary. |
| In addition:- | |
| 106 Passed stones.<br>26 Had large untreated stones, primary or recurrent.<br>71 Had small untreated stones, primary or recurrent. | |

# TABLE XII.

## Fate of 1,394 Stones Formed in the Kidneys of 1,038 Patients.

| | |
|---|---|
| Retained in the Kidney | 711 |
| Entered the Ureter | 683 |
| Total | 1,394 |

Stones Retained in Kidney.

| | | |
|---|---|---|
| Operative treatment | 534 | (75 per cent.) |
| Untreated (Primary and Recurrent) | 177 | (53 large, 124 small) |
| Total | 711 | |

Stones Entering Ureter.

| | | |
|---|---|---|
| Ureterolithotomy | 146 | (21 per cent.) |
| Passed | 521 | |
| Retained | 16 | |
| | 683 | |

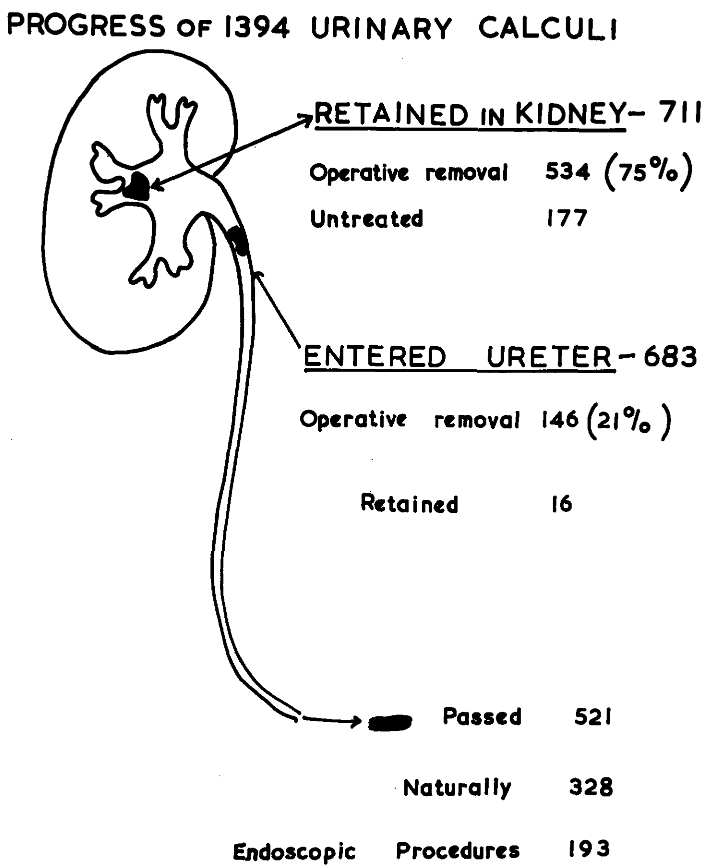

PROGRESS OF 1394 URINARY CALCULI
RETAINED IN KIDNEY - 711
Operative removal 534 (75%)
Untreated 177
ENTERED URETER - 683
Operative removal 146 (21%)
Retained 16
Passed 521
Naturally 328
Endoscopic Procedures 193

FIG. 14.

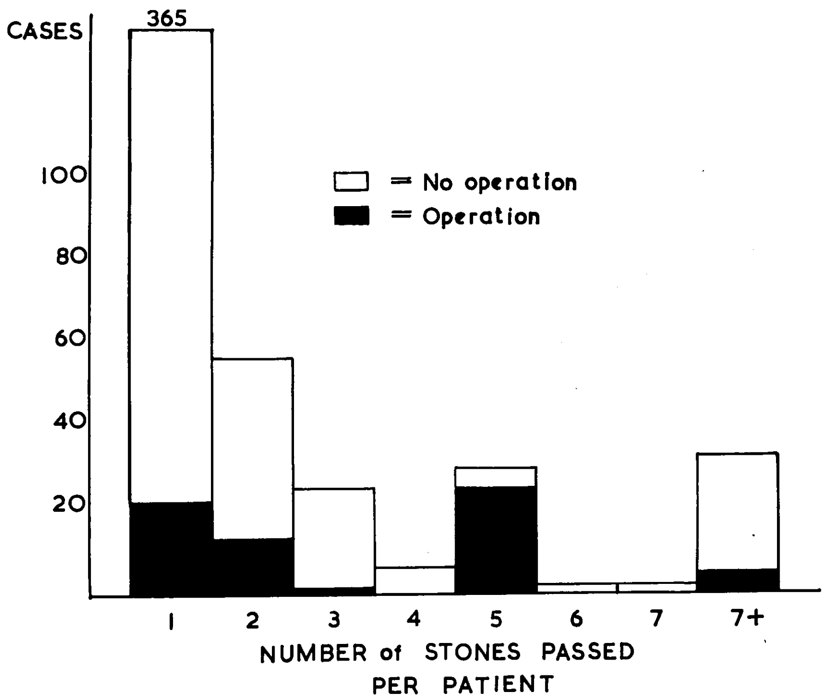

CASES
365
100
80
60
40
20
= No operation
= Operation
1
2
3
4
5
6
7
7+
NUMBER of STONES PASSED
PER PATIENT

FIG. 15.

## TABLE XIII.

Total Stones Known to have Passed.

| Number of Stones | Number of Cases | Product |
|---|---|---|
| 1 | 365 | 365 |
| 2 | 56 | 112 |
| 3 | 25 | 75 |
| 4 | 6 | 24 |
| 5 | 31 | 155 |
| 6 | 2 | 12 |
| 7 | 1 | 7 |
| 9 | 2 | 18 |
| 10 | 27 | 270 |
| 13 | 2 | 26 |
| 17 | 1 | 17 |
| 560 | 1 | 560 |
| | Total | 1,641 |

## TABLE XIV.

Study of 521 Stone-Passers.

| | Total Passing Stones | One Stone Passed | More than one Passed | Per cent. Passing more than One |
|---|---|---|---|---|
| Operation Series | 106 | 60 | 46 | 43.4 |
| No Operation Series | 415 | 305 | 110 | 26.5 |
| Total | 521 | 365 | 156 | 30.0 |

Hence: If the passage of a subsequent stone is regarded as "recurrence", this happened in 156/521 or 30 per cent.

---

## TABLE XV.

Stone-Passers in Operation Series.

106 of 403 interviewed = 25%

of the 106 Cases :-

12% started only after operation.

44% passed before and after operation.

44% passed stones before operation and stopped after operation.

FIG. 16.

Large right lower ureteric calculus which passed naturally.

FIG. 17.

Right lower ureteric stone (smaller than that in Fig.16) for which operation was required.

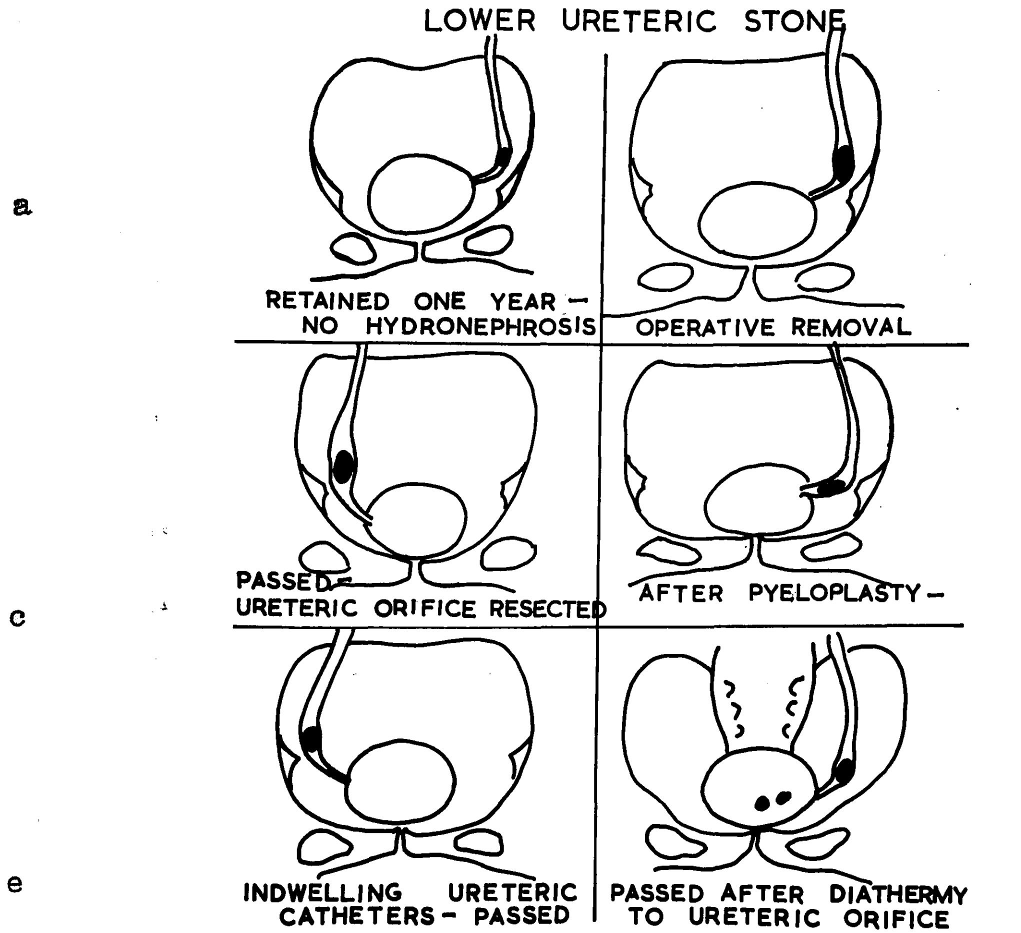



FIG. 18.

Examples of lower ureteric stone illustrating their management.

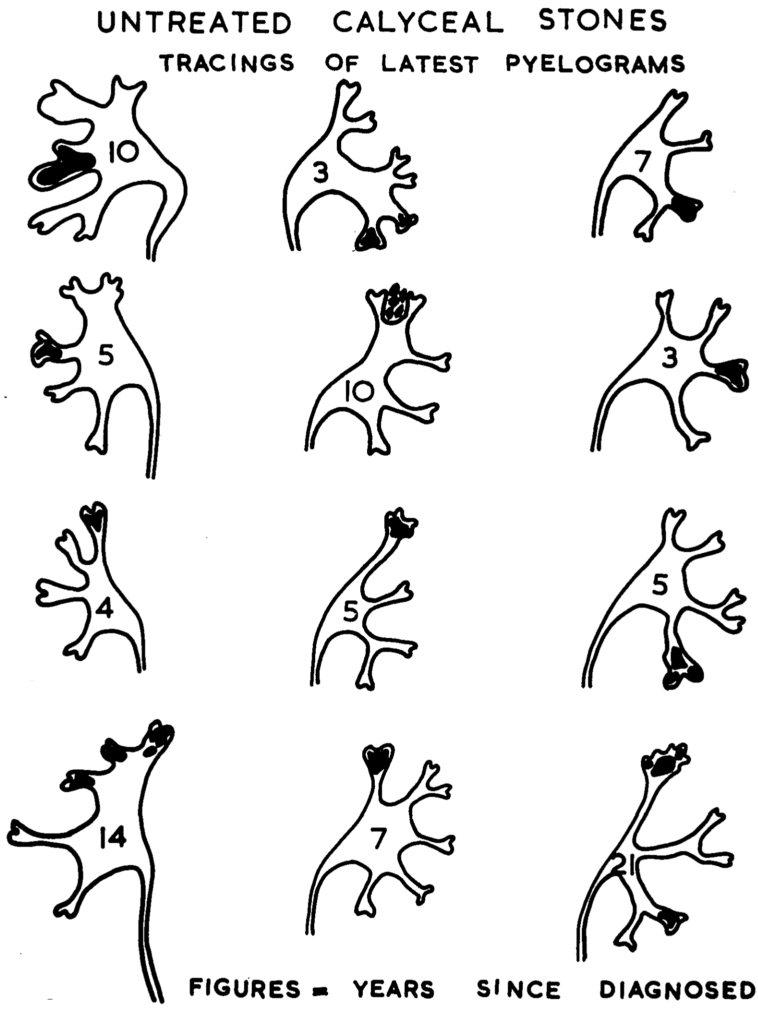

UNTREATED CALYCEAL STONES
TRACINGS OF LATEST PYELOGRAMS
10
3
7
5
10
3
4
5
5
14
7
21
FIGURES = YEARS SINCE DIAGNOSED

FIG. 19.

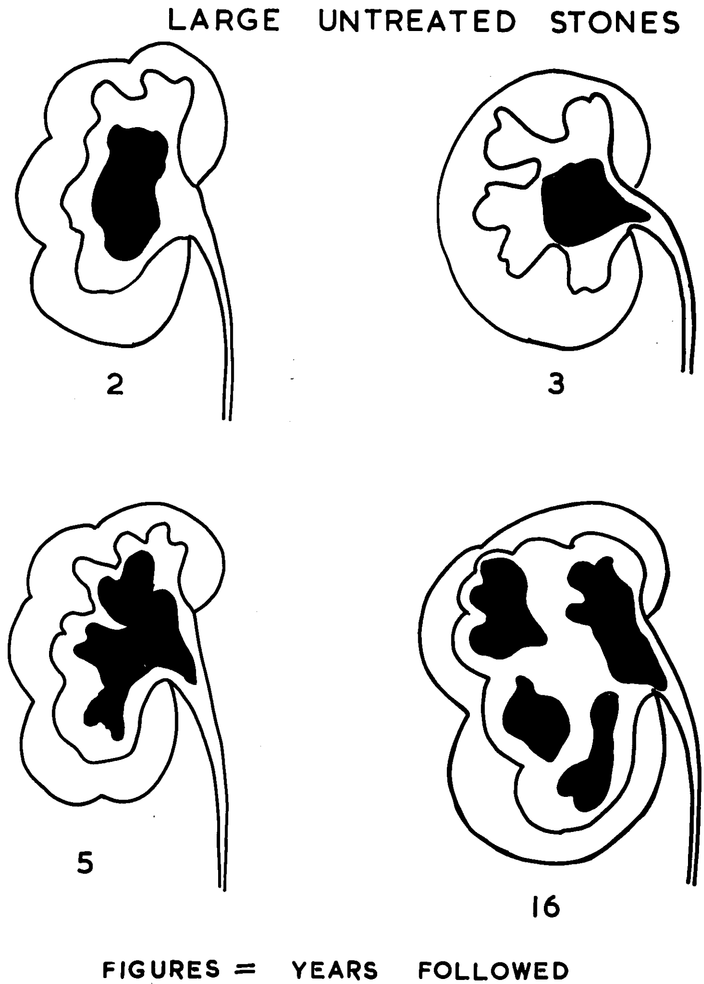



FIG. 20.

Large stones treated conservatively.


FIG. 21.

Large discrete stones known to have been present for 16 years in non-functioning right kidney. No "spread" to the opposite side.

FIG. 22 (a).

Plain film.

FIG. 22 (b).

Intravenous pyelogram.

FIG. 23 (a).

Plain film.

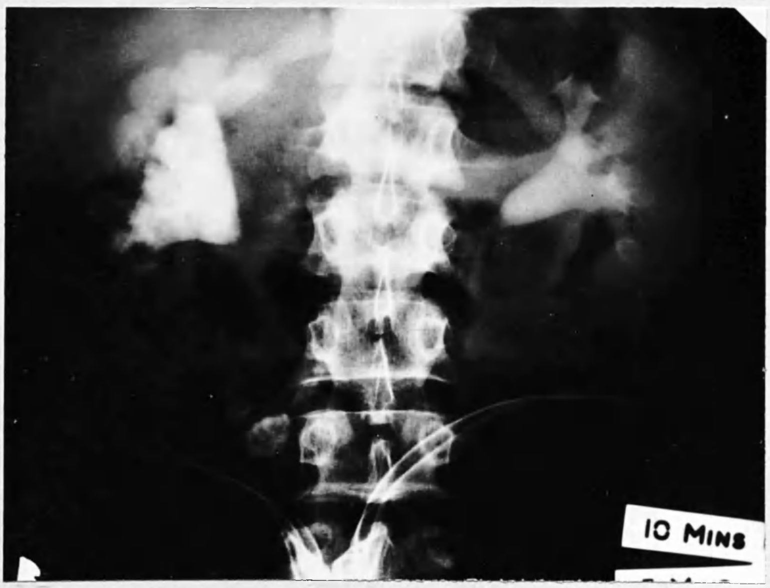



Fig. 23 (b).

Intravenous pyelogram.

FIG. 24 (a)
Plain film
6.8.1947.

FIG. 24 (b)
Plain film
25.11.1953.

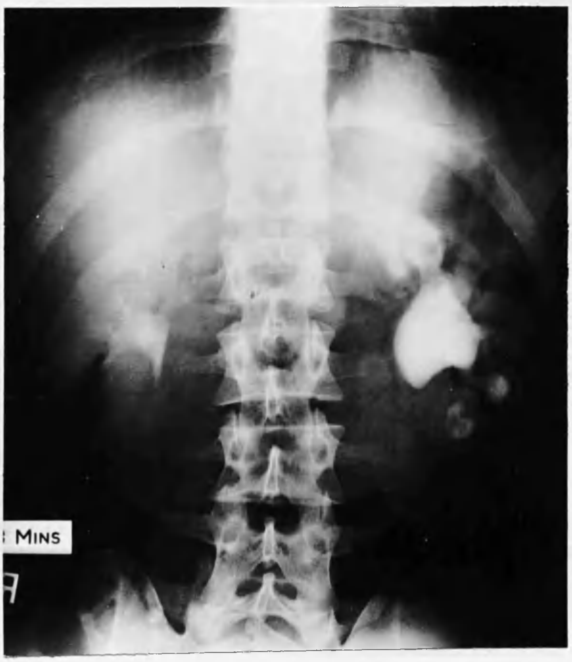



FIG. 24 (c)
Intravenous pyelogram.
25.11.1953.

FIG. 25 (a)

Plain film. 10.10.51.

FIG. 25 (b)

Intravenous pyelogram 10.10.51.
The films for 1955 are on the next page.


FIG. 25 (c)

Plain film. 14.9.55.


FIG. 25 (d)

Intravenous pyelogram. 14.9.55.

# TABLE XVI.

## Comparison of End-Results of Operative and Expectant Treatment of Bilateral Branched Calculi

| | Expectant Treatment | Operative Treatment | Total |
|---|---|---|---|
| Total | 8 | 23 | 31 |
| Died from Disease | 3 | 9 | 12 |
| Died from other causes | 0 | 1 | 1 |
| Untraced | 1 | 3 | 4 |
| Alive (all have stones) | 4 | 10 | 14 |
| Symptoms | 1 | 5 | |
| No symptoms | 3 | 3 | |
| One kidney - poor function | 0 | 2 | |

BILATERAL CALCULI TREATED CONSERVATIVELY for 16 YEARS

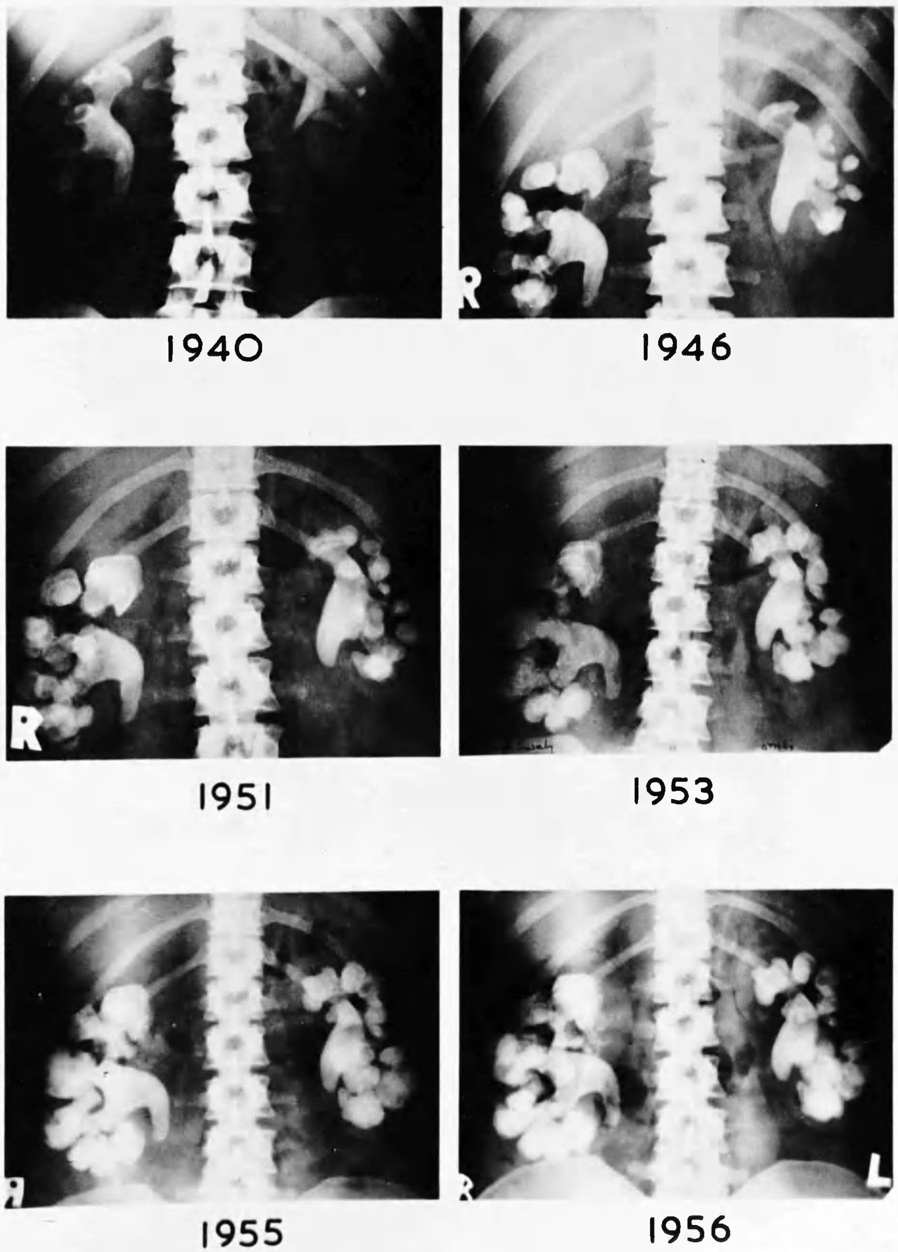



FIG. 26.

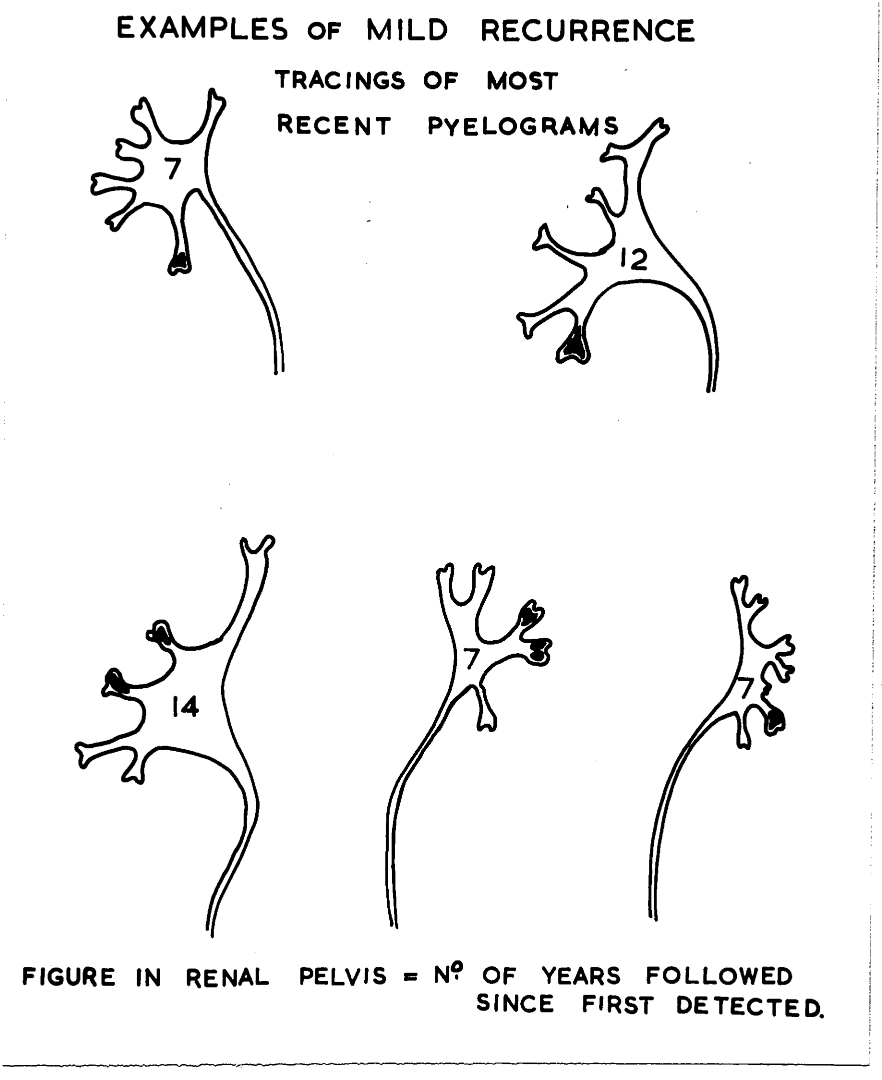

EXAMPLES OF MILD RECURRENCE
TRACINGS OF MOST
RECENT PYELOGRAMS
7
12
14
7
7
FIGURE IN RENAL PELVIS = Nº OF YEARS FOLLOWED
SINCE FIRST DETECTED.

FIG. 27.

FIG. 28.

Plain film. Branched stones in remaining portion of right kidney.

# TABLE XVII.

## Study of 29 Cases of Untreated Severe Recurrence

### Disposal

| | | | | |
|---|---|---|---|---|
| Untraced | 7 | | | |
| Leaving | 22 | → | Unfit | 10 |
| | | | Unwilling | 10 |
| | | | Waiting for operation | 2 |
| | | | | 22 |

| Followed | Number |
|---|---|
| 0 - 5 years | 3 |
| 6 - 10 " | 7 |
| 11 - 15 " | 8 |
| 16 - 20 " | 2 |
| 21 - 25 " | 1 |
| 26 - 30 " | 0 |
| over 30 " | 1 |
| | 22 |

### Died (6)

| | |
|---|---|
| Other causes | 5 |
| Urinary causes | 1 |
| | 6 |

### X-ray Examination (22 cases)

| | |
|---|---|
| Good function | 4 |
| Fair function | 6 |
| Poor function | 12 |
| | 22 |

### General Condition (29 Cases)

| | |
|---|---|
| Good | 18 |
| Poor | 11 |
| | 29 |

### Symptoms

| | |
|---|---|
| No symptoms - | 9 |
| Symptoms - | 20 |
| | 29 |

# FIGURES and TABLES

relating to

# PART III

# TABLE XVIII

## Disposal of 546 Open Operation Cases

| Disposal | Total | Urological Dept. | Vic. Infy. Surgeons | Others |
|---|---|---|---|---|
| Interviewed | 403 (74%) | 246 (80%) | 99 (60%) | 58 |
| Questionnaire or Social Service visit | 50 | 26 | 24 | - |
| Post-operative deaths | 23 | 11 | 10 | 2 |
| Too recent | 32 | 30 | - | 2 |
| Untraced | 38 | 10 | 28 | - |
| Total | 546 | 323 | 161 | 62 |

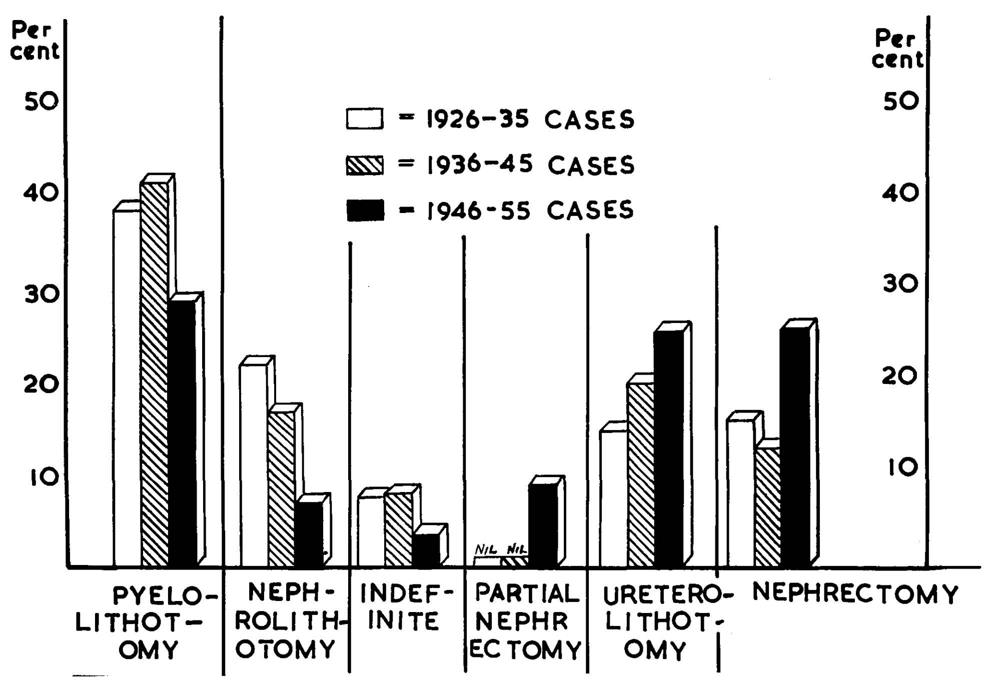



FIG. 29.

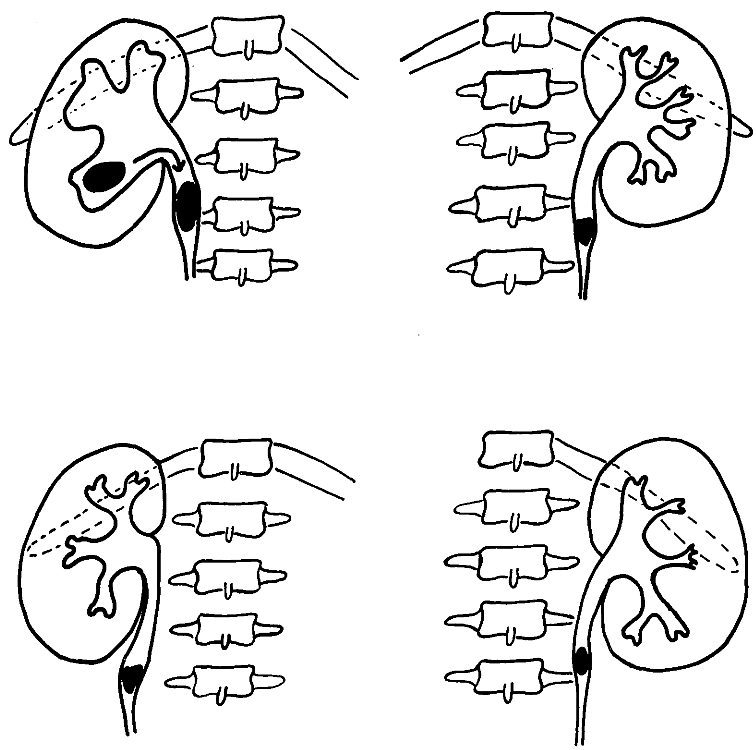
Incidence of operations performed in three decades.

# TABLE XIX.

OPERATIVE TECHNIQUES EMPLOYED (HELLSTROM)

| | 1911-14 | 1935-38 | 1940-47 |
|---|---|---|---|
| NEPHROLITHOTOMY | 40%. | 10%. | 5% |
| PYELOLITHOTOMY | 20%. | 35%. | 45%. |
| URETEROLITHOTOMY | 15%. | 35%. | 25%. |
| NEPHRECTOMY | 25%. | 20%. | 25%. |

UPPER URETERIC CALCULI



STONES SUITABLE FOR REMOVAL THROUGH THE TRIANGLE OF PETIT

FIG. 30.

TABLE XX.

Bilateral Primary Operations in 34 Cases.

(simultaneous in one only)

| | |
|---|---|
| Bilateral Renal | 26 |
| Bilateral Ureteric | 2 |
| (Unilateral Renal & (Unilateral Ureteric | 6 |
| | 34 |

Recurrence Rates in other Investigations

| Writer | Year | Total Cases | Re-examined | RECURRENCE PER CENT FOLLOWING Pyelo-litho-tomy | Nephro-litho-tomy | Uretero-litho-tomy | Total Recurr perCent |
|---|---|---|---|---|---|---|---|
| Cabot and Crabtree | 1915 | 155 | 87 | 51.0 | 56.0 | 29.0 | ... |
| Barney | 1922 | 70 | 35 | 39.0 | 52.9 | ... | ... |
| Braasch & Foulds | 1923 | ... | ... | 11.85 | 24.03 | ... | ... |
| Brongersma | 1924 | 100 | 100 | 23.6 | 35.5 | ... | ... |
| Rovsing | 1924 | 109 | ... | ... | ... | ... | 40.0 |
| Hunner | 1928 | 302 | 78 | ... | ... | 4.4 | 9.5 |
| Hellström | 1933 | 348 | ... | ... | ... | ... | 25.0 |
| Higgins | 1936 | ... | ... | ... | ... | ... | 16.4 |
| Twinem | 1937 | 252 | 115 | 20.9 | 28.0 | ... | ... |
| Oppenheimer | 1937 | 169 | 141 | 24.0 | 58.6 | ... | ... |
| Spence and Baird | 1939 | 164 | ... | ... | ... | 18.0 | 38.4 |
| Hamilton Stewart | 1952 | 101 | 87 | ... | ... | ... | 6.8 |
| Pyrah | 1954 | 156 | 156 | 34.9 | 60.0 | 20.9 | ... |
| Sutherland | 1954 | 345 | 216 | 47.0 | 62.5 | 37.0 | 46.7 |
| Kairis | 1955 | 1676 | 39 | 3.8 | 7.4 | 0.9 | |

TABLE XXI.

# TABLE XXII.

Incidence of Pseudo-Recurrence

| Site of Pseudo-Recurrence | Total Cases Reviewed | Mild Pseudo Recurr. | Severe Pseudo Recurr. | Total Pseudo Recurr. | Pseudo-R Per cent. |
|---|---|---|---|---|---|
| Kidney | 201 | 7 | 25 | 32 | 16 |
| Ureter | 104 | 1 | 5 | 6 | 6 |
| Totals | 305 | 8 | 30 | 38 | 12.5 |

## TRACINGS—EXAMPLES OF PSEUDO-RECURRENCE

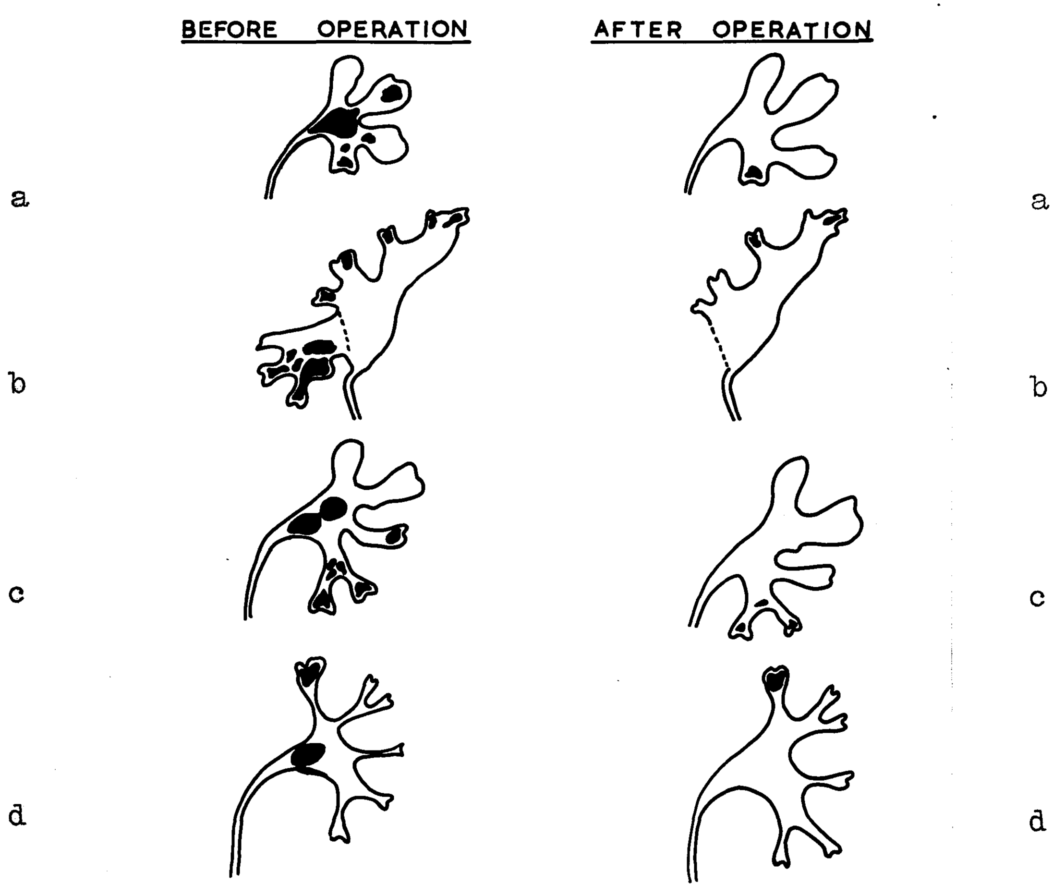



FIG. 31.

FIG. 32.

Radiograph of kidney after removal illustrating the difficulty of removing the multiple tiny fragments of stone present.

SEVERE RECURRENCE

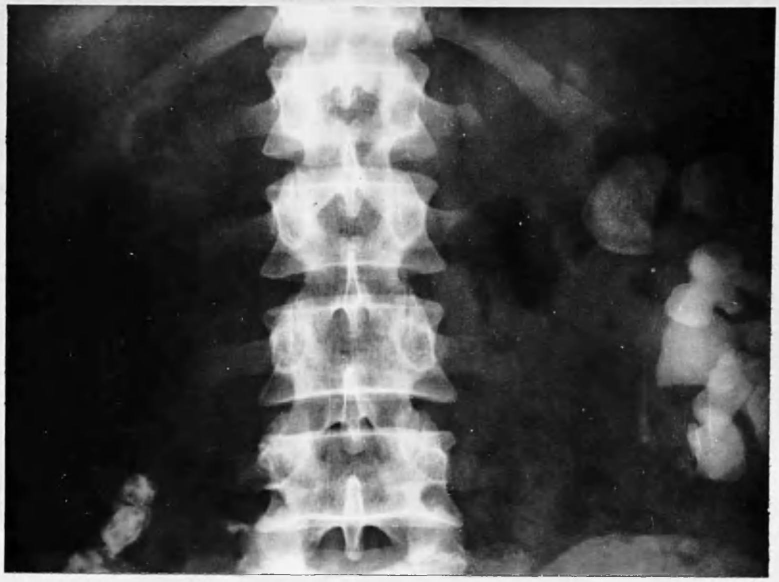


FIG. 33 (a)

Plain film upper urinary tract.
Severe recurrence.

FIG. 33 (b)

Plain film lower urinary tract (same patient).
Severe recurrence.

SEVERE RECURRENCE

FIG. 34 (a)

Plain film. Three recurrent stones in left kidney (plus pyjama button). Previous right nephrectomy.


FIG. 34 (b)

Intravenous pyelogram (same patient). No hydronephrosis.

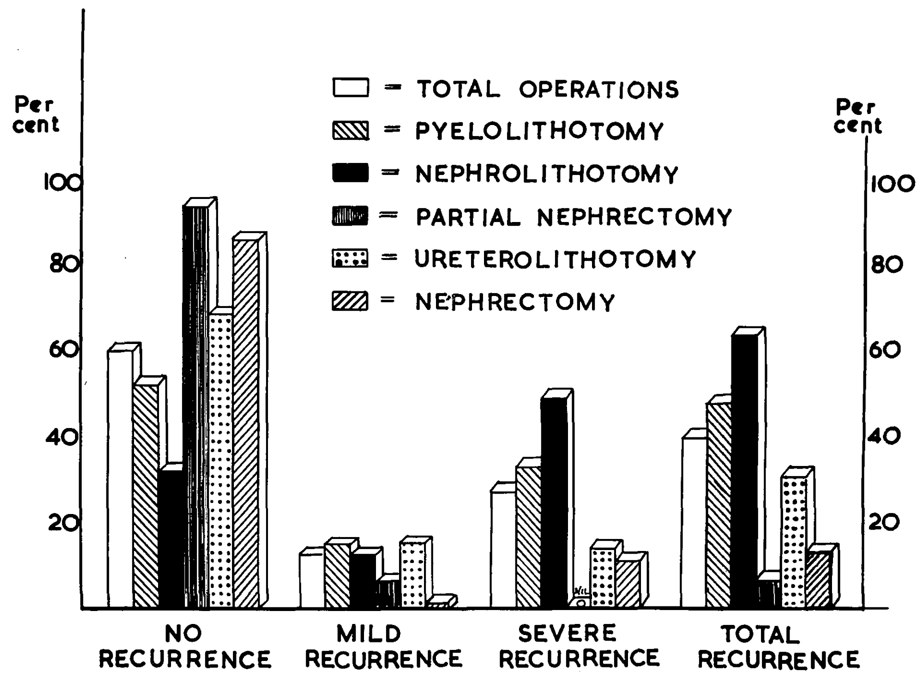



FIG. 35.

Percentage Incidence of Recurrence in Total Series
(416 operations)

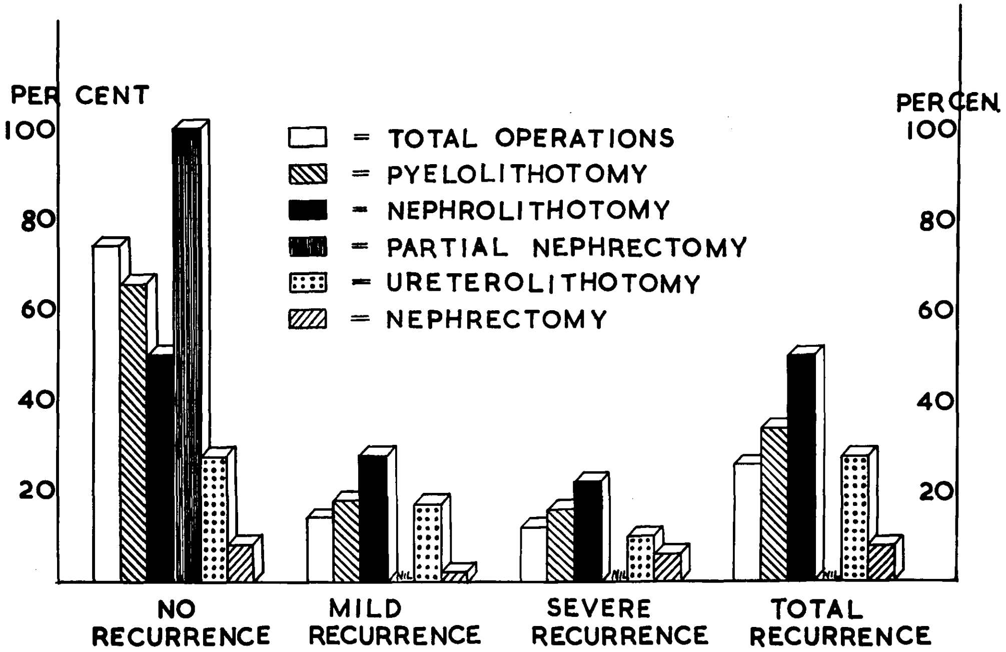



FIG. 36.

Percentage Incidence of Recurrence in Urological Series. (246 Operations)

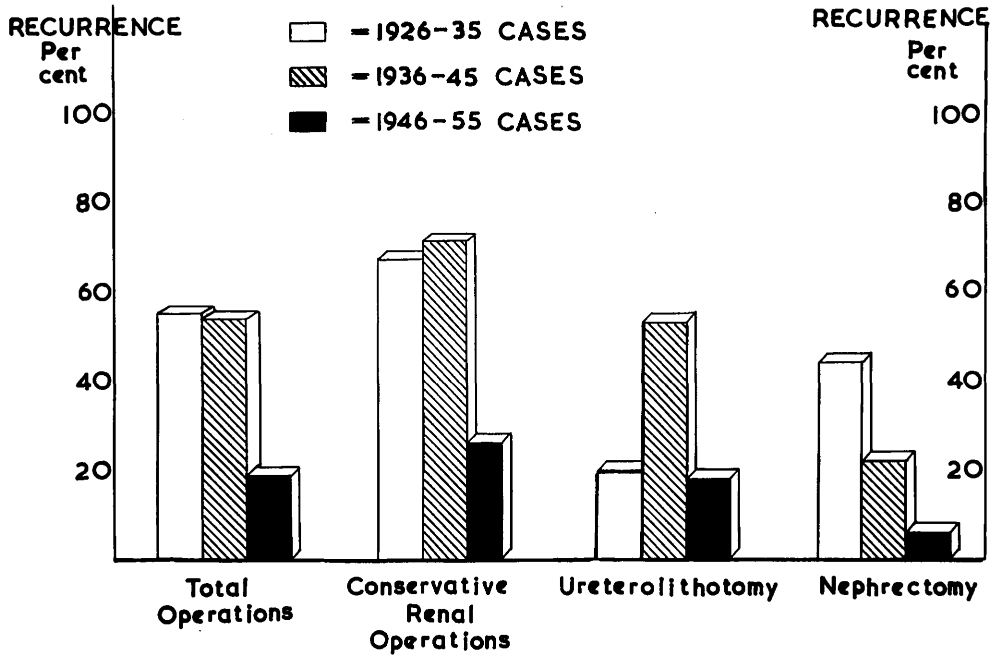



FIG. 37.

Percentage Incidence of Recurrence in Three Decades.

# TABLE XXIII.

INCIDENCE OF CONTRALATERAL RECURRENCE.

| AUTHOR | INCIDENCE OF CONTRALATERAL RECURRENCE. | |
|---|---|---|
| | AFTER CONSERVATIVE OPERATIONS PER. CENT. | AFTER NEPHRECTOMY PER. CENT. |
| BRONGERSMA (1924) | | 2 |
| CIFUENTES (1924) | | 13 |
| ROVSING (1924) | | 3.2 |
| QUINBY (1933) | | 12.5 |
| HELLSTROM (1933) | 8.6 | 10.11 |
| TWINEM (1937) | | 4.2 |
| OPPENHEIMER (1937) | 15.1 | 14.8 |

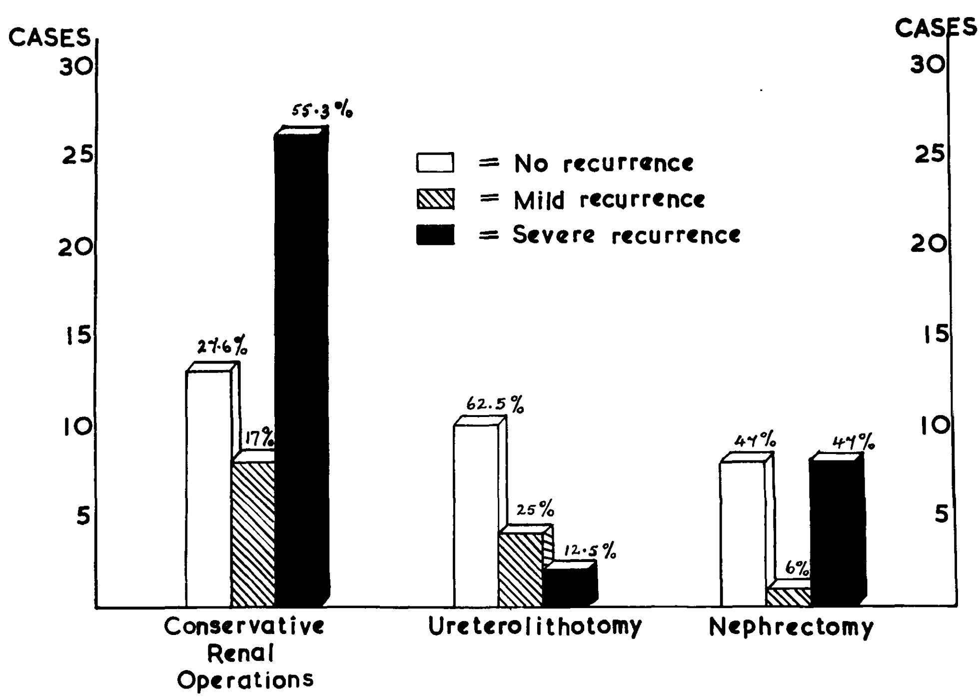



FIG. 38.

Incidence of Recurrence in Patients with Bilateral Stone.


FIG. 39 (a)

Plain film. 22.11.49.

FIG. 39 (b)

Intravenous pyelogram.
22.11.49.

FIG. 39 (c)

Plain film. 14.5.51.

FIG. 39 (d)

Plain film. 2.8.56.

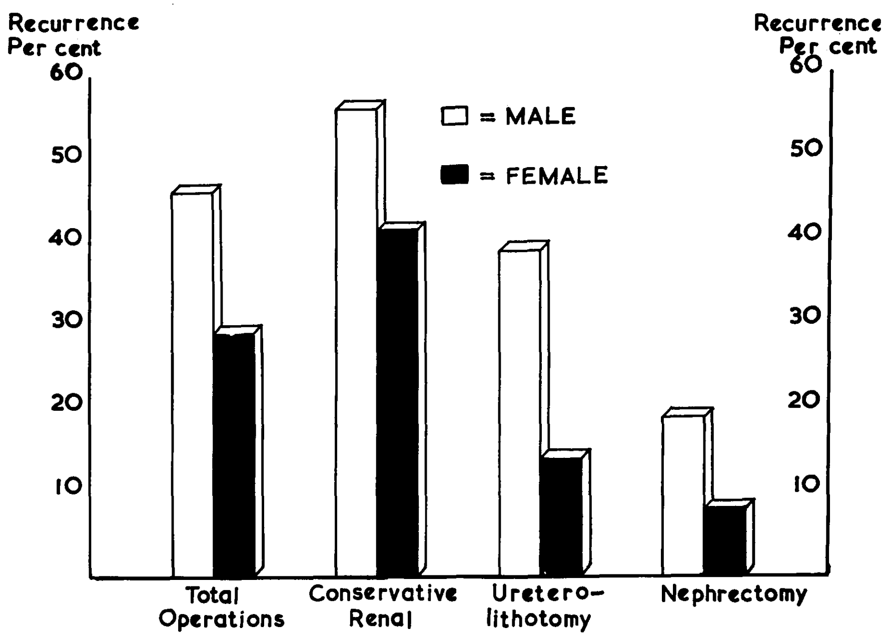



FIG. 40.

Sex Incidence of Recurrence in Total Series.

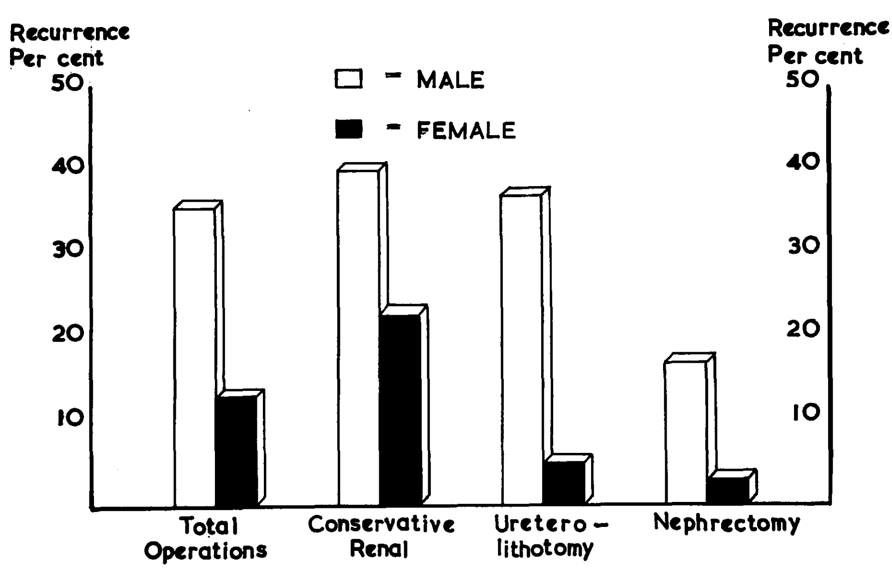



FIG. 41.

Sex Incidence of Recurrence in Urological Series.

## TABLE XXIV.

**Symptoms in Recurrence in 132 Cases.**

| Recurrence | Total | No Symptoms | Symptoms | Per cent. Free from Symptoms |
|---|---|---|---|---|
| Mild | 60 | 21 | 39 | 35.0 |
| Severe | 72 | 26 | 46 | 36.1 |
| Total | 132 | 47 | 85 | 35.6 |

**Hence:** one-third of recurrent cases had no symptoms and would have been missed without X-ray examination.


FIG. 42 (a)

Plain film. Symptomless recurrence 28 years after operation.


FIG. 42 (b)

Intravenous pyelogram. No hydronephrosis.

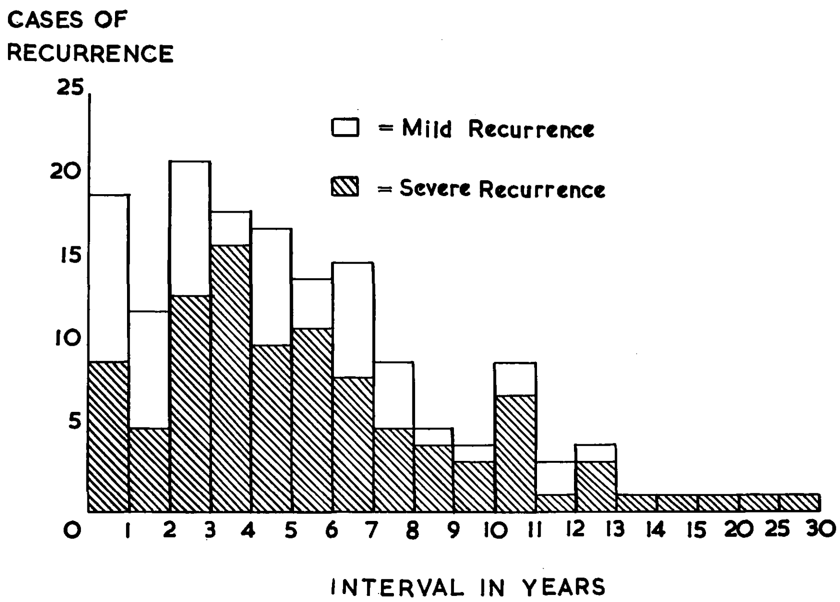



FIG. 43.

Interval Between Operation and Detection of Recurrence.

Very Early Recurrence.

FIG. 44.

Plain film. Massive bilateral recurrent stones within one year of operation.

Example of Very Late Detection of Recurrence.

FIG. 45 (a)

Plain film.
27.2.52.

FIG. 45 (b)

Plain film.
16.11.55.


FIG. 45 (c)

Intravenous pyelogram.

16.11.55.

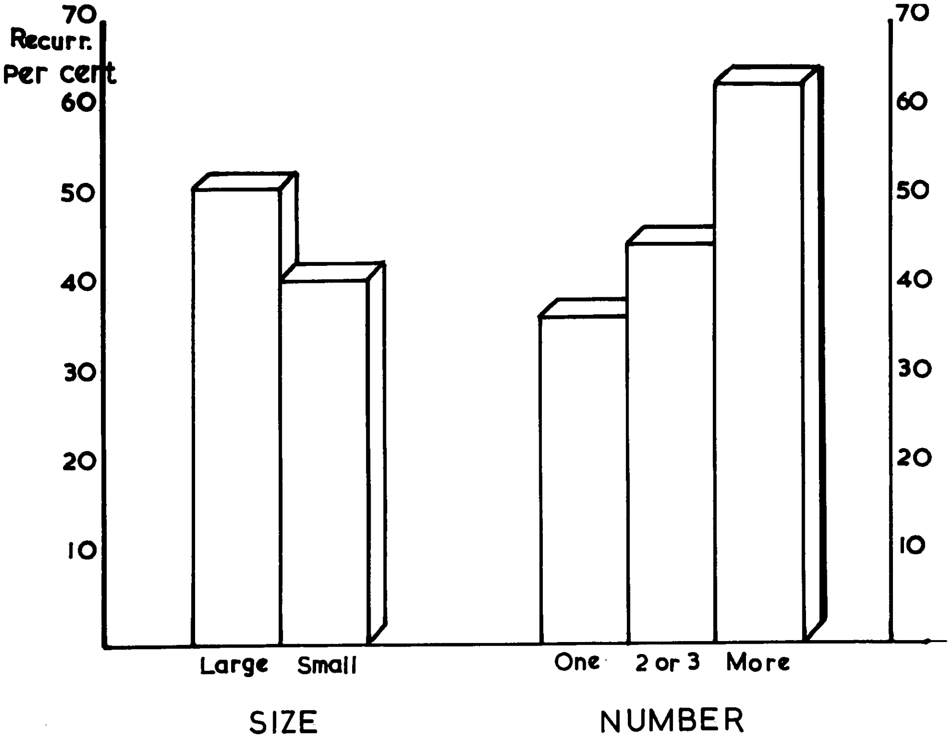



FIG. 46.

Relationship of Size and Number of Initial Stones to Recurrence.

FIG. 47 (a)

Plain film. Recurrence due to Proteus.

FIG. 47 (b)

Intravenous pyelogram of same patient.
Poor function in left side. Right normal.

## TABLE XXVII.

Severe Recurrence

Relationship of Renal Function to Calculous State

(72 Cases)

| Calculous State at time of X-ray | Total Cases | Normal | Early Hydro-neph. | Fair | Poor | None one side | None (Practically) on both sides |
|---|---|---|---|---|---|---|---|
| Clear | 14 | 13 | - | - | 1 | - | - |
| Mild Recurrence | 3 | 3 | - | - | - | - | - |
| Severe Recurrence | 55 | 12 | 5 | 8 | 17 | 9 | 4 |
| Totals | 72 | 28 | 5 | 8 | 18 | 9 | 4 |

## TABLE XXVIII.

RELATIONSHIP OF CHEMICAL NATURE OF STONE TO RECURRENCE.

TWINEM (1937).

| CHEMICAL NATURE. | NO. OF CASES. | RECURRENCES. |
|---|---|---|
| PHOSPHATE. | 79 | 28 |
| OXALATE. | 74 | 11 |
| URIC ACID. | 7 | 2 |
| CYSTINE. | 3 | 3 |

## TABLE XXIX.

### The Various Types of Mild Recurrence.

**Mild Recurrence - 60 Cases.**

| Type of Mild Recurrence | Number |
|---|---|
| 1. Pseudo-recurrence | 8 |
| 2. Contralateral calyceal | 9 |
| 3. Calyceal stone after renal op.<br>Unilateral 17<br>Bilateral 6 | 23 |
| 4. Calyceal stone after lower ureterolithotomy | 5 |
| 5. Ureteric stone after ureterolithotomy | 4 |
| 6. Passed stone (5) after operation - now clear | 11 |
| Total | 60 |

Hence: 52 True Mild Recurrences

## TABLE XXX.

Symptoms in Mild Recurrence - 60 Cases.

| Symptoms | Number of Cases |
|---|---|
| None | 21 |
| Lumbar pain | 11 |
| Colic - no stone passed | 11 |
| Colic - Passed stone(s) | 17 |
| Total | 60 |

## TABLE XXXI.

Relationship to Type of Operation - 52 Cases
(False recurrence excluded)

| Operation | Total Cases | Mild Recurrence | Mild Recurr. Per cent. |
|---|---|---|---|
| Pyelolithotomy | 160 | 24 | 15.0 |
| Nephrolithotomy | 72 | 9 | 12.5 |
| Partial nephrectomy | 16 | 1 | 6.2 |
| Nephrectomy | 70 | 1 | 1.4 |
| Ureterolithotomy | 98 | 7 | 17.4 |
| Total | 416 | 52 | 12.4 |

# TABLE XXXII.

## Incidence of Urinary Infection in Mild Recurrence.

**Post-operative Urine Examination - 54 Cases**

| Findings | Number | Per cent. |
|---|---|---|
| Sterile | 32 | 60 |
| Infected | 22 | 40 |
| Total | 54 | 100 |

| Organisms | Number |
|---|---|
| W.B.C. alone | 3 |
| B.coli | 10 |
| B.coli + Strep.faec. | 3 |
| Proteus | 1 |
| Proteus + Strep.faec | 1 |
| Staph. Aur. | 1 |
| Staph. Alb. | 3 |
| Total | 22 |

# TABLE XXXIII.

**Mild Recurrence**
**Post-operative Radiological Examination**
**40 Cases**

| X-ray Findings | Number | Per cent. |
|---|---|---|
| Normal function | 28 | 70.0 |
| Early hydronephrosis - Good function | 8 | 20.0 |
| Moderate hydronephrosis - Fair function | 4 | 10.0 |
| Total | 40 | 100.0 |

# TABLE XXXIV.

Relationship of 112 True Severe Recurrences to Primary Operation

| Primary Operation | Total Primary Operation | Severe Recurr-ence | Severe Recurrence per Cent. |
|---|---|---|---|
| Pyelolithotomy | 160 | 53 | 33.1 |
| Nephrolithotomy | 72 | 37 | 51.5 |
| Partial nephrectomy | 16 | 0 | - |
| Nephrectomy | 70 | 8 | 11.5 |
| Ureterolithotomy | 98 | 14 | 14.2 |
| Total | 416 | 112 | 27.0 |

# TABLE XXXV.

Severe Recurrence
Treatment of 107 Cases

| Treatment | Number | Comments |
|---|---|---|
| No secondary operation | 29 | Reasons<br>Unfit 10<br>Unwilling -no symptoms 10<br>Waiting for operation 2<br>Untraced 7<br>29 |
| Secondary operation<br>Unilateral 55<br>Bilateral 23<br>78 | 78 | Conservative (43 Cases)<br>Single unilateral conserv. 27<br>Multiple " " 4<br>Single bilateral conserv. 7<br>Multiple " " 5<br>43<br>Radical (35 Cases)<br>Nephrectomy after S.U.C. 17<br>Nephrectomy after M.U.C. 7<br>Nephrec.+ S.U.C. 4<br>" + M.U.C. 7<br>35 |
| Total | 107 | |

FIG. 48 (a)

Plain film. Staghorn Recurrence in Solitary Kidney.

FIG. 48 (b)

Intravenous Pyelogram. Hydronephrosis. Poor function.

# TABLE XXXVI.

## Study of 78 Cases of Severe Recurrence Treated by Secondary Operation

### Disposal

| | |
|---|---|
| Total | 78 |
| Died | 14 |
| Untraced | 8 |
| Leaving | 56 |

### Causes of Death

| | |
|---|---|
| Post-operative | 4 |
| Urinary | 5 |
| Other | 5 |
| Total | 14 |

### Period of Follow-up

| | Cases |
|---|---|
| 0 - 5 years | 13 |
| 6 - 10 " | 17 |
| 11 - 15 " | 21 |
| 16 - 20 " | 14 |
| 21 - 25 " | 3 |
| 26 - 30 " | 8 |
| Over 30 " | 2 |
| Total | 78 |

# TABLE XXXVII.

## Symptoms in Severe Recurrence.

### Symptoms at Present in 56 Cases.

| Present Condition | Total | Symptoms | No Symptoms |
|---|---|---|---|
| Clear | 32 | 6 | 26 |
| Mild Recurrence | 11 | 2 | 9 |
| Severe Recurrence still present | 13 | 9 | 4 |
| Total | 56 | 17 | 39 |

# TABLE XXXVIII.

## Severe Recurrence.

**Renal Function**
**(31 Cases)**

| | |
|---|---|
| Good | 17 |
| Fair | 2 |
| Poor | 12 |
| Total | 31 |

**Present Condition**
**(56 Cases)**

| | |
|---|---|
| Clear | 32 |
| Mild Recurrence | 11 |
| Still Severe Recurrence | 13 |
| Total | 56 |

**General Health**
**(56 Cases)**

| | |
|---|---|
| Good | 35 |
| Fair | 15 |
| Poor | 6 |
| Total | 56 |

# TABLE XXXIX.

**Severe Recurrence**

**Relationship of Urinary Infection to Calculous State**
**(96 Cases)**

| Urine Examination Findings | Total Cases | Calculous State at Time: No stone present | Small stone present | Large stone present |
|---|---|---|---|---|
| Sterile | 40 | 27 | 3 | 10 |
| RBC + WBC only | 8 | 0 | 1 | 7 |
| B.coli | 23 | 2 | 0 | 21 |
| B.coli + Proteus | 3 | 0 | 0 | 3 |
| B.coli + Strep.faec. | 3 | 0 | 0 | 3 |
| Proteus Vulgaris | 5 | 0 | 1 | 4 |
| Ps. Pyocyanea | 3 | 0 | 0 | 3 |
| Staph. aureus | 6 | 0 | 2 | 4 |
| Staph. albus | 5 | 1 | 1 | 3 |
| Totals | 96 | 30 | 8 | 58 |

# FIGURES and TABLES

relating to

# PART IV

RECURRENT UPPER CALYCEAL STONE SUITABLE FOR PARTIAL NEPHRECTOMY.

FIG. 49 (a)

Plain film. Dendritic recurrent stone in left upper calyx.

FIG. 49 (b).

Intravenous pyelogram. Double pelvis and incomplete double ureter on left side. Suitable case for partial nephrectomy.

# TABLE XL.

## The Stone-forming Diet.

### "Stone-forming" Diet. (Damanski)

| | |
|---|---|
| Ammonium oxalate | 24 Gm. |
| Ammonium chloride | 80 Gm. |
| Dried brewer's yeast | 120 Gm. |
| Calf meal - OA (see below) | To make a total of 4,000 Gm. of food mixture. |

### Formula for Calf meal - OA

| | | | | |
|---|---|---|---|---|
| Yellow corn meal | 417 | parts | by | weight |
| 34 per cent. protein O.P. linseed meal | 300 | " | " | " |
| Ground malt barley | 200 | " | " | " |
| Wheat red dog | 440 | " | " | " |
| Oat flour | 300 | " | " | " |
| Dried skimmed milk | 260 | " | " | " |
| Soluble blood flour | 40 | " | " | " |
| Irradiated Yeast | 0.50 | " | " | " |
| Dicalcium phosphate | 15 | " | " | " |
| Ground limestone | 5 | " | " | " |
| Iodized salt | 20 | " | " | " |

FIG. 50.

Multiple opacities, all proven at autopsy to be artefacts. One appears to lie in the left renal pelvis.

FIG. 51.

Two opacities in right renal area proven at autopsy to be calculi.

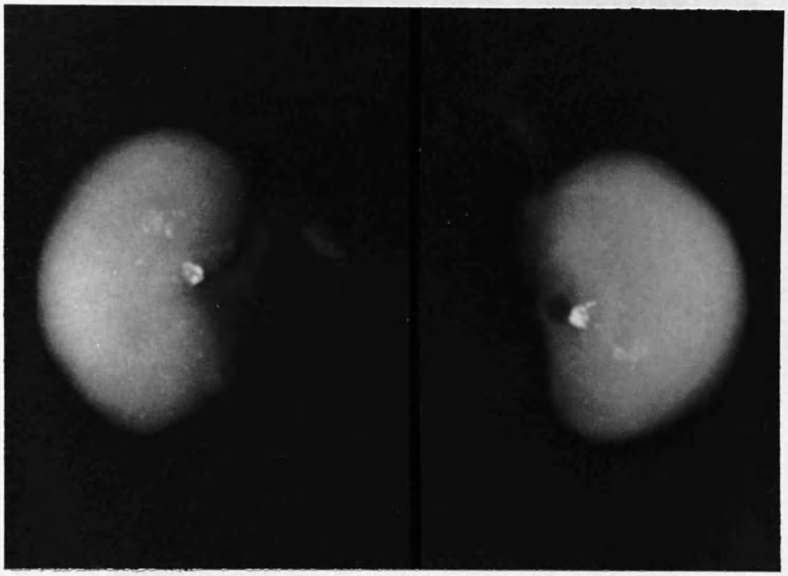


FIG. 52.

Radiograph of rat's kidneys. Bilateral pelvic stones and papillary calcification.

FIG. 53.

Rat kidneys opened. The two stones on the right side appeared to have originated from eroded papillae immediately to their right.

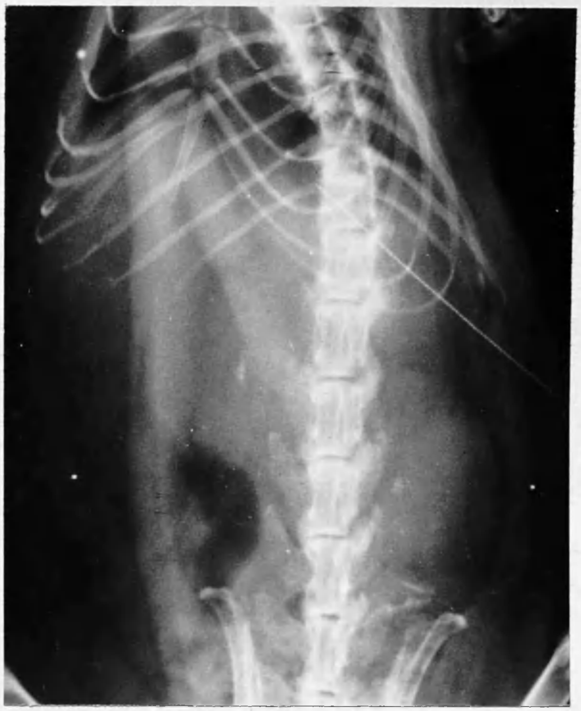


FIG. 54.

Bilateral calculi.

FIG. 55.

Left kidney from rat shown in x-ray above.
Stone in renal pelvis.

# TABLE XLIV.

## "Therapeutic" Diet. (Hammarsten)

### Diet 211 (Diet A)

| | |
|---|---|
| Ground rice | 666 parts |
| Casein | 150 " |
| Arachis oil | 37 " |
| Cod liver oil (Vitamins A & D) | 3 " |
| Wheat Germ (Vitamins B & E) | 30 " |
| Sugar | 10 " |
| Hip meal (Vitamin C) | 5 " |
| Dry brewer's Yeast (Vitamin B) | 30 " |
| Salt mixture 110 (q.v.) | 61.6 " |
| Sodium bicarbonate | 7 " |
| | 1,000 parts |

### Salt Mixture 110

| | |
|---|---|
| Sodium chloride | 83 grammes |
| Magnesium sulphate $MgSO_4, 7H_2O$ | 113 " |
| $K_2HPO_4$ | 100 " |
| Calcium lactate | 540 " |
| $Ca(H_2PO_4)_2 H_2O$ | 380 " |
| Ferr. citrate | 35 " |
| Magnesium oxide | 64 " |
| | 1,315 |

Diet B = Diet A + 10 c.c. milk and a few leaves of lettuce.

# FIGURES and TABLES

## relating to

# PART V

# TABLE XLV.

**Figures Relating to Bilateral Stone Expressed as Percentage of Total Series.**

| Case Groups | Total Cases (number) | Bilateral Cases (number) | Bilateral Cases expressed as percentage of Total Cases |
|---|---|---|---|
| Complete series | 1,114 | 149 | 13.4 |
| No operation series | 568 | 53 | 9.3 |
| Operation series | 546 | 96 | 17.6 |
| No Recurrence | 252 | 31 | 12.3 |
| Mild Recurrence (True) | 52 | 13 | 25.0 |
| Severe Recurrence (True) | 112 | 36 | 32.1 |
| Mild + Severe (True) | 164 | 49 | 30.0 |

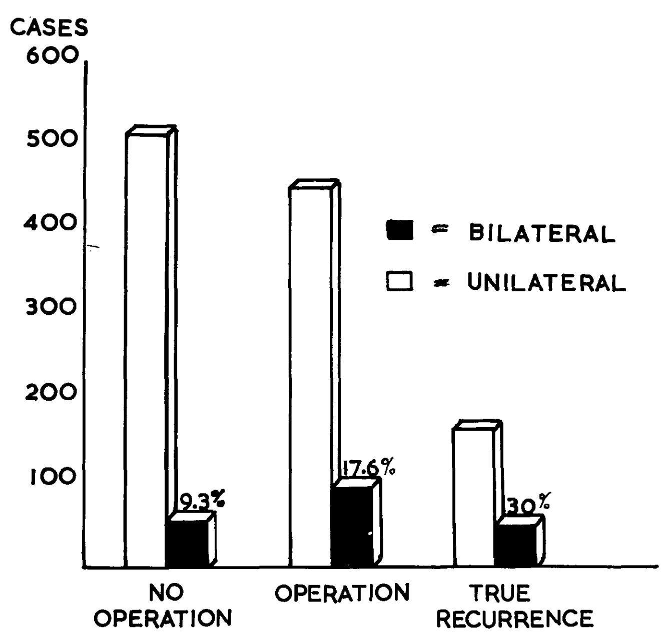



FIG. 56.

Bilateral and Unilateral Cases Contrasted.

# TABLE XLVI

## Sex Incidence and Length of Follow-up.

### Bilateral Stone.

**Sex (149 Cases)**

| | |
|---|---|
| Males | 98 |
| Females | 51 |
| Total | 149 |
| Male: Female | 2:1 |

**Length of Follow-up (149 Cases)**

| Duration in years | Number |
|---|---|
| 0 - 5 | 58 |
| 6 - 10 | 34 |
| 11 - 15 | 27 |
| 16 - 20 | 18 |
| 21 - 25 | 6 |
| 26 - 30 | 5 |
| over 30 | 1 |
| Total | 149 |

| Hence: | Number | per Cent. |
|---|---|---|
| Followed more than 5 years | 91 | 61.1 |
| " " " 10 " | 57 | 38.3 |
| " " " 15 " | 30 | 20.1 |
| " " " 20 " | 12 | 8.1 |

## TABLE XLVII.

Bilateral Stone
Simultaneity (149 Cases)

| Simultaneity | No Operation | Operation | Total Cases | Per cent. of All Cases |
|---|---|---|---|---|
| Simultaneously Bilateral at some time | 32 | 70 | 102 | 68.5 |
| Bilateral at Different times | 21 | 26 | 47 | 31.5 |
| Totals | 53 | 96 | 149 | 100.0 |

On first Examination - 91 (61.1%) were simultaneous.
On later " 102 (68.5%) " "

## TABLE XLVIII.

Urine Examination in Bilateral Stone Cases
Urine Analysis on First Examination - 77 Cases
i.e. Pre-operative

| Findings | No Op. | OPERATION | | | |
|---|---|---|---|---|---|
| | | No Recurr. | Recurr. | Total Operation | Percentage Recurr. |
| Sterile | 13 | 9 | 2 | 11 | 18.2 |
| Infected | 16 | 12 | 25 | 37 | 67.6 |
| Total | 29 | 21 | 27 | 48 | 56.2 |
| Percentage Infection | | 57.1 | 92.6 | 77.1 | |

# INITIAL RADIOLOGICAL FINDINGS.

## TABLE XLIX

(Size)

**Size (149 Cases)**

| Size | No Operation | Operation | Total Cases | Per cent. of Total |
|---|---|---|---|---|
| Bilateral (small or medium) unbranched | 42 | 47 | 89 | 60.0 |
| Unilateral unbranched, Unilateral branched. | 3 | 26 | 29 | 19.5 |
| Bilateral large or branched. | 8 | 23 | 31 | 20.5 |
| Totals | 53 | 96 | 149 | 100.0 |

## TABLE L.

(Site)

**Distribution of Bilateral Stone (149 Cases.)**

**Site (149 Cases)**

| Site | No Operation | Operation | Total Cases | Per cent. of Total |
|---|---|---|---|---|
| Both kidneys | 29 | 62 | 91 | 61.1 |
| One kidney opposite ureter | 15 | 14 | 29 | 19.5 |
| Both ureters | 7 | 6 | 13 | 8.7 |
| Both kidneys, one ureter | 1 | 14 | 15 | 10.1 |
| Both kidneys, both ureters | 1 | 0 | 1 | 0.6 |
| Totals | 53 | 96 | 149 | 100.0 |

## TABLE LI.

(Number and Renal Function)

**Number (78)**

| | | |
|---|---|---|
| 2 | - | 38 |
| 3 | - | 3 |
| more | - | 37 |
| | | 78 |

**Renal Function (76)**

| | |
|---|---|
| Normal | 18 |
| Fair | 33 |
| Poor | 25 |
| | 76 |

## TABLE LII.

### Bilateral Stone
### Treatment of 149 Cases.

| Treatment | Number of Cases | Comments | |
|---|---|---|---|
| No open operation | 53 | Expectant | 37 |
| | | Endoscopic procedures | 16 |
| | | | 53 |
| Open operation | 96 | Unilateral Surgery | 62 |
| | | Bilateral Surgery | 34 |
| | | | 96 |
| Total | 149 | | |

Primary Operations on Both Sides (34 Cases)

| | |
|---|---|
| Bilateral Renal | 26 |
| Bilateral Ureteric | 2 |
| Unilateral Renal, Unilateral Ureteric | 6 |
| Total | 34 |

---

## TABLE LIII.

### Bilateral Calculi

Operations Performed in 96 Cases (130 Primary; 35 Secondary) } 62 Unilateral Surgery
34 Bilateral Surgery

| Operation | Total | Primary | Secondary |
|---|---|---|---|
| Pyelolithotomy | 73 | 58 | 15 |
| Nephrolithotomy | 31 | 24 | 7 |
| Partial Nephrectomy | 7 | 6 | 1 |
| Nephrectomy | 22 | 17 | 5 |
| Ureterolithotomy | 32 | 25 | 7 |
| | 165 | 130 | 35 (in 25 patients) |

## TABLE LIV.

### Bilateral Stone.

### Post-Operative Mortality.

| Groups | Total Cases | Post-op deaths | Post-op deaths per Cent. |
|---|---|---|---|
| All Cases | 96 | 7 | 7.3 |
| Cases having Unilateral Surgery | 62 | 4 | 6.5 |
| Cases having Bilateral Surgery | 34 | 3 | 9.0 |
| Primary Operation Cases | 71 | 5 | 7.0 |
| Secondary Operation Cases | 25 | 2 | 8.0 |

## TABLE LV.

### Bilateral Stone

### Contralateral Recurrence in Series of 96 Cases.

| Operation Groups (according to first operation) | Total Cases | Contralateral Recurrence | | | |
|---|---|---|---|---|---|
| | | Mild | Severe | Total | Total per Cent. |
| Conservative Renal | 61 | 10 | 9 | 19 | 31.1 |
| Nephrectomy | 17 | 1 | 5 | 6 | 35.3 |
| Ureterolithotomy | 18 | 3 | 1 | 4 | 22.2 |
| Totals | 96 | 14 | 15 | 29 | 30.0 |

## TABLE LVI.

### Post-operative Progress of 23 Bilateral Branched Calculi

### Summary

| | | |
|---|---|---|
| Total | 23 | |
| Untraced | 3 | |
| Dead | 10 | (9 from urinary causes) |
| Alive | 10 | (none free from stone ) |

↓

Present state of these 10.

| | |
|---|---|
| Bilateral Recurrence | 5 |
| Unilateral Recurrence | 3 |
| Recurrence in Solitary Kidney | 2 |
| | 10 |

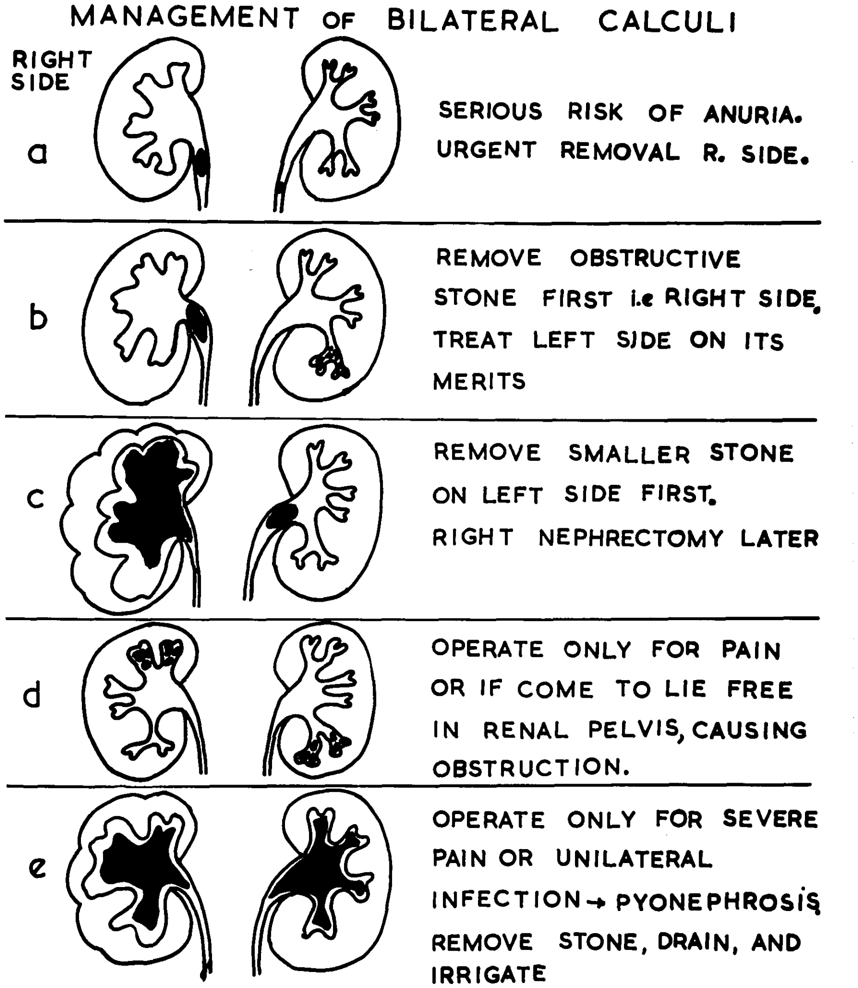



FIGURE 57.

Diagrammatic examples illustrating the policy of management of bilateral calculi.


FIG. 58 (a).

Right ureteric catheter in place.
Description in text.

FIG. 58 (b).

Plain film two weeks later. Little change.

Obstructive on One side, Non-Obstructive on the Other.


FIG. 59 (a)

Plain film upper urinary tract.
Early stag-horn calculus in right kidney.

FIG. 59 (b)

Plain film lower urinary tract.
Large recurrent left lower ureteric stones.

Bilateral Small Calyceal Non-Obstructive Calculi

FIG. 60

Plain film. Bilateral small widespread calyceal stones.

Bilateral Non-Obstructive Stones; Large on One Side, Small on the Other. Expectant Treatment.

FIG. 61.

Plain film. Stag-horn calculus in right kidney. Dendritic stone in left lower calyx.

Bilateral Non-Obstructive Calculi, Large on One Side, Small on the Other. Operation for Pyonephrosis.

FIG. 62 (a).

Plain film.

FIG. 62 (b).

Intravenous pyelogram. Non-functioning right kidney. Stone in left lower calyx. Left pyelogram normal.

Bilateral Non-Obstructive Calculi, Large on One side, Smaller on the other. Operation for Severe Pain.

FIG. 63 (a).

Plain film.
Stag-horn calculus in left kidney and dendritic stone in right upper calyx.

FIG. 63 (b).

Intravenous pyelogram. No function on left side. Normal pyelogram on right side.

Large Bilateral Non-Obstructive Calculi: No Operation.

FIG. 64.

Incidental finding during barium enema examination.

FIG. 65.

Massive "silent" recurrent stones.

Large Bilateral Non-Obstructive Calculi - Operation for Pain.

FIG. 66 (a).

Plain film 1949.
Bilateral stag-horn calculi.

FIG. 66 (b).

Plain film 1956.
Multiple recurrent stones in right kidney after operation for severe pain.

Large Bilateral Non-Obstructive Calculi + Operation for Pyonephrosis.

FIG. 67 (a)

Plain film.
Large bilateral calculi.

FIG. 67 (b)

Intravenous pyelogram.
No function on left.
Function only in upper half of right kidney.
Ureter filled with dye.

FIG. 67 (c)

Plain film after drainage of pyenephrosis and removal of stones from right kidney.

# FIGURES and TABLES

relating to

# PART VI

# TABLE LVIII

## LOW CALCIUM/LOW PHOSPHORUS DIET.

Ca. = 100 mg.
P. = 500 mg.

**FOODS ALLOWED, FREELY.**

Sugar, glucose.
Boiled sweets, e.g., barley sugar, fruit drops.

Lucozade.

**FOODS FORBIDDEN.**

Milk, cheese, fish, liver, kidney.
Brown bread, cereals.
Porridge, breakfast cereals.
Vegetables, fresh or tinned.
Cakes, biscuits, teabread.
Oranges, dried fruits.
Soups.

**DAILY RATIONS.**

7 oz. white bread.
2 oz. butter.
3 portions fruit, e.g., 1 apple, 1 pear, 1 banana.
½ oz. marmalade, 1 oz. jam.
1 lemon for use in tea, if desired.

**NOTES.**

(1) 3 water biscuits or 2 tea biscuits may be taken instead of 1 oz. bread.

(2) 1 Egg may be taken instead of 4 oz. bread.

**SPECIMEN DIET.**

| | |
|---|---|
| BREAKFAST. | One portion of fruit from ration.<br>2 oz. white bread with butter and marmalade from ration.<br>Tea with sugar and lemon. |
| MID-MORNING. | 1 oz. white bread or 2 tea biscuits with butter from ration. Tea with sugar and lemon. |
| DINNER. | 1½ oz. lean meat or poultry.<br>5 oz. potato.<br>One portion of fruit from ration, e.g., apple, cooked or raw.<br>1 oz. white bread with butter from ration. |
| AFTERNOON TEA. | 1½ oz. white bread with butter and jam from ration.<br>Tea with sugar and lemon. |
| TEA. | 1½ oz. lean meat or poultry.<br>3 oz. potato.<br>One portion of fruit from ration.<br>1½ oz. white bread with butter and jam from ration.<br>Tea with lemon and sugar. |

# TABLE LIX

Summary of Urinary Calcium Output Studies in 73 Cases (including Hyperparathyroidism) and of Sulkowitch Test in further 19 cases

| Test & Result | Total | Operation | | No Operation |
|---|---|---|---|---|
| | | No Recurrence | Recurrence | |
| **Urinary Calcium Output on low intake.** | | | | |
| Normal | 39 | 21 | 14 | 4 |
| Hypercalcuria | 34 | 13 | 20 | 1 |
| Totals | 73 | 34 | 34 | 5 |
| **Sulkowitch** | | | | |
| Normal or Low | 10 | 7 | 3 | 0 |
| Increased | 9 | 0 | 7 | 2 |
| Totals | 19 | 7 | 10 | 2 |
| **Combined figures** | | | | |
| Normal | 49 | 28 | 17 | 4 |
| Hypercalcuria | 43 | 13 | 27 | 3 |
| Totals | 92 | 41 | 44 | 7 |

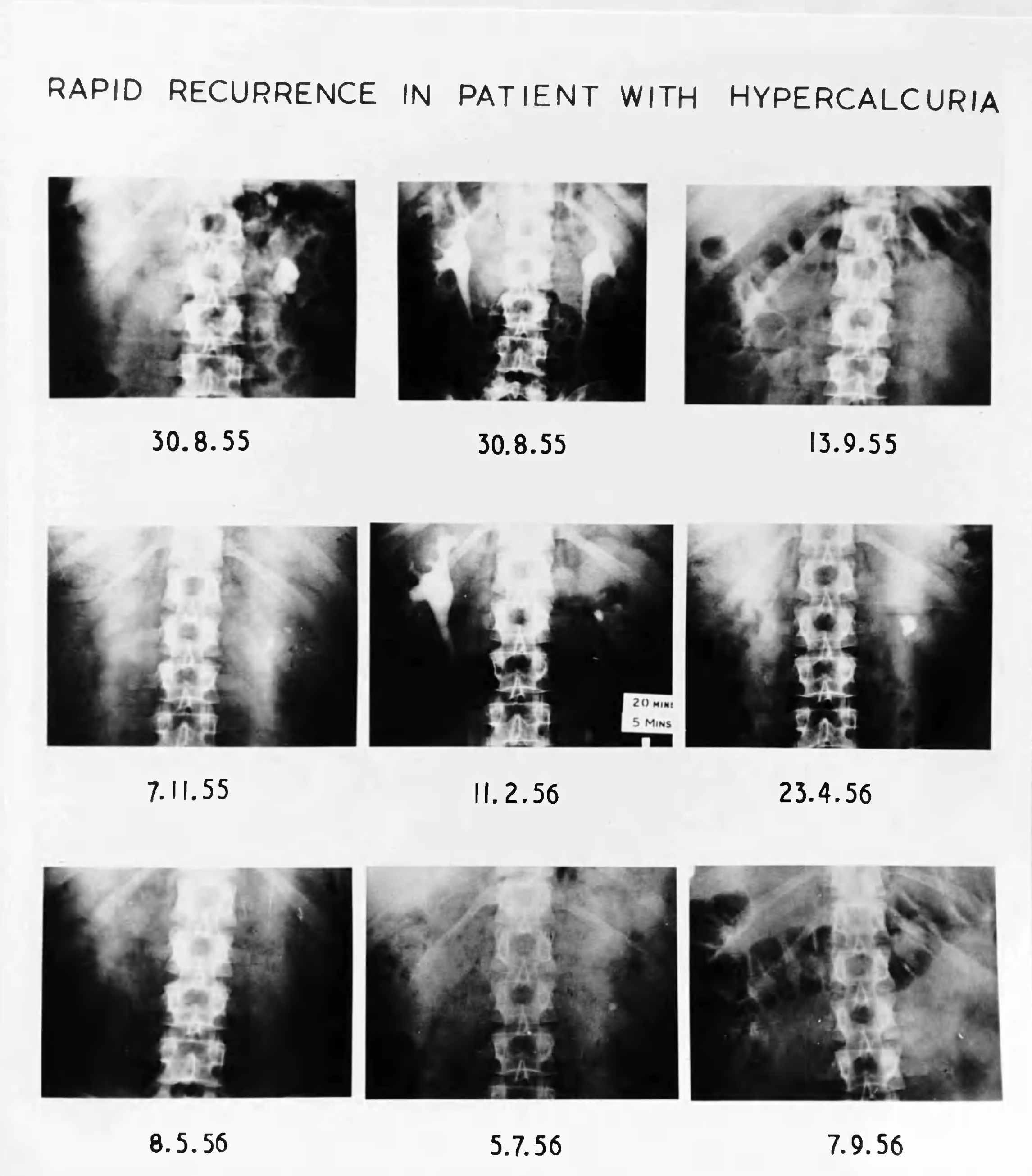

RAPID RECURRENCE IN PATIENT WITH HYPERCALCURIA
30.8.55
30.8.55
13.9.55
7.11.55
11.2.56
20 MINS
5 MINS
23.4.56
8.5.56
5.7.56
7.9.56

FIG. 68.

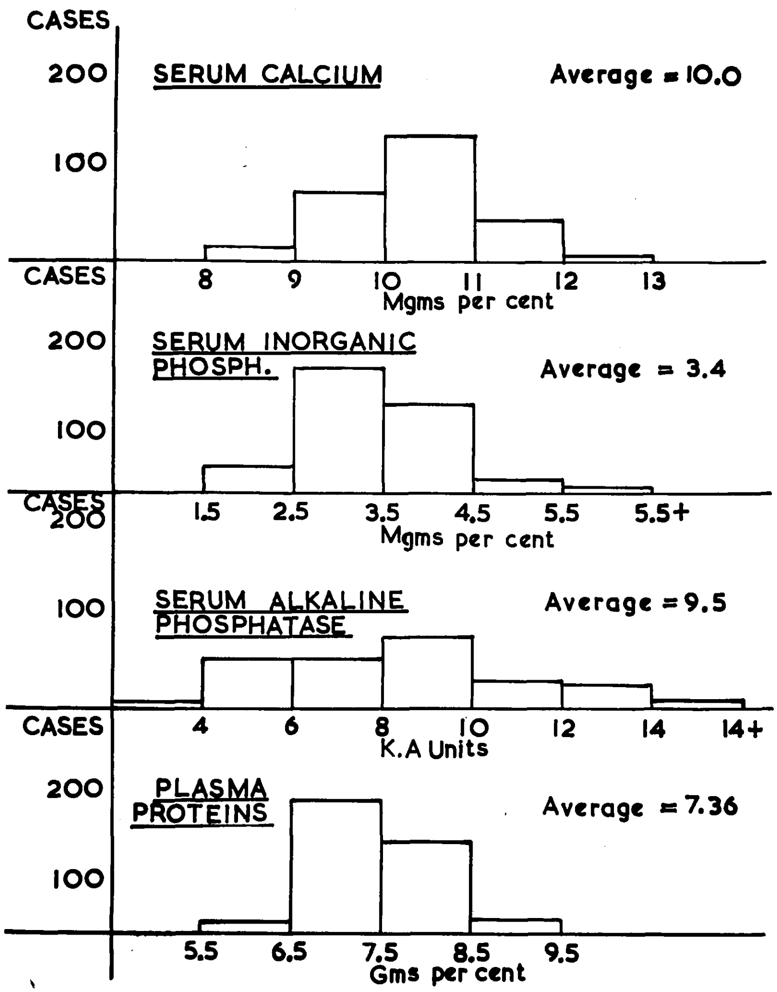



FIG. 69.

"Normal" range of Serum Calcium, Serum Inorganic Phosphorus, Serum Alkaline Phosphatase and Plasma Proteins.

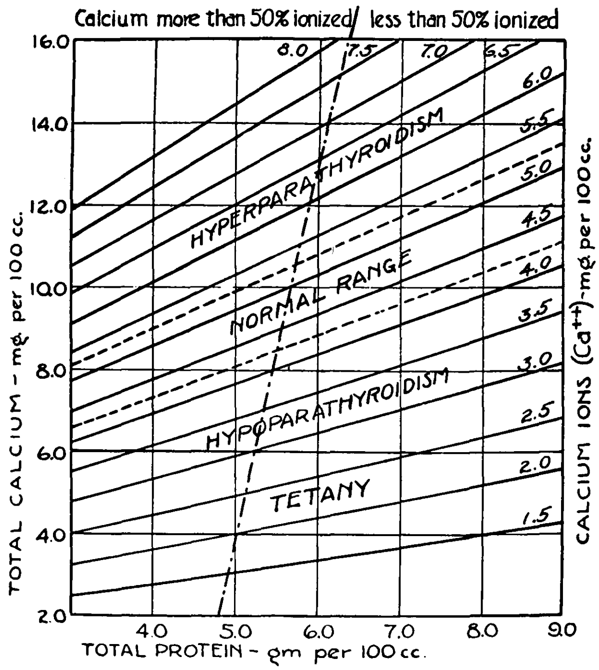



Fig. 70.

McLean and Hastings' Nomogram
Showing Relationship of Plasma Proteins
and Total Calcium to Ionized Calcium.

# TABLE LX

## Summary of Biochemical Findings

**Biochemical Summary : Urinary Calcium Output**

| | | |
|---|---|---|
| **Normal: Recurrence in** | $\frac{17}{45}$ | = 37.8 Per cent. |
| **Hypercalcuria: Recurrence in** | $\frac{27}{40}$ | = 67.5 Per cent. |

Blood Chemistry

| | No Recurr. | Recurr. | Total | Recurr. Per cent. |
|---|---|---|---|---|
| **Normal** | 88 | 56 | 144 | 39.0 |
| **Abnormal** | 13 | 20 | 33 | 60.6 |
| **Total** | 101 | 76 | 177 | 43.0 |
| **Percentage Abnormal** | 12.9 | 26.3 | 18.7 | |

**See Table for Stone Analysis.**

FIG. 71 (a)

Plain film 14.4.53 showing
several opacities in left renal area.

FIG. 71 (b)

Intravenous pyelogram 14.4.53 showing
left calculous hydronephrosis.

FIG. 71 (c)

Plain film, two years later.
No marked increase in size of calculi.

FIG. 71 (d)

Intravenous pyelogram.
Slight increase in left hydronephrosis.

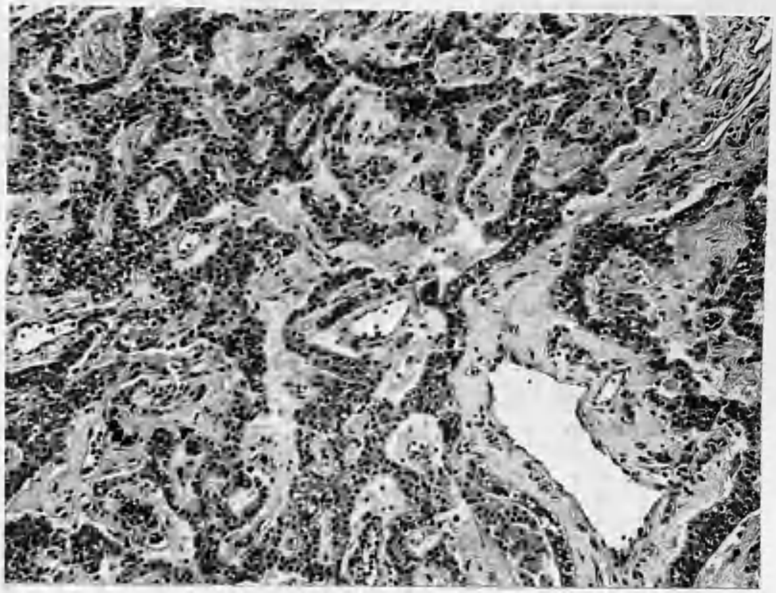


FIG. 72 (a)

Parathyroid adenoma composed of chief cells with reticular arrangement. Many cells contain clear vacuoles.
Haemalum and Eosin x 130 (Blue-green filter)

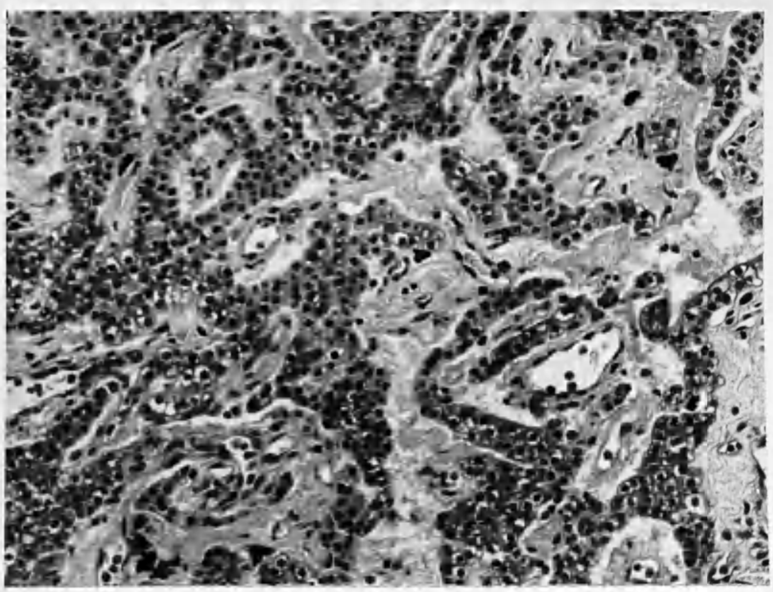


FIG. 72 (b)

High power of same show cellular detail vacuolation is distinct.
Haemalum and Eosin x 220 (Blue-green filter)

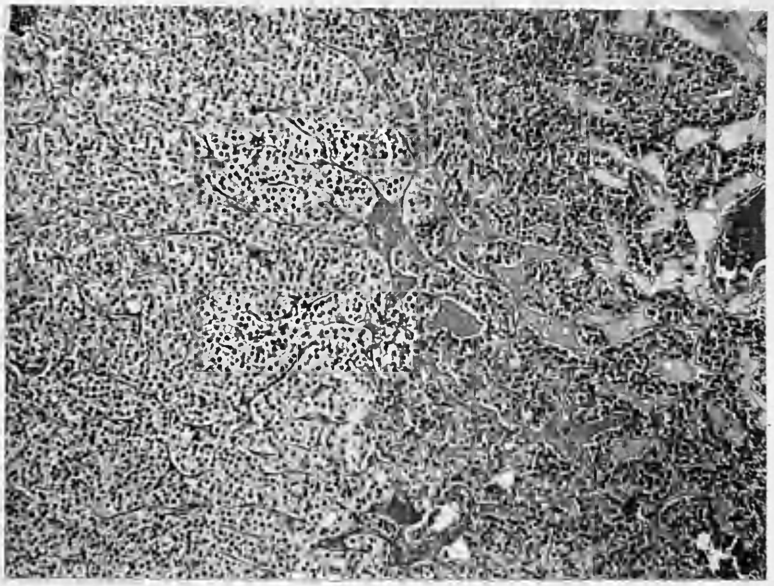


FIG. 73.

Parathyroid Adenoma showing area of Clear Cells on Left (above), and Denser Chief Cells on Right (below). The Clear Cells are arranged in Irregular Columns, the Chief Cells in Poorly Differentiated Alveoli which contain Colloid Secretion.
Haemalum and Eosin x 130
(Blue-green Filter)

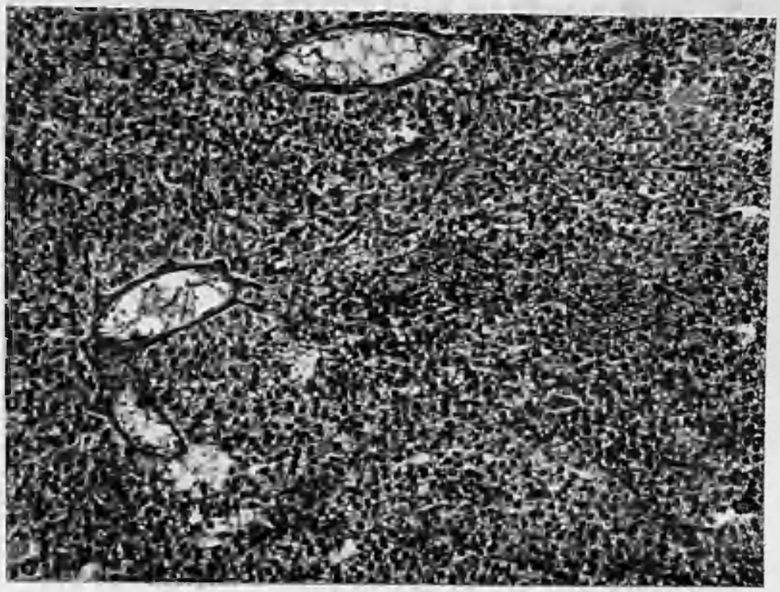


FIG. 74 (a)

Parathyroid adenoma showing highly cellular diffuse tumour composed of chief cells.
Haemalum and Eosin x 220 (Blue-green filter)

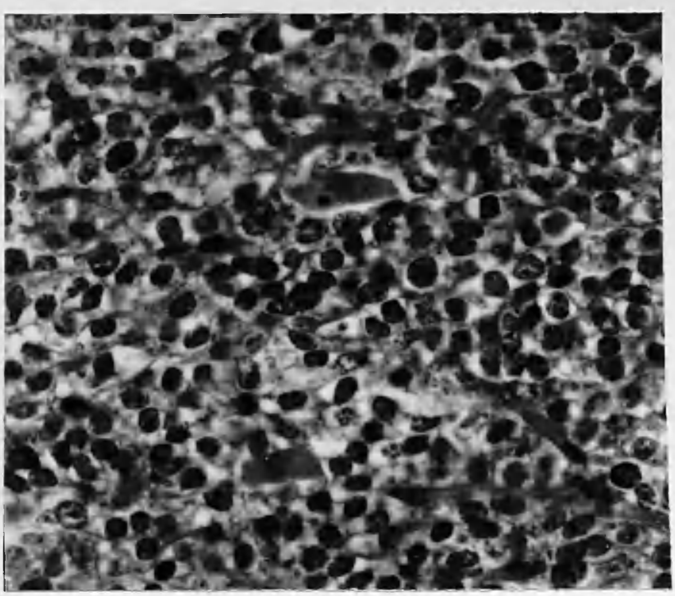


FIG. 74 (b)

Higher magnification of the same showing two large non-granular oxyphil cells.
Haemalum and Eosin x 650 (Blue-green filter)

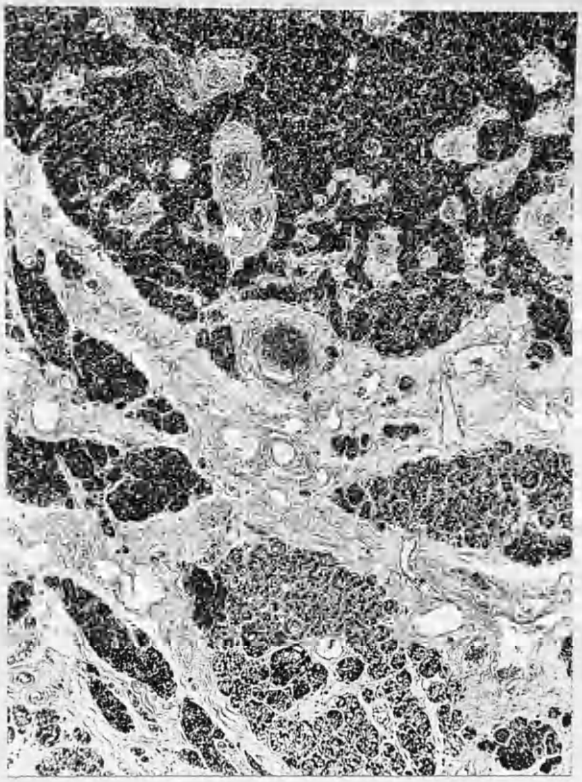


FIG. 75 (a)

Low power view showing variable structure.
Above is an area of small dark chief cells having a reticular arrangement. There is an alveolar area below composed mostly of clear cells with a few dark chief cells.
Haemalum and Eosin x 650 (Blue-green filter)

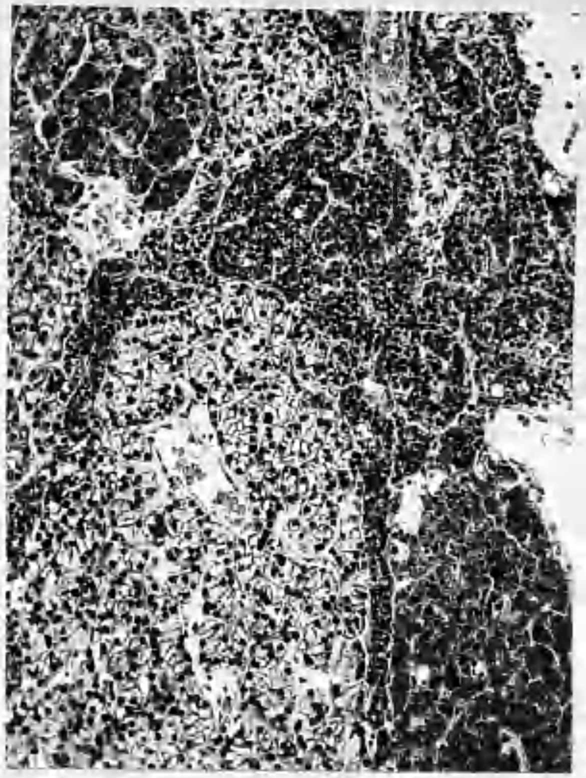


FIG. 75 (b)

Higher magnification to show:

(1) Large clear cells
(2) Small dark chief cells and
(3) Large dark oxyntic cells
in top left hand corner. The nuclei are of much the same size and configuration in all the cells.

Haemalum and Eosin x 170 (Blue-green filter)

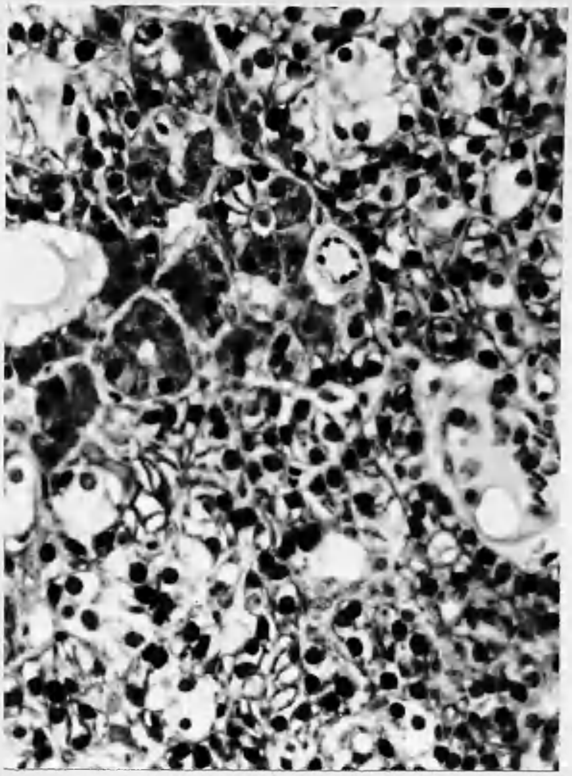


FIG. 75 (c)

High power view to show large clear
cells and large dark oxyntic
cells with granular cytoplasm.
Haemalum and Eosin x 170 (Blue-green filter)

FIG. 76.

Operation photograph
showing parathyroid adenoma discussed in
Fig. 75.

## LIST of the TABLES in the APPENDIX

The Tables are arranged in the sequence encountered in the text. For convenience they are divided according to the six parts of the thesis. Arabic numerals have been used to avoid confusion with the short photographed Tables.

### PART I.

#### General Incidence, Diagnostic Findings and Aetiological Factors.



* * * * * * *

## PART II.

## The Results of Conservative Management Studies of Some Aspects of the Natural History



* * * * * * *

# PART III.

## The Late Results of Operative Treatment

## With Special Reference to:-

## Post-Operative Recurrence.

## PART III. (Continued).



* * * * * * *

## PART IV.

### The Prevention of Post-Operative Recurrence



* * * * * * *

## PART V.

## Bilateral Upper Urinary Tract Stone.



* * * * * * *

## PART VI.

## Biochemical Studies



* * * * * * *

TABLE I.

## LENGTH OF FOLLOW-UP - 974 CASES

| Number of years followed | No Operation | Operation | Total |
|---|---|---|---|
| 0-1 | 14 | 0 | 14 |
| 1-2 | 75 | 57 | 132 |
| 2-3 | 44 | 30 | 74 |
| 3-4 | 44 | 25 | 69 |
| 4-5 | 35 | 25 | 60 |
| 5-6 | 46 | 32 | 78 |
| 6-7 | 38 | 36 | 74 |
| 7-8 | 29 | 26 | 55 |
| 8-9 | 19 | 19 | 38 |
| 9-10 | 20 | 20 | 40 |
| 10-11 | 20 | 20 | 40 |
| 11-12 | 16 | 19 | 35 |
| 12-13 | 15 | 17 | 32 |
| 13-14 | 9 | 11 | 20 |
| 14-15 | 9 | 20 | 29 |
| 15-16 | 7 | 15 | 22 |
| 16-17 | 8 | 15 | 23 |
| 17-18 | 11 | 12 | 23 |
| 18-19 | 10 | 8 | 18 |
| 19-20 | 12 | 17 | 29 |
| 20-21 | 5 | 9 | 14 |
| 21-22 | 2 | 5 | 7 |
| 22-23 | 0 | 5 | 5 |
| 23-24 | 0 | 1 | 1 |
| 24-25 | 0 | 3 | 3 |
| 25-26 | 1 | 6 | 7 |
| 26-27 | 1 | 3 | 4 |
| 27-28 | 0 | 2 | 2 |
| 28-29 | 1 | 4 | 5 |
| 29-30 | 1 | 9 | 10 |
| Over 30 | 2 | 9 | 11 |
| Total | 494 | 480 | 974 |

## ESTIMATED AGE AT ONSET OF SYMPTOMS - 1007 CASES

| Age in Years | MALE | | | FEMALE | | | Total Male and Female |
|---|---|---|---|---|---|---|---|
| | No operation | Operation | Total Male | No operation | Operation | Total Female | |
| 0-5 | 1 | 2 | 3 | 0 | 0 | 0 | 3 |
| 6-10 | 2 | 2 | 4 | 1 | 6 | 7 | 11 |
| 11-15 | 0 | 9 | 9 | 0 | 5 | 5 | 14 |
| 16-20 | 6 | 12 | 18 | 4 | 8 | 12 | 30 |
| 21-25 | 20 | 25 | 45 | 12 | 20 | 32 | 77 |
| 26-30 | 46 | 40 | 86 | 13 | 26 | 39 | 125 |
| 31-35 | 47 | 41 | 88 | 19 | 29 | 48 | 136 |
| 36-40 | 57 | 36 | 93 | 20 | 26 | 46 | 139 |
| 41-45 | 74 | 30 | 104 | 11 | 27 | 38 | 142 |
| 46-50 | 47 | 35 | 82 | 12 | 26 | 38 | 120 |
| 51-55 | 36 | 24 | 60 | 11 | 18 | 29 | 89 |
| 56-60 | 25 | 8 | 33 | 11 | 16 | 27 | 60 |
| 61-65 | 16 | 9 | 25 | 5 | 6 | 11 | 36 |
| 66-70 | 7 | 3 | 10 | 4 | 1 | 5 | 15 |
| 71-75 | 3 | 2 | 5 | 2 | 1 | 3 | 8 |
| 76-80 | 1 | 0 | 1 | 1 | 0 | 1 | 2 |
| | 388 | 278 | 666 | 126 | 215 | 341 | 1007 |
| Average Age | 41.5 | 37.0 | 39.4 | 40.6 | 37.6 | 38.7 | 39.1 |

TABLE 3.

AGE AT FIRST OPERATION (OR AT DIAGNOSIS WHEN NO OPERATIVE TREATMENT) - 1007 CASES

| Age in Years | MALE | | | FEMALE | | | Total Male and Female |
|---|---|---|---|---|---|---|---|
| | No operation (Age at diagnosis) | Operation | Total Male Cases | No operation (Age at diagnosis) | Operation | Total Female Cases | |
| 0-5 | 0 | 1 | 1 | 0 | 0 | 0 | 1 |
| 6-10 | 1 | 1 | 2 | 1 | 2 | 3 | 5 |
| 11-15 | 0 | 4 | 4 | 0 | 7 | 7 | 11 |
| 16-20 | 5 | 10 | 15 | 5 | 3 | 8 | 23 |
| 21-25 | 11 | 15 | 26 | 8 | 13 | 21 | 47 |
| 26-30 | 41 | 39 | 80 | 9 | 22 | 31 | 111 |
| 31-35 | 37 | 41 | 78 | 18 | 31 | 49 | 127 |
| 36-40 | 61 | 30 | 91 | 21 | 23 | 44 | 135 |
| 41-45 | 73 | 31 | 104 | 12 | 30 | 42 | 146 |
| 46-50 | 54 | 41 | 95 | 12 | 24 | 36 | 131 |
| 51-55 | 43 | 32 | 75 | 15 | 26 | 41 | 116 |
| 56-60 | 30 | 17 | 47 | 12 | 17 | 29 | 76 |
| 61-65 | 17 | 11 | 28 | 5 | 11 | 16 | 44 |
| 66-70 | 8 | 3 | 11 | 5 | 4 | 9 | 20 |
| 71-75 | 5 | 2 | 7 | 2 | 2 | 4 | 11 |
| 76-80 | 2 | 0 | 2 | 1 | 0 | 1 | 3 |
| | 388 | 278 | 666 | 126 | 215 | 341 | 1007 |
| Average Age | 42.6 | 37.0 | 41.8 | 43.5 | 40.8 | 41.1 | 41.6 |

TABLE 4.

INCIDENCE OF SYMPTOMS IN 1061 CASES AT PRIMARY EXAMINATION

| Symptom or Sign | No Operation | Operation | Total |
|---|---|---|---|
| Painless | 39 | 50 | 89 |
| Colic | 386 | 231 | 617 |
| Lumbar pain | 137 | 218 | 355 |
| Haematuria | 184 | 196 | 380 |
| Passed one stone | 101 | 48 | 149 |
| Passed many stones | 54 | 29 | 83 |
| Pyuria | 86 | 74 | 160 |
| Frequency | 53 | 60 | 113 |
| Painful micturition | 114 | 66 | 180 |
| Sickness | 158 | 99 | 257 |
| Loss of weight | 32 | 48 | 80 |
| Loss of energy | 82 | 84 | 166 |
| Poor general health | 52 | 51 | 103 |
| Other | 2 | 7 | 9 |

TABLE 5.

ESTIMATED DURATION OF SYMPTOMS IN 641 CASES

| Duration of Symptoms | No Operation | Operation | Total |
|---|---|---|---|
| Less than 2 weeks | 98 | 43 | 141 |
| 2 weeks to 6 months | 34 | 31 | 65 |
| 6 months to 1 year | 21 | 35 | 56 |
| 1-2 years | 16 | 52 | 68 |
| 2-3 | 16 | 46 | 62 |
| 3-4 | 15 | 23 | 38 |
| 4-5 | 13 | 17 | 30 |
| 5-6 | 11 | 20 | 31 |
| 6-7 | 7 | 8 | 15 |
| 7-8 | 4 | 7 | 11 |
| 8-9 | 5 | 9 | 14 |
| 9-10 | 6 | 6 | 12 |
| 10-11 | 11 | 9 | 20 |
| 11-12 | 5 | 4 | 9 |
| 12-13 | 3 | 8 | 11 |
| 13-14 | 1 | 5 | 6 |
| 14-15 | 5 | 4 | 9 |
| 15-16 | 2 | 7 | 9 |
| 16-17 | 1 | 3 | 4 |
| 17-18 | 1 | 2 | 3 |
| 18-19 | 0 | 2 | 2 |
| 19-20 | 0 | 2 | 2 |
| 20-21 | 2 | 5 | 7 |
| 21-22 | 0 | 1 | 1 |
| 22-23 | 1 | 0 | 1 |
| 23-24 | 1 | 0 | 1 |
| 24-25 | 1 | 0 | 1 |
| 25-26 | 1 | 1 | 2 |
| 26-27 | 1 | 0 | 1 |
| 27-28 | 1 | 1 | 2 |
| 28-29 | 1 | 0 | 1 |
| 29-30 | 0 | 0 | 0 |
| More than 30 years | 4 | 2 | 6 |
| | 288 | 353 | 641 |

# TABLE 6.

## URINE EXAMINATION WHEN FIRST SEEN

## 665 CASES

| Bacteriology & Cytology. | Total | RENAL | | | URETERIC | | | BILATERAL | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Total Renal | OP. | No OP. | Total Uret. | OP. | No OP. | Total Bilat. | OP. | No OP. |
| Sterile | 334 | 143 | 76 | 67 | 167 | 36 | 131 | 24 | 11 | 13 |
| Sterile pyuria | 173 | 83 | 61 | 22 | 66 | 13 | 53 | 24 | 16 | 8 |
| Organisms + W.B.C. | 158 | 87 | 67 | 20 | 42 | 17 | 25 | 29 | 21 | 8 |
| Total | 665 | 313 | 204 | 109 | 275 | 66 | 209 | 77 | 48 | 29 |

### Organisms (158 cases).

| | |
|---|---|
| B.Coli. | 93 |
| B.Coli + strep.faec. | 11 |
| B.Coli + proteus. | 4 |
| B.Coli + staph.albus. | 2 |
| B.Coli + staph.aureus. | 2 |
| B.Coli + pyocyanea. | 1 |
| Staph.aureus. | 7 |
| Staph.aureus + proteus. | 1 |
| Strep.faecalis. | 15 |
| Strep.faecalis + pyocyanea. | 1 |
| Ps.pyocyanea. | 2 |
| Proteus vulgaris. | 13 |
| Staph.albus. | 6 |
| Total | 158 |

### Crystals.

| | |
|---|---|
| Oxalates | 35 |
| Oxalates + urates | 2 |
| Urates | 8 |
| Phosphates | 22 |
| Cystine | 1 |
| Total | 68 |

### Reaction.

| | |
|---|---|
| Acid | 270 |
| Alkaline | 125 |
| Amphoteric | 86 |
| Total | 481 |

TABLE 7.

## URINE EXAMINATION AT FIRST VISIT

665 CASES

| Groups | Total | Sterile | Infected | Per cent Infected |
|---|---|---|---|---|
| 1. **Renal.** | | | | |
| Total cases | 313 | 143 | 170 | |
| No operation | 109 | 67 | 42 | 38.5 |
| Operation | 204 | 76 | 128 | |
| Recurrence | 73 | 21 | 52 | 71.2 |
| No recurrence | 131 | 55 | 76 | 58.0 |
| Percentage recurrence | 35.8 | 27.6 | 40.6 | |
| 2. **Ureteric.** | | | | |
| Total cases | 275 | 167 | 108 | |
| No operation | 209 | 131 | 78 | 37.3 |
| Operation | 66 | 36 | 30 | |
| Recurrence | 13 | 2 | 11 | 84.6 |
| No recurrence | 53 | 34 | 19 | 36.0 |
| Percentage recurrence | 20.0 | 5.5 | 36.7 | |
| 3. **Bilateral.** | | | | |
| Total cases | 77 | 24 | 53 | |
| No Operation | 29 | 13 | 16 | 55.2 |
| Operation | 48 | 11 | 37 | |
| Recurrence | 27 | 2 | 25 | 92.6 |
| No recurrence | 21 | 9 | 12 | 57.0 |
| Percentage recurrence | 56.3 | 18.2 | 67.6 | |
| 4. **Total cases.** | | | | |
| Total cases | 665 | 334 | 331 | |
| No operation | 347 | 211 | 136 | 39.2 |
| Operation | 318 | 123 | 195 | |
| Recurrence | 113 | 25 | 88 | 78.0 |
| No recurrence | 205 | 98 | 107 | 52.2 |
| Percentage recurrence | 35.5 | 20.3 | 45.1 | |

TABLE 8.

**RADIOLOGICAL FINDINGS WHEN FIRST SEEN**

**TOTAL SERIES (1027 CASES)**

| Site of Stones | Totals | Number of Stones | | | | Size of Stones | | | Renal Function | | | Total Renal Funct. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | More | Small | Med. | Large | Good | Fair | Poor | |
| 1. Renal | | | | | | | | | | | | |
| Indefinite | 108 | 91 | 4 | 3 | 10 | 22 | 58 | 28 | 18 | 18 | 7 | 43 |
| Pelvic | 145 | 127 | 10 | 3 | 5 | 2 | 109 | 34 | 31 | 84 | 20 | 135 |
| Calyceal | 99 | 82 | 6 | 3 | 8 | 44 | 48 | 7 | 62 | 31 | 1 | 94 |
| Pelvic + Calyceal | 52 | 13 | 7 | 4 | 28 | 5 | 29 | 18 | 10 | 26 | 16 | 52 |
| Staghorn | 65 | 65 | 0 | 0 | 0 | 0 | 0 | 65 | 0 | 4 | 60 | 64 |
| Total Renal | 469 | 378 | 27 | 13 | 51 | 73 | 244 | 152 | 121 | 163 | 104 | 388 |
| 2. Ureteric | | | | | | | | | | | | |
| Indefinite | 39 | 39 | 0 | 0 | 0 | 28 | 10 | 1 | 29 | 3 | 2 | 34 |
| Upper | 51 | 48 | 0 | 3 | 0 | 10 | 41 | 0 | 15 | 30 | 4 | 49 |
| Middle | 46 | 42 | 4 | 0 | 0 | 15 | 31 | 0 | 17 | 27 | 2 | 46 |
| Lower | 330 | 317 | 9 | 2 | 2 | 211 | 111 | 8 | 196 | 106 | 23 | 325 |
| Total Ureteric | 466 | 446 | 13 | 5 | 2 | 264 | 193 | 9 | 257 | 166 | 31 | 454 |
| 3. Simultaneous Renal + Ureteric | 14 | 6 | 3 | 1 | 4 | 5 | 7 | 2 | 3 | 5 | 6 | 14 |
| Total Unilateral | 949 | 830 | 43 | 19 | 57 | 342 | 444 | 163 | 381 | 334 | 141 | 856 |
| 4. Bilateral | | | | | | | | | | | | |
| Renal | 31 | 0 | 11 | 1 | 19 | 4 | 15 | 12 | ,9 | 13 | 7 | 29 |
| Ureteric | 6 | 0 | 6 | 0 | 0 | 4 | 2 | 0 | 3 | 3 | 0 | 6 |
| Renal & Ureteric | 28 | 0 | 15 | 2 | 11 | 7 | 19 | 2 | 6 | 17 | 5 | 28 |
| Staghorn | 13 | 0 | 6 | 0 | 7 | 0 | 0 | 13 | 0 | 0 | 13 | 13 |
| Total Bilateral | 78 | 0 | 38 | 3 | 37 | 15 | 36 | 27 | 18 | 33 | 25 | 76 |
| GRAND TOTAL | 1027 | 830 | 81 | 22 | 94 | 357 | 480 | 190 | 399 | 367 | 166 | 932 |

TABLE 9.

## RADIOLOGICAL FINDINGS WHEN FIRST SEEN

## 481 "NO OPERATION" CASES

| Site of Stones | Totals | Number of Stones | | | | Size of Stones | | | Renal Function | | | Total Renal Funct. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | More | Small | Med. | Large | Good | Fair | Poor | |
| 1. Renal | | | | | | | | | | | | |
| Indefinite | 28 | 22 | 2 | 1 | 3 | 19 | 8 | 1 | 18 | 6 | 4 | 28 |
| Pelvic | 14 | 12 | 2 | 0 | 0 | 2 | 9 | 3 | 5 | 7 | 2 | 14 |
| Calyceal | 49 | 40 | 4 | 1 | 4 | 42 | 7 | 0 | 40 | 8 | 1 | 49 |
| Pelvic + Calyceal | 5 | 1 | 0 | 1 | 3 | 5 | 0 | 0 | 5 | 0 | 0 | 5 |
| Staghorn | 13 | 13 | 0 | 0 | 0 | 0 | 0 | 13 | 0 | 1 | 12 | 13 |
| Total Renal | 109 | 88 | 8 | 3 | 10 | 68 | 24 | 17 | 68 | 22 | 19 | 109 |
| 2. Ureteric | | | | | | | | | | | | |
| Indefinite | 32 | 32 | 0 | 0 | 0 | 28 | 4 | 0 | 27 | 3 | 2 | 32 |
| Upper | 16 | 14 | 0 | 2 | 0 | 9 | 7 | 0 | 8 | 8 | 0 | 16 |
| Middle | 29 | 27 | 2 | 0 | 0 | 14 | 15 | 0 | 15 | 14 | 0 | 29 |
| Lower | 260 | 254 | 6 | 0 | 0 | 210 | 48 | 2 | 195 | 51 | 14 | 260 |
| Total Ureteric | 337 | 327 | 8 | 2 | 0 | 261 | 74 | 2 | 245 | 76 | 16 | 337 |
| 3. Simultaneous Renal & Ureteric | 7 | 0 | 5 | 0 | 2 | 5 | 2 | 0 | 3 | 2 | 2 | 7 |
| Total Unilateral | 453 | 415 | 21 | 5 | 12 | 334 | 100 | 19 | 316 | 100 | 37 | 453 |
| 4. Bilateral | | | | | | | | | | | | |
| Indefinite | 9 | 0 | 2 | 0 | 7 | 6 | 1 | 2 | 5 | 1 | 3 | 9 |
| Renal | 3 | 0 | 0 | 0 | 3 | 1 | 0 | 2 | 1 | 0 | 2 | 3 |
| Ureteric | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Renal & Ureteric | 11 | 0 | 3 | 0 | 8 | 5 | 6 | 0 | 5 | 5 | 1 | 11 |
| Staghorn | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 5 | 0 | 0 | 5 | 5 |
| Total Bilateral | 28 | 0 | 5 | 0 | 23 | 12 | 7 | 9 | 11 | 6 | 11 | 28 |
| GRAND TOTAL | 481 | 415 | 26 | 5 | 35 | 346 | 107 | 28 | 327 | 106 | 48 | 481 |

TABLE 10. **RADIOLOGICAL FINDINGS WHEN FIRST SEEN**

**OPERATION CASES (546)**

| Site of Stones | Totals | Number of Stones | | | | Size of Stones | | | Renal Function | | | Total Renal Funct. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | More | Small | Med. | Large | Good | Fair | Poor | |
| 1. Renal | | | | | | | | | | | | |
| Indefinite | 80 | 69 | 2 | 2 | 7 | 3 | 50 | 27 | 0 | 12 | 3 | 15 |
| Pelvic | 131 | 115 | 8 | 3 | 5 | 0 | 100 | 31 | 26 | 77 | 18 | 121 |
| Calyceal | 50 | 42 | 2 | 2 | 4 | 2 | 41 | 7 | 22 | 23 | 0 | 45 |
| Pelvic + Calyceal | 47 | 12 | 7 | 3 | 25 | 0 | 29 | 18 | 5 | 26 | 16 | 47 |
| Staghorn | 52 | 52 | 0 | 0 | 0 | 0 | 0 | 52 | 0 | 3 | 48 | 51 |
| Total Renal | 360 | 290 | 19 | 10 | 41 | 5 | 220 | 135 | 53 | 141 | 85 | 279 |
| 2. Ureteric | | | | | | | | | | | | |
| Indefinite | 7 | 7 | 0 | 0 | 0 | 0 | 6 | 1 | 2 | 0 | 0 | 2 |
| Upper | 35 | 34 | 0 | 1 | 0 | 1 | 34 | 0 | 7 | 22 | 4 | 33 |
| Middle | 17 | 15 | 2 | 0 | 0 | 1 | 16 | 0 | 2 | 13 | 2 | 17 |
| Lower | 70 | 63 | 3 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total Ureteric | 129 | 119 | 5 | 3 | 2 | 3 | 119 | 7 | 12 | 90 | 15 | 117 |
| 3. Simultaneous Renal + Ureteric | 7 | 0 | 4 | 1 | 2 | 0 | 5 | 2 | 0 | 3 | 4 | 7 |
| Total Unilateral | 496 | 409 | 28 | 14 | 45 | 8 | 344 | 144 | 65 | 234 | 104 | 403 |
| 4. Bilateral | | | | | | | | | | | | |
| Indefinite | 3 | 0 | 2 | 0 | 1 | 0 | 0 | 3 | 0 | 0 | 1 | 1 |
| Renal | 23 | 0 | 9 | 1 | 13 | 1 | 15 | 7 | 6 | 12 | 5 | 23 |
| Ureteric | 4 | 0 | 4 | 0 | 0 | 2 | 2 | 0 | 1 | 3 | 0 | 4 |
| Renal & Ureteric | 14 | 0 | 12 | 2 | 0 | 0 | 12 | 2 | 0 | 12 | 2 | 14 |
| Staghorn | 6 | 0 | 6 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 6 | 6 |
| Total Bilateral | 50 | 0 | 33 | 3 | 14 | 3 | 29 | 18 | 7 | 27 | 14 | 48 |
| Total Unilateral & Bilateral | 546 | 409 | 61 | 17 | 59 | 11 | 373 | 162 | 72 | 261 | 118 | 451 |

TABLE 11.

## POSSIBLE AETIOLOGICAL FACTORS IN STONE-FORMATION

(Excluding Biochemical & Urinary Infection)

| Aetiological Factor | Number Affected | Possible Total | Incidence per cent | Method by which determined |
|---|---|---|---|---|
| 1. Vitamin A lack. (Poor night vision.) | 87 | 517 | 17.0 | History and questionnaire. |
| 2. Peptic ulcer. | 24 | 335 | 7.1 | History. |
| 3. Prolonged recumbency. | 39 | 891 | 4.4 | History. |
| 4. Pulmonary tuberculosis. | 14 | 891 | 1.6 | History and examination. |
| 5. Sweating - poor intake. | 35 | 335 | 10.5 | History. |
| 6. Family history. | 20 | 335 | 5.9 | History. |
| 7. Pyelitis. | 36 | 778 | 4.6 | Interview. |
| 8. Pyelitis in parous. | 36 | 139 | 26.0 | Interview. |
| 9. Previous "nephritis". | 21 | 778 | 2.7 | Interview. |
| 10. Renal trauma. | 8 | 778 | 1.0 | Interview. |
| 11. Congenital anomaly.<br>6 Horseshoe kidney.<br>1 Pelvic ectopia. | 7 | 301 | 2.3 | Intravenous pyelography. |
| 12. Kidney or ureteric stasis. | 10 | 301 | 3.3 | Intravenous pyelography. |
| 13. Bladder neck obstruction. | 7 | 301 | 2.3 | Intravenous pyelography. |
| 14. Others.<br>1 Bilharzia.<br>1 Cystinuria.<br>2 Tumour.<br>3 Cns disease. | 7 | | | |

TABLE 12.

STUDY OF 521 STONE - PASSERS

(415 in "No Operation" Series and 106 in "Operation" Series)

| Number of years Followed. | Total | Number of stones passed 1 | 2 | 3 | 4 | 5 | 6 | 7 | More than 7 |
|---|---|---|---|---|---|---|---|---|---|
| 0 - 1 | 25 | 24 | | | 1 | | | | |
| 1 - 2 | 48 | 38 | 5 | 1 | 1 | | | | 3 |
| 2 - 3 | 45 | 35 | 5 | | 1 | | | | 4 |
| 3 - 4 | 36 | 24 | 4 | 4 | | | | | 4 |
| 4 - 5 | 31 | 21 | 4 | 2 | 2 | | | | 2 |
| 5 - 6 | 42 | 30 | 4 | 2 | | 1 | 1 | | 4 |
| 6 - 7 | 35 | 26 | 2 | 3 | | | 1 | | 3 |
| 7 - 8 | 31 | 22 | 3 | 1 | | | | | 5 |
| 8 - 9 | 23 | 15 | 2 | | | 1 | | | 5 |
| 9 - 10 | 18 | 13 | 3 | | | 1 | | | 1 |
| 10 - 11 | 28 | 18 | 2 | 2 | | 1 | | | 5 |
| 11 - 12 | 20 | 17 | 1 | | | | | | 2 |
| 12 - 13 | 15 | 8 | 3 | 1 | 1 | | | | 2 |
| 13 - 14 | 11 | 7 | 1 | 2 | | | | | 1 |
| 14 - 15 | 12 | 10 | | 1 | | 1 | | | |
| 15 - 16 | 12 | 7 | 2 | 2 | | | | | 1 |
| 16 - 17 | 8 | 5 | 2 | | | | | | 1 |
| 17 - 18 | 12 | 9 | 3 | | | | | | |
| 18 - 19 | 11 | 6 | 2 | 1 | | | | | 2 |
| 19 - 20 | 19 | 15 | 2 | | | | | 1 | 1 |
| 20 - 21 | 12 | 7 | 1 | | | | | | 4 |
| 21 - 22 | 3 | 2 | 1 | | | | | | |
| 22 - 23 | 3 | 1 | 1 | | | | | | 1 |
| 23 - 24 | 0 | | | | | | | | |
| 24 - 25 | 1 | | | | | | | | 1 |
| 25 - 26 | 0 | | | | | | | | |
| 26 - 27 | 7 | 2 | 1 | | | | | | 4 |
| 27 - 28 | 1 | | | | | | | | 1 |
| 28 - 29 | 2 | | | 1 | | | | | 1 |
| 30 - 31 | 5 | | 2 | 1 | | | | | 2 |
| 32 - 33 | 2 | 2 | | | | | | | |
| 37 - 38 | 1 | | | | | 1 | | | |
| 40 - 41 | 2 | 1 | | 1 | | | | | |
| Total | 521 | 365 | 56 | 25 | 6 | 6 | 2 | 1 | 60 |

TABLE 13.

ENDOSCOPIC PROCEDURES IN 193 CASES

| Endoscopic Procedure | Total Cases | PASSED Within Two Weeks | Within Three Months | After Three Months | Total Passed | Not Passed | Not Known |
|---|---|---|---|---|---|---|---|
| Ureteric catheterisation | 137 | 28 | 31 | 28 | 87 | 32 | 18 |
| Ureteric meatotomy | 26 | 16 | 2 | 3 | 21 | 1 | 4 |
| Diathermy to orifice | 4 | 2 | 1 | 1 | 4 | - | - |
| Bougie dilatation | 8 | 1 | 2 | 2 | 5 | - | 3 |
| Evacuated from bladder | 18 | 18 | - | - | 18 | - | - |
| Total | 193 | 65 | 36 | 34 | 135 | 33 | 25 |

Of 168 cases, 135 (80 per cent) passed.

RECURRENCE AFTER ENDOSCOPIC PROCEDURES

| Interval in years | Total cases | Not known | Cases followed | No recurr. | Recurr. | Rec. %. |
|---|---|---|---|---|---|---|
| 0 - 5 | 120 | 40 | 80 | 71 | 9 | 11.25 |
| 6 - 10 | 51 | - | 51 | 47 | 4 | 7.8 |
| 11 - 15 | 8 | - | 8 | 7 | 1 | 14.3 |
| 16 - 20 | 12 | - | 12 | 9 | 3 | 25.0 |
| More than 20 | 2 | - | 2 | 2 | 0 | Nil |
| Totals | 193 | 40 | 153 | 136 | 17 | 12.5 |

TABLE 14.

## NATURAL HISTORY

### 156 CASES FOLLOWED MORE THAN 10 YEARS WITHOUT OPERATION

| ORIGINAL STATE | TOTAL | PROGRESS | | | | | |
|---|---|---|---|---|---|---|---|
| | | I.S.Q. NO SYMPTOMS | FURTHER STONES PASSED | FURTHER STONES FORMED | DIED URINARY CAUSES | INCREASED IN SIZE. NO OPERATION | OPERATION REQUIRED |
| Clear - Having passed stone | 106 | 87 | 15 | 4 | - | - | - |
| Unilateral large | 14 | 8 | - | - | - | 3 | 3 |
| Unilateral small | 29 | 9 | 3 | 2 | - | 9 | 6 |
| Bilateral large | 4 | - | - | - | 1 | 3 | - |
| Bilateral small | 2 | - | - | 1 | - | 1 | - |
| Large on one side, small on other. | 1 | 1 | - | - | - | - | - |
| TOTALS: | 156 | 105 | 18 | 7 | 1 | 16 | 9 |

#### SUMMARY

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Originally clear | 106 | 87 | 15 | 4 | - | - | - |
| Stone originally present | 50 | 18 | 3 | 3 | 1 | 16 | 9 |
| | 156 | 105 | 18 | 7 | 1 | 16 | 9 |

TABLE 15.

NATURAL HISTORY

PROGRESS OF 156 UNTREATED SMALL CALYCEAL STONES

| Progress | | Total | Per cent |
|---|---|---|---|
| (a) Now Clear. | | 12 | 7.7 |
| Alive - no symptoms | 9 | | |
| Died - other causes | 3 | | |
| | 12 | | |
| (b) No increase in size. | | 111 | 71.2 |
| Alive - no symptoms | 74 | | |
| Alive - symptoms | 30 | | |
| Died - other causes | 7 | | |
| | 111 | | |
| (c) Increased in size. | | 33 | 21.1 |
| No symptoms | 1 | | |
| Symptoms - no operation | 13 | | |
| Operation required | 19 | | |
| | 33 | | |
| Totals | | 156 | 100.0 |

Hence:
1. 33 had increased.
2. 30 had mild symptoms without increase in size.
3. 10 had died from other causes.
4. More than half were symptom-free.

Followed.

| | |
|---|---|
| 0 - 5 years | 67 |
| 6 - 10 " | 36 |
| 11 - 15 " | 46 |
| 16 - 20 " | 3 |
| 21 - 25 " | 4 |
| Total | 156 |

TABLE 16.

NATURAL HISTORY

68 CASES OF LARGE UNTREATED STONE

| Period followed in years | Total | Unilateral (44) | | Bilateral (24) | | Total (68) | |
|---|---|---|---|---|---|---|---|
| | | Symptoms | No Symptoms | Symptoms | No Symptoms | Symptoms | No Symptoms |
| 0 - 1 | 6 | 5 | | 1 | | 6 | |
| 1 - 2 | 2 | | 1 | | 1 | | 2 |
| 2 - 3 | 2 | | 2 | | | | 2 |
| 3 - 4 | 10 | | 5 | 1 | 4 | 1 | 9 |
| 4 - 5 | 5 | | 2 | | 3 | | 5 |
| 5 - 6 | 8 | 1 | 5 | 1 | 1 | 2 | 6 |
| 6 - 7 | 3 | 1 | - | 1 | 1 | 2 | 1 |
| 7 - 8 | 5 | | 5 | | | | 5 |
| 8 - 9 | 5 | | 2 | 2 | 1 | 2 | 3 |
| 9 - 10 | 1 | | 1 | | | | 1 |
| 10 - 11 | 9 | 2 | 2 | 3 | 2 | 5 | 4 |
| 11 - 12 | 2 | | 2 | | | | 2 |
| 13 - 14 | 2 | | 1 | 1 | | 1 | 1 |
| 15 - 16 | 1 | 1 | | | | 1 | |
| 16 - 17 | 1 | | 1 | | | | 1 |
| 17 - 18 | 2 | 1 | - | | 1 | 1 | 1 |
| 20 - 21 | 2 | | 2 | | | | 2 |
| 31 - 32 | 2 | 1 | 1 | | | 1 | 1 |
| Totals | 68 | 12 | 32 | 10 | 14 | 22 | 46 |
| Died -other causes. | | 2 | 5 | 1 | 4 | 3 | 9 |
| -urinary causes. | | 1 | | 7 | | 8 | |
| Total died | | 3 | 5 | 8 | 4 | 11 | 9 |
| Still alive | | 9 | 27 | 2 | 10 | 11 | 37 |

## TABLE 17

## NATURAL HISTORY

## 34 CASES TREATED CONSERVATIVELY FOR 1 TO 30 YEARS BEFORE COMING TO OPERATION

### SIZE

| | |
|---|---|
| Large | 16 |
| Medium | 18 |
| | 34 |

### PROGRESS

| | |
|---|---|
| Rapid | 3 |
| Slow | 31 |
| | 34 |

### YEARS FOLLOWED

| | Cases |
|---|---|
| 0-2 | 4 |
| 3-5 | 8 |
| 6-10 | 14 |
| 11-15 | 5 |
| 16-20 | 2 |
| 21-25 | 0 |
| 26-30 | 1 |
| Total | 34 |

### "SPREAD" TO OPPOSITE SIDE

9 were bilateral when first seen. During the period of observation none had spread to the other side in spite of the infection and the presence of stag-horn calculi for periods of 7, 8, 11, 20, 15, 7 and 4 years.

### OPERATION EVENTUALLY PERFORMED

| | |
|---|---|
| Nephrectomy | 17 |
| Conservative | 17 |
| | 34 |

### REASON FOR CONSERVATIVE ATTITUDE

| | |
|---|---|
| Mild or no symptoms | 30 |
| Unfit at time | 2 |
| Refused operation | 2 |
| | 34 |

## TABLE 18.

## NATURAL HISTORY

## BILATERAL CALCULI - 53 CASES TREATED CONSERVATIVELY

**SIZE.**

| | |
|---|---|
| Bilateral unbranched | 42 |
| Bilateral branched | 8 |
| One side branched, other unbranched | 3 |
| | 53 |

**PROGRESS.**

(a) Bilateral unbranched (42)

| Condition. | Total. | Summary. | |
|---|---|---|---|
| 1. Passed stones - now clear. | 14 | Both sides clear. | 14 |
| 2. Passed stones - one side clear. | 13 | One side clear. | 14 |
| 3. Passed stones - still present both sides. | 2 | Stones present both sides. | 9 |
| 4. Calyceal stones unchanged. | 4 | Condition unknown. | 5 |
| 5. Untraced. | 4 | | 42 |
| 6. Died other causes - unchanged. | 1 | | |
| 7. Calyceal and ureteric unchanged. | 2 | | |
| 8. Died other causes - state unknown. | 1 | | |
| 9. Died - one side clear. | 1 | | |
| | 42 | | |

TABLE 18 (Cont)

NATURAL HISTORY

BILATERAL CALCULI - 53 CASES TREATED CONSERVATIVELY (Contd).

PROGRESS. (Contd.)

(b) Unilateral branched, unilateral unbranched (3).

1. W.D. Dead - other causes. Lived 7 years. No symptoms.
2. J.B.S.R. Dead - other causes, aged 74. Lived 4 years. No symptoms.
3. T.W. Alive - aged 33. Two years since first seen. No symptoms.

(c) Bilateral Branched (8).

| Init. | Alive or Dead. | Followed or Survived. | Symptoms | Age | Comments |
|---|---|---|---|---|---|
| 1. L.B. | Alive | 8 years | Present | 60 | Unfit for operation. |
| 2. W.B. | Alive | 5 years | None | 68 | Moved house. |
| 3. J.E. | Alive | 5 years | None | 12 | Recumbency stones. |
| 4. Mrs.E.L. | Dead | Few months. | Present | 62 | Bilateral poor function |
| 5. Mrs.J.McC. | Dead | Few months. | Present | 62 | Bilateral poor function |
| 6. Mrs.J.McG. | Dead | Few months. | Present | 32 | Renal function 3% of normal |
| 7. Mrs.M.S. | Alive | 17 years | None | 59 | Blood urea normal. |
| 8. Mrs.J.S. | Un-traced | - | None | 76 | Present many years possibly |

Summary

| | |
|---|---|
| Alive | 4 |
| Dead - urinary causes | 3 |
| Untraced (aged 76) | 1 |
| | 8 |

# TABLE 19

## NATURAL HISTORY

## PROGRESS OF 43 CASES OF MILD RECURRENCE FOLLOWED FOR FURTHER 7 YEARS.

| Original State | Total | Progress | |
|---|---|---|---|
| Passed stone(s) after operation. | 10 | No further stones passed.<br>Passed further stones. | 3<br>7 |
| Bilateral small stone(s). | 5 | One side now clear.<br>Operation required | 4<br>1 |
| Contralateral stone(s). | 5 | Clear.<br>Unchanged. | 1<br>4 |
| Ipsilateral stone(s). | 23 | Clear.<br>Unchanged.<br>Operation required.<br>Died other causes. | 5<br>14<br>1<br>3 |
| Total | 43 | | 43 |

**Hence:**

| | |
|---|---|
| Improved | 13 |
| Unchanged | 25 |
| Operation needed | 2 |
| Died - other causes | 3 |
| | 43 |

## TABLE 20

## NATURAL HISTORY

## URINE EXAMINATIONS EARLY & LATE IN 223 CASES TREATED CONSERVATIVELY.

| URINE EXAMINATION | Total | CLINICAL GROUPS | | | |
|---|---|---|---|---|---|
| Formerly → Latterly | | Passed stones now clear. | Continue to pass stones. | Small stones present. | Large stones present. |
| Sterile → Sterile | 161 | 104 | 32 | 25 | - |
| Infected → Sterile | 19 | 14 | 4 | 1 | |
| Total | 180 | 118 | 36 | 26 | - |
| Sterile → Infected | 7 | 3 | 1 | 3 | - |
| Infected → Infected | 36 | 10 | 6 | 14 | 6 |
| Total | 43 | 13 | 7 | 17 | 6 |
| Grand Total | 223 | 131 | 43 | 43 | 6 |

Organisms. (43 cases)

| | |
|---|---|
| B. Coli | 32 |
| Proteus | 5 |
| Strep.faec. | 4 |
| Staph.aur. | 2 |
| | 43 |

TABLE 21

INCIDENCE OF OPERATIONS IN 3 DECADES

680 OPERATIONS

| Operation | Total | 1926-1935 | | 1936-1945 | | 1946-1955 | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Pyelolithotomy | 238 | 41 | 39.2 | 104 | 41.8 | 93 | 28.5 |
| Nephrolithotomy | 65 | 19 | 18.0 | 35 | 14.0 | 11 | 3.4 |
| Indefinite | 39 | 8 | 7.6 | 20 | 8.0 | 11 | 3.4 |
| Pyelonephrolithotomy | 24 | 4 | 3.8 | 7 | 2.8 | 13 | 4.0 |
| Partial nephrectomy | 30 | Nil | Nil | Nil | Nil | 30 | 9.2 |
| Nephrectomy | 134 | 17 | 16.2 | 32 | 13.0 | 85 | 26.0 |
| Ureterolithotomy | 150 | 16 | 15.2 | 51 | 20.4 | 83 | 25.5 |
| Totals | 680 | 105 | 100.0 | 249 | 100.0 | 326 | 100.0 |

Nepholithotomy and Pyelonephrolithotomy are combined in the summary in the text under the heading of nephrolithotomy.

TABLE 22

POST-OPERATIVE MORTALITY - 23 IN 546 CASES (4.2%)

DETAILS

| No | Init | Age | Operation. | Cause. | Interval. |
|---|---|---|---|---|---|
| 1 | Mrs. J.B. | 62 | Nephrolithotomy | Uraemia - Bilat.Stone | One week |
| 2 | Mrs. J.D. | 50 | Nephrolithotomy | Shock - Haemorrhage | Day of operation |
| 3 | Mrs. B.F. | 64 | Nephrolithotomy | Shock - Haemorrhage | Day of operation |
| 4 | Mrs. H. | 47 | Nephrectomy | Shock | Day of operation |
| 5 | Mrs. McG. | 46 | Nephrolithotomy | Cardiac dilatation | Four weeks |
| 6 | Mrs. McG. | 60 | Nephrolithotomy | Uraemia | Two weeks |
| 7 | Miss J.R. | 50 | Pyelolithotomy | Pneumonia | Three months |
| 8 | Mrs. M.S. | 47 | Partial Nephrectomy | Shock | Day of Operation |
| 9 | Mrs. E.B. | 52 | Pyelolithotomy | Shock | Day of Operation |
| 10 | T.B. | 44 | Excision of half of Horseshoe Kidney | Haemorrhage and Infection | Several months |
| 11 | Mrs. C. | 37 | Pyelolithotomy | Shock | Day of Operation |
| 12 | R.G. | 49 | Ureterolithotomy | Peritonitis from Ruptured Diverticulitis | Three weeks |
| 13 | D.H. | 44 | Ureterolithotomy | Anuria | Six days |
| 14 | W.M. | 59 | Partial Nephrectomy | Haemorrhage | Three days |

TABLE 22 (Continued)

| No. | Init. | Age. | Operation. | Cause. | Interval. |
|---|---|---|---|---|---|
| 15 | J.McE. | 53 | Ureterolithotomy | Hyperpotassaemia | Ten days |
| 16 | C.McK. | 50 | Ureterolithotomy | Circulatory collapse | Two weeks |
| 17 | Mrs. A.McL. | 27 | Nephrolithotomy | Uraemia | Three weeks |
| 18 | W.T. | 74 | Pyelolithotomy | Uraemia and Bronchitis | Three weeks |
| 19 | E.B. | 35 | Nephrolithotomy | Uraemia | Two weeks |
| 20 | P.O. | 59 | Nephrolithotomy | Uraemia | Two weeks |
| 21 | Mrs. G. | 51 | Bilateral Nephrolithotomy | Uraemia | Four weeks |
| 22 | E.V. | 60 | Nephrolithotomy | Uraemia | One week |
| 23 | J.T. | 64 | Ureterolithotomy | Uraemia | One week |

TABLE 23.

## POST-OPERATIVE COMPLICATIONS

| Complication | Total | FOLLOWING Pyelo-Lithotomy | Nephro-Lithotomy | Partial Nephrectomy | Nephrectomy | Uretero-Lithotomy |
|---|---|---|---|---|---|---|
| 1. Urinary leakage. | 35 | 7 | - | 6 | - | 22 |
| 2. Secondary nephrectomy for: | | | | | | |
| a) Haemorrhage | 5 | 1 | 3 | 1 | - | - |
| b) Fistula | 8 | 2 | - | 3 | - | 3 |
| 3. Pseudo-recurrence. | 32 | 12 | 8 | 6 | - | 6 |
| 4. Haemorrhage. | 5 | 3 | - | 1 | - | 1 |
| 5. Pneumothorax. | 5 | 2 | 1 | - | 2 | - |
| 6. Wound infection. | 15 | 7 | 1 | 1 | 3 | 3 |
| 7. Peritonitis. | 1 | - | - | - | - | 1 |
| 8. Chest complications. | 8 | 3 | 1 | - | - | 4 |
| 9. Deep thrombosis. | 2 | 2 | - | - | - | - |
| 10. Loin sinus. | 2 | 1 | - | - | 1 | - |
| 11. Adrenal insufficiency. | 1 | - | - | - | 1 | - |
| 12. Uraemia. | 1 | - | - | 1 | - | - |
| 13. Injury to Inf. vena cava. | 1 | - | - | 1 | - | - |
| 14. Intestinal obstruction. | 1 | - | - | - | 1 | - |
| 15. Hernia. | 2 | - | - | 1 | 1 | - |
| Totals | 124 | 40 | 14 | 21 | 9 | 40 |
| Mortality | 23 | 4 | 10 | 2 | 2 | 5 |

TABLE 24.

INCIDENCE OF PSEUDO-RECURRENCE

(EVIDENCE AVAILABLE FOR 305/546 CASES)

| Operation | Total Cases | Total Clear | CLEAR Immediate Post-Op X-ray. | CLEAR Later X-Ray | PSEUDO-RECURRENCE Total pseudo-recurr. | PSEUDO-RECURRENCE Mild | PSEUDO-RECURRENCE Severe |
|---|---|---|---|---|---|---|---|
| Pyelolithotomy | 119 | 107 | 50 | 57 | 12 | 1 | 11 |
| Nephrolithotomy | 30 | 22 | 4 | 18 | 8 | 0 | 8 |
| Indefinite | 8 | 7 | Nil | 7 | 1 | 0 | 1 |
| Pyelonephro-lithotomy | 14 | 9 | 6 | 3 | 5 | 3 | 2 |
| Partial nephrectomy | 27 | 23 | 23 | Nil | 4 | 1 | 3 |
| Pyeloplasty + lithotomy | 3 | 1 | 1 | Nil | 2 | 2 | 0 |
| Upper uretero-lithotomy | 30 | 29 | 21 | 8 | 1 | 1 | 0 |
| Middle uretero-lithotomy | 6 | 6 | 3 | 3 | 0 | 0 | 0 |
| Lower uretero-lithotomy | 68 | 63 | 29 | 34 | 5 | 0 | 5 |
| | 305 | 267 | 137 | 130 | 38 | 8 | 30 |

TABLE 25.

INCIDENCE OF RECURRENCE (EXCLUDING PSEUDO-RECURRENCE) IN 416 PRIMARY OPERATIONS, i.e. 437 - 21.

| | Urological Department | | Vict.Inf. Surgeons | | Others | | Total Operations | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| No recurrence | 182 | 74.0 | 52 | 48.6 | 18 | 28.6 | 252 | 60.6 |
| Mild recurrence | 35 | 14.2 | 5 | 4.7 | 12 | 19.0 | 52 | 12.5 |
| Severe recurrence | 29 | 11.8 | 50 | 46.7 | 33 | 52.4 | 112 | 26.9 |
| Total recurrence | 64 | 26.0 | 55 | 51.4 | 45 | 71.4 | 164 | 39.4 |
| Total operations | 246 | 100.0 | 107 | 100.0 | 63 | 100.0 | 416 | 100.0 |

INCIDENCE OF TRUE RECURRENCE IN 403 PATIENTS

| | Urological Department | | Vict.Inf. Surgeons | | Others | | Total cases | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| No recurrence | 171 | 70.0 | 47 | 47.5 | 17 | 30.0 | 236 | 58.3 |
| Mild recurrence | 42 | 17.0 | 7 | 7.1 | 12 | 20.0 | 60 | 15.0 |
| Severe recurrence | 33 | 13.0 | 45 | 45.4 | 29 | 50.0 | 107 | 26.7 |
| Total recurrence | 75 | 30.0 | 52 | 52.5 | 41 | 70.0 | 167 | 41.7 |
| Total cases | 246 | 100.0 | 99 | 100.0 | 58 | 100.0 | 403 | 100.0 |

TABLE 26. INCIDENCE OF TRUE RECURRENCE AFTER 437 PRIMARY OPERATIONS

| Recurrence | Total | | Pyelo-lithotomy | | Nephro-lithotomy | | Partial Nephrect. | | Nephrec-tomy. | | Uretero-lithotomy. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| Total operations | 437 | | 169 | | 78 | | 19 | | 70 | | 101 | |
| Pseudo-recurrences | 21 | | 9 | | 6 | | 3 | | 0 | | 3 | |
| Leaving for study | 416 | 100.0 | 160 | 100.0 | 72 | 100.0 | 16 | 100.0 | 70 | 100.0 | 98 | 100.0 |
| No recurrence | 252 | 60.0 | 83 | 51.9 | 26 | 36.0 | 15 | 93.8 | 61 | 87.1 | 67 | 68.4 |
| Mild recurrence | 52 | 12.5 | 24 | 15.0 | 9 | 12.5 | 1 | 6.2 | 1 | 1.4 | 17 | 17.4 |
| Severe recurrence | 112 | 27.5 | 53 | 33.1 | 37 | 51.5 | 0 | - | 8 | 11.5 | 14 | 14.2 |
| TOTAL TRUE RECURRENCE | 164 | 40.0 | 77 | 48.1 | 46 | 64.0 | 1 | 6.2 | 9 | 12.9 | 31 | 31.6 |

TABLE 27.

SUMMARY OF INCIDENCE OF TRUE RECURRENCE

416 PRIMARY OPERATIONS ON 403 PATIENTS

(21 PSEUDO-RECURRENCES OMITTED)

| Operations | Total Operations | | No Recurrence | | Mild Recurrence | | Severe Recurrence | | Total Recurrence | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| Pyelo-lithotomy | 160 | 100.0 | 83 | 51.9 | 24 | 15.0 | 53 | 33.1 | 77 | 48.1 |
| Nephro-lithotomy | 72 | 100.0 | 26 | 36.0 | 9 | 12.5 | 37 | 51.5 | 46 | 64.0 |
| Partial nephrectomy | 16 | 100.0 | 15 | 93.8 | 1 | 6.2 | 0 | - | 1 | 6.2 |
| Nephrectomy | 70 | 100.0 | 61 | 87.1 | 1 | 1.4 | 8 | 11.5 | 9 | 12.9 |
| Uretero-lithotomy | 98 | 100.0 | 67 | 68.4 | 17 | 17.4 | 14 | 14.2 | 31 | 31.6 |
| Totals | 416 | 100.0 | 252 | 60.6 | 52 | 12.4 | 112 | 27.0 | 164 | 39.4 |

TABLE 28. INCIDENCE OF RECURRENCE AFTER 260 PRIMARY OPERATIONS

UROLOGICAL DEPARTMENT SERIES

| Recurrence | Total | | Pyelo-lithotomy | | Nephro-lithotomy | | Partial nephrect. | | Nephrec-tomy. | | Uretero-lithotomy. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| Total operations | 260 | | 98 | | 22 | | 18 | | 51 | | 71 | |
| Pseudo-recurrences | 14 | | 5 | | 4 | | 3 | | 0 | | 2 | |
| Leaving for study | 246 | 100.0 | 93 | 100.0 | 18 | 100.0 | 15 | 100.0 | 51 | 100.0 | 69 | 100.0 |
| No recurrence | 182 | 74.0 | 61 | 65.6 | 9 | 50.0 | 15 | 100.0 | 47 | 92.1 | 50 | 72.5 |
| Mild recurrence | 35 | 14.2 | 17 | 18.3 | 5 | 27.8 | 0 | - | 1 | 2.0 | 12 | 17.4 |
| Severe recurrence | 29 | 11.8 | 15 | 16.1 | 4 | 22.2 | 0 | - | 3 | 5.9 | 7 | 10.1 |
| TOTAL TRUE RECURRENCE | 64 | 26.0 | 32 | 34.4 | 9 | 50.0 | 0 | - | 4 | 7.9 | 19 | 27.5 |

TABLE 29. INCIDENCE OF TRUE RECURRENCE (i.e. EXCLUDING PSEUDO-RECURRENCE) AFTER 246 OPERATIONS (PRIMARY)

UROLOGICAL DEPARTMENT SERIES

| Operation | Total Operations | | No Recurrence | | Mild Recurrence | | Severe Recurrence | | Total Recurrence | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| Pyelo-lithotomy | 93 | 100.0 | 61 | 65.6 | 17 | 18.3 | 15 | 16.1 | 32 | 34.4 |
| Nephro-lithotomy | 18 | 100.0 | 9 | 50.0 | 5 | 27.8 | 4 | 22.2 | 9 | 50.0 |
| Partial nephrectomy | 15 | 100.0 | 15 | 100.0 | 0 | - | 0 | - | 0 | - |
| Nephrectomy | 51 | 100.0 | 47 | 92.1 | 1 | 2.0 | 3 | 5.9 | 4 | 7.9 |
| Uretero-lithotomy | 69 | 100.0 | 50 | 72.5 | 12 | 17.4 | 7 | 10.1 | 19 | 27.5 |
| Total | 246 | 100.0 | 182 | 74.0 | 35 | 14.2 | 29 | 11.8 | 64 | 26.0 |

TABLE 30

INCIDENCE OF RECURRENCE IN 3 DECADES

437 PRIMARY OPERATIONS

| Decades. | Total Operations | | OPERATIONS: Conservative Renal | | Nephrectomy | | Uretero-lithotomy. | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| **1926-1935.** | | | | | | | | |
| Total ops. | 75 | | 52 | | 12 | | 11 | |
| Pseudo-recurr. | 7 | | 6 | | 0 | | 1 | |
| Leaving | 68 | 100.0 | 46 | 100.0 | 12 | 100.0 | 10 | 100.0 |
| No recurr. | 30 | 44.4 | 15 | 32.6 | 7 | 58.3 | 8 | 80.0 |
| Mild recurr. | 9 | 13.2 | 3 | 6.5 | 5 | 41.7 | 1 | 10.0 |
| Severe recurr. | 29 | 42.4 | 28 | 60.9 | 0 | - | 1 | 10.0 |
| Total true recurrence. | 38 | 55.6 | 31 | 67.4 | 5 | 41.7 | 2 | 20.0 |
| **1936-1945.** | | | | | | | | |
| Total ops. | 194 | | 133 | | 23 | | 38 | |
| Pseudo-recurr. | 7 | | 7 | | 0 | | 0 | |
| Leaving | 187 | 100.0 | 126 | 100.0 | 23 | 100.0 | 38 | 100.0 |
| No recurr. | 84 | 44.8 | 48 | 38.1 | 18 | 78.0 | 18 | 47.4 |
| Mild recurr. | 26 | 14.0 | 18 | 14.3 | 1 | 4.4 | 7 | 18.4 |
| Severe recurr. | 77 | 41.2 | 60 | 47.6 | 4 | 17.6 | 13 | 34.2 |
| Total true recurrence. | 103 | 55.2 | 78 | 71.9 | 5 | 22.0 | 20 | 52.6 |
| **1946-1955.** | | | | | | | | |
| Total ops. | 268 | | 140 | | 67 | | 61 | |
| Pseudo-recurr. | 22 | | 16 | | 0 | | 6 | |
| Leaving | 246 | 100.0 | 124 | 100.0 | 67 | 100.0 | 55 | 100.0 |
| No recurr. | 200 | 81.3 | 92 | 74.2 | 63 | 94.0 | 45 | 81.8 |
| Mild recurr. | 25 | 10.2 | 19 | 15.3 | 0 | - | 6 | 10.9 |
| Severe recurr. | 21 | 8.5 | 13 | 10.5 | 4 | 6.0 | 4 | 7.3 |
| Total true recurrence. | 46 | 18.7 | 32 | 25.8 | 4 | 6.0 | 10 | 18.2 |

TABLE 31. SUMMARY OF RECURRENCE IN 3 DECADES IN 537 OPERATIONS

| | 1926 - 1935 | | | | 1936 - 1945 | | | | 1946 - 1955 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Operations | | Total less Pseudo-R. | | Total Operations | | Total less Pseudo-R. | | Total Operations | | Total less Pseudo-R. | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| Total | 75 | 100.0 | 68 | 100.0 | 194 | 100.0 | 187 | 100.0 | 268 | 100.0 | 246 | 100.0 |
| No recurrence. | 30 | 40.0 | 30 | 44.4 | 84 | 43.3 | 84 | 44.8 | 200 | 74.6 | 200 | 81.3 |
| Mild recurrence. | 9 | 12.0 | 9 | 13.2 | 27 | 14.0 | 26 | 14.0 | 34 | 12.7 | 25 | 10.2 |
| Severe recurrence. | 36 | 48.0 | 29 | 42.4 | 83 | 42.7 | 77 | 41.2 | 34 | 12.7 | 21 | 8.5 |
| Total Recurrence | 45 | 60.0 | 38 | 55.6 | 110 | 56.7 | 103 | 55.2 | 68 | 25.4 | 46 | 20.7 |

TABLE 32

CONTRALATERAL RECURRENCE

IN TOTAL SERIES OF 416 (FALSE RECURRENCE OMITTED)

| Operation | Total Operations | Contralateral recurrence Mild | Severe | Total | Contralat. recurrence per cent. |
|---|---|---|---|---|---|
| Conservative Operations | 346 | 16 | 16 | 32 | 9.2 |
| Nephrectomy | 70 | 1 | 8 | 9 | 12.9 |
| Total | 416 | 17 | 24 | 41 | 10.0 |

IN UROLOGICAL DEPARTMENT SERIES OF 246 (FALSE RECURRENCE OMITTED)

| Operation | Total Operations | Contralateral recurrence Mild | Severe | Total | Contralat. recurrence per cent. |
|---|---|---|---|---|---|
| Conservative Operations | 195 | 12 | 3 | 15 | 7.7 |
| Nephrectomy | 51 | 1 | 3 | 4 | 7.9 |
| Total | 246 | 13 | 6 | 19 | 7.8 |

TABLE 33

BILATERAL STONE - 96 CASES

POST OPERATIVE RECURRENCE.

| | Totals | Conservative Renal | Nephrectomy + Conservative - Renal | Uretero-Lithotomy |
|---|---|---|---|---|
| Total Cases | 96 | 61 | 17 | 18 |
| Untraced | 4 | 4 | 0 | 0 |
| Post-op. deaths | 3 | 3 | 0 | 0 |
| Pseudo-recurrence | 9 | 7 | 0 | 2 |
| Leaving for study | 80 | 47 | 17 | 16 |
| No recurrence | 31 | 13 | 8 | 10 |
| Mild recurrence | 13 | 8 | 1 | 4 |
| Severe recurrence | 36 | 26 | 8 | 2 |
| Total recurrence | 49 | 34 | 9 | 6 |
| Recurrence % (of those available for study) | 61.3% | 72.4% | 53.0% | 37.5% |

TABLE 34.

## OPERATIONS FOR BILATERAL CALCULI
## RECURRENCE IN 130 PRIMARY OPERATIONS

| Primary Operation | Total Ops. | Not Traced | Post-Op deaths. | Pseudo-recurr. | Leav-ing. | No recurr. | Mild recurr. | Severe recurr. | Total true recurr. | True recurr. %. |
|---|---|---|---|---|---|---|---|---|---|---|
| Pyelo-lithotomy. | 58 | 6 | 1 | 6 | 45 | 15 | 7 | 23 | 30 | 66.7 |
| Nephro-lithotomy. | 24 | 4 | 3 | 1 | 16 | 4 | 1 | 11 | 12 | 75.0 |
| Partial nephrectomy. | 6 | - | - | - | 6 | 5 | 1 | - | 1 | 16.7 |
| Nephrectomy. | 17 | - | - | - | 17 | 12 | 1 | 4 | 5 | 29.4 |
| Uretero-lithotomy. | 25 | - | 1 | 3 | 21 | 15 | 3 | 3 | 6 | 28.6 |
| Totals | 130 | 10 | 5 | 10 | 105 | 51 | 13 | 41 | 54 | 51.4 |
| Conservative renal alone (i.e. pyelo-lithotomy nephro-lithotomy & partial nephrectomy. | 88 | 10 | 4 | 7 | 67 | 24 | 9 | 34 | 43 | 64.2 |
| Conservative renal + ure-terolithotomy | 113 | 10 | 5 | 10 | 88 | 39 | 12 | 37 | 49 | 55.7 |

TABLE 35

SEX INCIDENCE OF RECURRENCE

TOTAL SERIES (416) - PSEUDO-RECURRENCE OMITTED

| Sex Incidence of Recurrence. | Totals No. | Totals % | OPERATIONS: Conservative Renal No. | Conservative Renal % | Nephrectomy No. | Nephrectomy % | Uretero-lithotomy No. | Uretero-lithotomy % |
|---|---|---|---|---|---|---|---|---|
| Males. | | | | | | | | |
| Total ops. | 250 | 100.0 | 149 | 100.0 | 31 | 100.0 | 70 | 100.0 |
| No recurr. | 134 | 53.6 | 66 | 44.3 | 25 | 80.7 | 43 | 61.4 |
| Mild recurr. | 40 | 16.0 | 24 | 16.1 | 1 | 3.2 | 15 | 21.4 |
| Severe recurr. | 76 | 30.4 | 59 | 39.6 | 5 | 16.1 | 12 | 17.2 |
| Total Male Recurrence | 116 | 46.4 | 83 | 55.7 | 6 | 19.3 | 27 | 38.6 |
| Females. | | | | | | | | |
| Total ops. | 166 | 100.0 | 99 | 100.0 | 39 | 100.0 | 28 | 100.0 |
| No recurr. | 118 | 71.1 | 58 | 58.5 | 36 | 92.3 | 24 | 85.7 |
| Mild recurr. | 11 | 6.6 | 10 | 10.2 | 0 | - | 1 | 3.6 |
| Severe recurr. | 37 | 22.3 | 31 | 31.3 | 3 | 7.7 | 3 | 10.7 |
| Total Female Recurrence | 48 | 28.9 | 41 | 41.5 | 3 | 7.7 | 4 | 14.3 |

TABLE 36

SEX INCIDENCE OF RECURRENCE
UROLOGICAL DEPT. SERIES (246)

| Sex Incidence of Recurrence. | Totals No. | Totals % | OPERATIONS Conservative Renal No. | % | Nephrectomy No. | % | Uretero-lithotomy No. | % |
|---|---|---|---|---|---|---|---|---|
| Males. | | | | | | | | |
| Total ops. | 140 | 100.0 | 73 | 100.0 | 18 | 100.0 | 49 | 100.0 |
| No recurr. | 90 | 64.3 | 44 | 60.3 | 15 | 83.3 | 31 | 63.3 |
| Mild recurr. | 28 | 20.0 | 15 | 20.5 | 1 | 5.6 | 12 | 24.5 |
| Severe recurr. | 22 | 15.7 | 14 | 19.2 | 2 | 11.1 | 6 | 12.2 |
| Total Male Recurrence | 50 | 35.7 | 29 | 39.7 | 3 | 16.7 | 18 | 36.7 |
| Females. | | | | | | | | |
| Total ops. | 106 | 100.0 | 53 | 100.0 | 33 | 100.0 | 20 | 100.0 |
| No recurr. | 92 | 86.8 | 41 | 77.4 | 32 | 97.0 | 19 | 95.0 |
| Mild recurr. | 7 | 6.6 | 7 | 13.2 | 0 | - | 0 | - |
| Severe recurr. | 7 | 6.6 | 5 | 9.4 | 1 | 3.0 | 1 | 5.0 |
| Total Female Recurrence | 14 | 13.2 | 12 | 22.6 | 1 | 3.0 | 1 | 5.0 |

TABLE 37. INTERVAL BETWEEN OPERATION AND RECURRENCE

| Interval | Total Recurr. | Mild | Severe | Total Ops. | Pyelo-lithot. | Nephro-lithot. | Partial Nephr-ectomy. | Nephr-ectomy. | Uretero-lithot-omy. | Contra-lateral recurr-ence. |
|---|---|---|---|---|---|---|---|---|---|---|
| 0-3 mns | 5 | 3 | 2 | 5 | 3 | - | - | - | 2 | - |
| 3-6 mns | 5 | 2 | 3 | 5 | 2 | - | - | - | 3 | - |
| 6-12mns | 9 | 5 | 4 | 10 | 5 | 1 | - | - | 4 | - |
| 1-2 yrs | 12 | 7 | 5 | 11 | 7 | 2 | - | - | 2 | 1 |
| 2-3 do | 21 | 8 | 13 | 21 | 14 | 1 | 2 | 1 | 3 | 2 |
| 3-4 do | 18 | 2 | 16 | 17 | 8 | 4 | - | 2 | 3 | 2 |
| 4-5 do | 17 | 7 | 10 | 18 | 11 | 4 | 1 | - | 2 | 1 |
| 5-6 do | 14 | 3 | 11 | 13 | 11 | 2 | - | - | - | - |
| 6-7 do | 15 | 7 | 8 | 13 | 5 | 4 | - | - | 4 | 3 |
| 7-8 do | 9 | 4 | 5 | 10 | 3 | 3 | - | 1 | 3 | 2 |
| 8-9 do | 5 | 1 | 4 | 5 | 4 | 1 | - | - | - | - |
| 9-10 do | 4 | 1 | 3 | 4 | 2 | 1 | - | 1 | - | 1 |
| 10-11 do | 9 | 2 | 7 | 9 | 7 | 1 | - | 1 | - | 2 |
| 11-12 do | 3 | 2 | 1 | 2 | 1 | 1 | - | - | - | - |
| 12-13 do | 4 | 1 | 3 | 5 | 4 | 1 | - | - | - | 1 |
| 13-14 do | - | - | - | - | - | - | - | - | - | - |
| 14-15 do | - | - | - | - | - | - | - | - | - | - |
| 15-16 do | 4 | - | 4 | 4 | 2 | - | - | 1 | 1 | 2 |
| 16-17 do | - | - | - | - | - | - | - | - | - | - |
| 17-18 do | - | - | - | - | - | - | - | - | - | - |
| 18-19 do | 1 | 1 | - | 1 | 1 | - | - | - | - | - |
| 19-20 do | - | - | - | - | - | - | - | - | - | - |
| 20-21 do | 2 | - | 2 | 2 | 1 | 1 | - | - | - | - |
| 21-22 do | 1 | - | 1 | 1 | - | 1 | - | - | - | - |
| 28-29 do | 2 | 1 | 1 | 2 | 1 | - | - | - | 1 | - |
| 30-31 do | 1 | - | 1 | 1 | 1 | - | - | - | - | - |
| | 161 | 57 | 104 | 159 | 93 | 28 | 3 | 7 | 28 | |

TABLE 38

RELATIONSHIP OF RECURRENCE TO SIZE OF CALCULI

355 CASES

| | Large calculi | | Medium or Small | | Totals |
|---|---|---|---|---|---|
| | Number | Per cent | Number | Per cent | |
| All Operations. | 86 | 100.0 | 269 | 100.0 | 355 |
| No recurrence | 62 | 72.1 | 163 | 60.6 | 225 |
| Mild recurrence | 6 | 7.0 | 48 | 18.0 | 54 |
| Severe recurrence | 18 | 20.9 | 58 | 21.4 | 76 |
| Total recurrence | 24 | 27.9 | 106 | 39.4 | 130 |
| Conservative Operations. | 43 | 100.0 | 257 | 100.0 | 300 |
| No recurrence | 21 | 48.8 | 152 | 59.1 | 173 |
| Mild recurrence | 6 | 14.0 | 47 | 18.3 | 53 |
| Severe recurrence | 16 | 37.2 | 58 | 22.6 | 74 |
| Total recurrence | 22 | 51.2 | 105 | 40.9 | 127 |

TABLE 39

## RELATIONSHIP OF RECURRENCE TO NUMBER OF CALCULI

355 CASES

| | One stone | | Two stones | | Three stones | | More than three | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | |
| All Operations. | 278 | 100.0 | 25 | 100.0 | 6 | 100.0 | 46 | 100.0 | 355 |
| No recurrence. | 191 | 68.7 | 13 | 52.0 | 4 | 66.6 | 17 | 37.0 | 225 |
| Mild recurrence. | 41 | 14.8 | 5 | 20.0 | 1 | 16.7 | 7 | 15.2 | 54 |
| Severe recurrence. | 46 | 16.5 | 7 | 28.0 | 1 | 16.7 | 22 | 47.8 | 76 |
| Total recurrences | 87 | 31.3 | 12 | 48.0 | 2 | 33.4 | 29 | 63.0 | 130 |
| Conservative Operations. | 231 | 100.0 | 25 | 100.0 | 6 | 100.0 | 38 | 100.0 | 300 |
| No recurrence. | 145 | 62.8 | 13 | 52.0 | 4 | 66.6 | 11 | 29.0 | 173 |
| Mild recurrence. | 41 | 17.7 | 5 | 20.0 | 1 | 16.7 | 6 | 15.8 | 53 |
| Severe recurrence. | 45 | 19.5 | 7 | 28.0 | 1 | 16.7 | 21 | 55.2 | 74 |
| Total recurrence | 86 | 37.2 | 12 | 48.0 | 2 | 33.4 | 27 | 71.0 | 127 |

TABLE 40. COMPARISON OF SINGLE VERSUS MULTIPLE

| | Single Stone | | More than one | | |
|---|---|---|---|---|---|
| | Number | Per cent | Number | Per cent | Total |
| All Operations. | 278 | 100.0 | 77 | 100.0 | 355 |
| No recurrence. | 191 | 68.7 | 34 | 44.1 | 225 |
| Mild recurrence. | 41 | 14.8 | 13 | 16.9 | 54 |
| Severe recurrence. | 46 | 16.5 | 30 | 39.0 | 76 |
| Total recurrence | 87 | 31.3 | 43 | 45.9 | 130 |
| Conservative Operations. | 231 | 100.0 | 69 | 100.0 | 300 |
| No recurrence. | 145 | 62.8 | 28 | 40.6 | 173 |
| Mild recurrence. | 41 | 17.7 | 12 | 17.4 | 53 |
| Severe recurrence. | 45 | 19.5 | 29 | 42.0 | 74 |
| Total recurrence | 86 | 37.2 | 41 | 59.4 | 127 |

## TABLE 41

## SUMMARY OF POST-OPERATIVE URINE EXAMINATION IN 499 CASES

### (a) EARLY EXAMINATION - 149 CASES

| | Sterile | Infected | Total | Per cent Infected |
|---|---|---|---|---|
| No recurrences | 75 | 26 | 101 | 25.7 |
| Recurrence | 7 | 41 | 48 | 85.4 |
| Total | 82 | 67 | 149 | 46.0 |
| Per cent recurred | 8.5 | 61.2 | 32.2 | |

### (b) LATE EXAMINATION - 350 CASES

| | Sterile | Infected | Total | Per cent Infected |
|---|---|---|---|---|
| No recurrence | 189 | 39 | 228 | 17.0 |
| Recurrence | 46 | 76 | 122 | 62.3 |
| Total | 235 | 115 | 350 | 33.0 |
| Per cent recurred | 17.3 | 66.0 | 35.0 | |

### (c) COMBINED EARLY & LATE EXAMINATIONS - 499 CASES

| | Sterile | Infected | Total | Per cent Infected |
|---|---|---|---|---|
| No recurrence | 264 | 65 | 329 | 19.8 |
| Recurrence | 53 | 117 | 170 | 68.8 |
| Total | 317 | 182 | 499 | 36.5 |
| Per cent recurred | 16.7 | 64.3 | 34.1 | |

TABLE 42

RELATIONSHIP OF POST-OPERATIVE URINARY INFECTION TO RECURRENCE

499 CASES

| Urine Examination | Total No. | Total % | No Recurrence No. | No Recurrence % | Recurrence No. | Recurrence % |
|---|---|---|---|---|---|---|
| Total cases | 499 | 100.0 | 329 | 100.0 | 170 | 100.0 |
| Sterile | 317 | 63.6 | 264 | 80.0 | 53 | 31.0 |
| Infected | 182 | 36.4 | 65 | 20.0 | 117 | 69.0 |
| Details of Infected.(182). | | | | | | |
| Sterile pyuria | 21 | | 4 | | 17 | |
| B.coli | 88 | | 38 | | 50 | |
| B.coli + strep.faec. | 8 | | 1 | | 7 | |
| B.coli + staph.aureus. | 3 | | 3 | | 0 | |
| B.coli + staph.albus. | 1 | | 1 | | 0 | |
| B.coli + proteus. | 5 | | 0 | | 5 | |
| B.coli + pyocyanea. | 6 | | 5 | | 1 | |
| Staph. aureus. | 12 | | 1 | | 11 | |
| Staph. albus. | 9 | | 4 | | 5 | |
| Proteus vulgaris. | 12 | | 2 | | 10 | |
| Ps. pyocyane. | 9 | | 3 | | 6 | |
| Strep. faecalis. | 5 | | 3 | | 2 | |
| Strep. faec. + proteus. | 1 | | 0 | | 1 | |
| Proteus + staph. aur. | 2 | | 0 | | 2 | |
| Totals | 182 | | 65 | | 117 | |

TABLE 43.

POST-OPERATIVE RENAL FUNCTION

(RELATIONSHIP TO RECURRENCE)

196 CASES

| Operation | Total | Normal | | | Early Hydronephrosis | | | Moderate hydro or Fair function | | | Severe hydro. or poor function. | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No Rec. | Mild Rec. | Sev. Rec. | No. Rec. | Mild Rec. | Sev. Rec. | No Rec. | Mild Rec. | Sev. Rec. | No Rec. | Mild Rec. | Sev. Rec. |
| Pyelo-lithotomy | 108 | 30 | 18 | 13 | 2 | 1 | 5 | 4 | 1 | 7 | - | 2 | 25 |
| Nephro-lithotomy | 29 | 5 | 3 | 2 | 1 | 3 | 1 | - | 1 | 6 | - | - | 7 |
| Partial neph-rectomy | 18 | 11 | 1 | - | 1 | - | - | 1 | - | - | 1 | 1 | 2 |
| Upper uretero-lithotomy | 8 | 5 | - | - | 1 | - | - | - | - | - | - | 1 | 1 |
| Middle ureter-olithotomy | 2 | 2 | - | - | - | - | - | - | - | - | - | - | - |
| Lower uretero-lithotomy | 31 | 14 | 7 | - | 1 | 1 | - | - | - | 1 | - | 1 | 6 |
| Total | 196 | 67 | 29 | 15 | 6 | 5 | 6 | 5 | 2 | 14 | 1 | 5 | 41 |

Normal = 111. Early H = 17. Moderate H = 21. Severe H = 47.

TABLE 43 (Continued)

SUMMARY

| | Total | Normal | | Early Hydronephrosis | | Moderate Hydronephrosis | | Severe Hydronephrosis | |
|---|---|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % | No. | % |
| No recurrence | 79 | 67 | 84.8 | 6 | 7.6 | 5 | 6.3 | 1 | 1.3 |
| Mild recurrence | 41 | 29 | 70.7 | 5 | 12.2 | 2 | 4.9 | 5 | 12.2 |
| Severe recurrence | 76 | 15 | 19.7 | 6 | 7.9 | 14 | 18.4 | 41 | 54.0 |
| Totals | 196 | 111 | 56.6 | 17 | 8.7 | 21 | 10.7 | 47 | 24.0 |

TABLE 44

RELATIONSHIP OF COMPOSITION OF STONE TO RECURRENCE

| Composition of Stone | Total | No Recurrence | Recurrence | Percentage Recurrence |
|---|---|---|---|---|
| 1. Calcium oxalate | 44 | 34 | 10 | 22.7 |
| 2. Calcium oxalate + calcium phosphate | 31 | 26 | 5 | 16.2 |
| 3. Calcium oxalate + apatite | 5 | 4 | 1 | 20.0 |
| 4. Calcium oxalate + $NH_4$ Mg. phos. | 4 | 4 | 0 | - |
| 5. Calcium phosphate | 20 | 14 | 6 | 30.0 |
| 6. Calcium phosphate + $NH_4$ Mg. phos. | 8 | 6 | 2 | 25.0 |
| 7. Apatite | 4 | 2 | 2 | 50.0 |
| 8. Calcium carbonate + $NH_4$ Mg. phos. | 1 | 1 | 0 | - |
| 9. Ammonium magnesium phosphate | 2 | 2 | 0 | - |
| 10. Ammonium urate | 2 | 2 | 0 | - |
| 11. Cystine | 1 | 1 | 0 | - |
| Totals | 122 | 96 | 26 | - |

Of 84 oxalate-containing stones 16 (19 per cent) recurred.

Of 75 phosphate-containing stones 16 (21.3 per cent) recurred.

## TABLE 45

## MILD RECURRENCE - BIOCHEMISTRY

BLOOD CHEMISTRY (26 CASES)

| | Number | Per cent |
|---|---|---|
| Normal | 21 | 84.0 |
| Hyperparathyroidism | 2 | 8.0 |
| 1st stage biochemical osteomalacia | 1 | 4.0 |
| 2nd stage biochemical osteomalacia | 1 | 4.0 |
| Total | 25 | 100.0 |

URINARY CALCIUM OUTPUT (16 CASES)

| Findings | | Number | Per cent |
|---|---|---|---|
| Normal | | 8 | 50.0 |
| Increased | | 8 | 50.0 |
| Sulkowitch | 3 | | |
| Output on low intake | 5 | | |
| Total | | 16 | 100.0 |

STONE ANALYSIS (16 CASES)

| Composition | Number |
|---|---|
| Calcium oxalate | 11 |
| Calcium oxalate + calcium phosphate | 1 |
| Calcium phosphate | 2 |
| Apatite | 1 |
| Complex polysaccharide | 1 |
| Total | 16 |

# TABLE 46

## BIOCHEMISTRY OF SEVERE RECURRENCE

### BLOOD CHEMISTRY (50 CASES)

| | |
|---|---|
| Normal | 36 |
| Hyperparathyroidism | 4 |
| Biochemical Osteomalacia | 5 |
| Raised Urea & Phosphorus & Phosphatase (Renal Osteodystrophy) | 5 |
| | 50 |

Hyperglobulinaemia in 7/50.

### URINARY CALCIUM (25 CASES)

| Test | Total | Normal | Raised |
|---|---|---|---|
| Urinary Calcium Output | 20 | 7 | 13 |
| Sulkowitch | 5 | 3 | 2 |
| Totals | 25 | 10 | 15 |

Hence Hypercalcuria in 60%.

### STONES ANALYSED (30)

| Composition | Primary | Recurrent | Total |
|---|---|---|---|
| Calcium Oxalate | 2 | 5 | 7 |
| Calcium Oxalate + Calcium Phosphate | 3 | 6 | 9 |
| Calcium Oxalate + Apatite | 0 | 1 | 1 |
| Calcium Phosphate | 4 | 4 | 8 |
| Calcium Phosphate + Amm. Mag. Phosphate | 2 | 2 | 4 |
| Calcium Oxalate + Amm.Mag. Phosphate. | 0 | 1 | 1 |
| Totals | 11 | 19 | 30 |

## Diet for oxalate stone formers (Hammarsten)

The patient takes a normal diet which must contain:-

**MILK:** One litre (approx. $1\frac{1}{2}$ pints) per day (if possible).

**BUTTER:** Better than margarine since it contains Vitamin A and fatty acids which facilitate calcium absorption.

**WHOLEMEAL BREAD:** Provided it does not cause indigestion.

**ASSORTED VEGETABLES:** (Note the exceptions below). They should be eaten uncooked, or taken with the cooking water, since the magnesium present dissolves easily and is quickly lost.

**FRUITS:** Particularly, APPLES, PEARS, CITROUS FRUITS and BLACK GRAPES for their rich Vitamin C content.

**MEAT BROTHS:** For their rich magnesium content.

**VITAMIN D:** In the form of fish, e.g. herring. In winter and spring supplement with fish liver oils containing Vitamins A & D.
Sunbathing is encouraged, since Vitamin D is formed in the skin.

**VITAMIN B:** A special preparation is unnecessary where wholemeal bread is eaten. Otherwise, a Vitamin B preparation is advisable and the cheapest form is wheat grain 10 to 20 Gm. daily, in a freshly cooked porridge.

**FORBIDDEN:** FOODS RICH IN OXALATE OR OXALIC ACID, viz.:

Rhubarb.
Cocoa and chocolates.
Strong tea in large quantities.
Spinach - more than 25 Gm. spread over the week.
Loganberries and strawberries in large quantities.

N.B. Laxative use of liquid paraffin is inadvisable, since it dissolves fat-soluble Vitamins which are lost to the body.

**THERAPEUTICS:** The most useful and cheapest therapy is the ingestion of calcium and magnesium in milk and vegetables. Special mineral therapy must be controlled to avoid digestive disturbances. Magnesium and calcium must be exhibited together, i.e., in equimolecular amounts.

R Ex. dicalcii phosphas Gm. 175.
Magnes. oxide levis Gm. 40.

Sig. One teaspoonful thrice daily with meals.

## Group I : Large Stones - Unfit.

CASE I. Male, aged 48.

**Previous History:** Bilateral calculi. Right side, single large stone in lower calyx with hydronephrosis. Left kidney contained two large stones and was non-functioning.

8.10.53: Right pyelolithotomy and drainage of pyonephrosis.

**Condition before hyaluronidase:**

I.V.P.: Left kidney as above. Right kidney clear.

Biochemistry: Azotaemia with low normal calcium and reciprocal elevation of phosphorus.

Stone: Mixed apatite and magnesium ammonium phosphate.

Urine: Persistent mixed B.Coli and Proteus infection.

**Hyaluronidase Therapy:** 1,000 to 1,500 T.R.U. per day for six months. Specific gravity of urine 1,014 - 1,020.

**Result:** Very slight reduction in size of one of the large stones on the left side, but no improvement in function.

CASE 2. Male, aged 61.

**Previous History:**
1942: Bilateral conservative renal operations.
1947: Bilateral recurrence - staghorn on left, two large lower ureteric stones on right.
1953: Right lower ureterolithotomy - very poor function both sides.

**Condition before hyaluronidase:**

I.V.P.: Large staghorn, poorly-functioning left kidney. Right side clear but poor function.

Urine: Persistent Staph.Aureus alkaline infection, Specific Gravity of urine 1,012.

Stone: Mixed apatite and magnesium ammonium phosphate.

Biochemistry: Calcium 9.7 mgms. per 100 ml.
Phosphorus 2.02 mgms. per 100 ml.
i.e. First stage biochemical osteomalacia.

Hyaluronidase Therapy: 1,000 to 2,000 T.R.U. every 48 hours for six months. At no time did the Specific Gravity of the urine exceed 1016.

Result: Steady deterioration in kidney function. No further stone-formation. Died from uraemia one year later.

CASE 3. Female, aged 56.

Previous History: Bilateral calculi. Staghorn in non-functioning left kidney, and dendritic stone in upper calyx of relatively normal right kidney.

23.3.54: Resection of right upper calyx.

Condition before hyaluronidase:

I.V.P.: Remaining portion of right kidney normal and free from stone. Staghorn in non-functioning left kidney.

Urine: Specific gravity 1,016, alkaline, B. Proteus.

Stone Analysis: Apatite and magnesium ammonium phosphate.

Biochemistry: Normal.

Hyaluronidase Therapy: 1,500 T.R.U. every 48 hours for six months.

Result: No reduction in size of stone on left and no improvement in kidney function. The specific gravity remained between 1,014 and 1,018.

Group II : Large Stone in Solitary Kidney.

CASE 4. Male, aged 31.

Previous History: 1946: Left nephrectomy for pyonephrosis.
1949: Stone removed from right kidney.

Condition before Hyaluronidase:

I.V.P.: Staghorn calculus in poorly-functioning right kidney.

Urine: Specific gravity 1,018, alkaline, B. Proteus.

Stone: Not available.

Biochemistry: Azotaemia, calcium and phosphorus normal.

Hyaluronidase Therapy: 1,000 to 1,500 T.R.U. daily for 18 months. Specific Gravity rose to 1,024.

Result: No change in size of stone. Renal function and pyelogram remained the same.

CASE 5. Female, aged 60.

Previous History: Bilateral calculi.
1949: Left nephrectomy for multiple calculi in non-functioning kidney.
1941: Right inferior calycectomy.

Condition before Hyaluronidase: I.V.P.: Staghorn calculus in poorly-functioning right kidney.

Biochemistry: Normal. Urea 43 mgm. per ml.

Stone Analysis: Magnesium ammonium Phosphate.

Urine: Specific gravity 1,010; alkaline; B. Coli and Proteus.

Hyaluronidase Therapy: 1,000 to 1,500 T.R.U. daily for six months.

Result: No change in size of stone or in renal function. Specific Gravity of urine never rose above 1,020.

CASE 6. Female, aged 45.

Previous History: Bilateral calculi.
1945: Right nephrolithotomy.
1949: Right nephrectomy.
1951: Left pyelolithotomy.

Condition before hyaluronidase: X-ray: 3 stones in poorly-functioning left kidney.

Urine: Persistent B.Coli infection. Specific Gravity 1,015.

Biochemistry: Hypercalcuria. Blood chemistry normal.

Stone Analysis: Apatite (calcium phosphate).

Hyaluronidase Therapy: 1,000 to 1,500 T.R.U. for six months.

Result: No change in size of stones or in renal function.

## Group III : Small Calyceal Stones.

CASE 7. Male, aged 35.

Previous History: Left pyelolithotomy, 14.10.50.

Condition before Hyaluronidase:

I.V.P.: Recurrent small stone in left lower calyx with normal pyelogram.

Urine: Acid, sterile, specific gravity 1,018.

Biochemistry: Normal.

Stone Analysis: Calcium Oxalate.

Hyaluronidase Therapy: 500 T.R.U. every 48 hours for six months.

Result: The small recurrent stone vanished. During the therapy the specific gravity of his urine rose to 1,024.

CASE 8. Male, aged 17.

Previous History. Previous tuberculosis of hip. Bilateral calculi.
6.11.51: Right pyelolithotomy.
6.3. 53: Left pyelolithotomy - principally calcium oxalate.

Condition before hyaluronidase:

I.V.P.: Small recurrent stone right middle calyx.
Pyelogram N.A.D.

Urine: Specific gravity 1,016, sterile.

**Biochemistry:** Normal, apart from minimal hypercalcuria.

**Hyaluronidase Therapy:** 500 to 1,000 T.R.U. every 48 hours for six months.

**Result:** No change in size of stone or function of the kidney. Urine specific gravity never rose above 1,020.

**CASE 9.** Male, aged 26.

**Previous History:** Tuberculosis left hip.

7.4.53.: Right pyelonephrolithotomy. A portion adherent to the lining of the middle calyx was left behind.

**Condition before Hyaluronidase:**

**I.V.P.:** Small stone right middle calyx. Pyelogram normal.

**Urine:** Specific gravity 1,018.

**Biochemistry:** Marked hypercalcuria and hyperphosphaturia.

**Stone Analysis:** Mixed calcium oxalate and apatite.

**Hyaluronidase Therapy:** 1,000 T.R.U. to 1,500 T.R.U. every 48 hours for six months.

**Result:** No change in the size of the plaque. The urinary specific gravity did not exceed 1,020.

## Group IV : The Stone-Passers.

**CASE 10.** Female, aged 42.

**Previous History:** Left upper calycectomy for stone. Passed numerous stones before and after operation.

**Condition before hyaluronidase:** Stones were passed with great regularity from both kidneys. They were small, (lentil size, or less), black and firm. They consisted almost entirely of a complex carbohydrate resembling mucopolysaccharide.

**I.V.P.:** No opaque stones and normal pyelograms.

Urine: Specific gravity 1,020; sterile.

Biochemistry: Normal.

Hyaluronidase Therapy: 500 to 1,000 T.R.U. for six months.

Result: Continued to pass stones.
Specific gravity of urine never rose above 1,020.

**CASE 11.** Male, aged 49.

**Previous History:** 1945: Left lower ureterolithotomy.
1948: Left pyelolithotomy.

Since operation passed 3 or 4 stones each year, composed of calcium phosphate.

Condition before hyaluronidase: I.V.P.: No stones in urinary tract.
Pyelograms normal.

Urine: Specific gravity 1,016. Sterile.

Biochemistry: Normal.

Hyaluronidase Therapy: 500 to 1,000 T.R.U. every 48 hours for nine months.

Result: Continued to pass stones.
Specific gravity rose to 1,026.

CASE 12. Male, aged 34.

**Previous History:** 1948: Left lower ureterolithotomy.
Since then has passed stones (oxalate) regularly.

Condition before hyaluronidase: I.V.P.: No stones, and pyelograms normal.

Urine: Specific gravity 1,022; sterile.

Biochemistry: Normal.

Hyaluronidase Therapy: 500 to 1,000 T.R.U. every 48 hours for six months.

Result: Passed three stones during this period.

# TABLE 47

## BILATERAL CALCULI

## AGE AT DIAGNOSIS OR OPERATION

| Age in Years | Number | |
|---|---|---|
| 0 - 5 | - | |
| 6 - 10 | 2 | |
| 11 - 15 | 2 | |
| 16 - 20 | 4 | |
| 21 - 25 | 3 | |
| 26 - 30 | 16 | |
| 31 - 35 | 14 | |
| 36 - 40 | 14 | |
| 41 - 45 | 26 | - 75.1% |
| 46 - 50 | 26 | |
| 51 - 55 | 16 | |
| 56 - 60 | 11 | |
| 60 - 65 | 4 | |
| 66 - 70 | 10 | |
| 76 - 80 | 1 | |

# TABLE 48

## BILATERAL STONE

## BIOCHEMISTRY

(a) BLOOD CHEMISTRY (53 CASES)

| | | |
|---|---|---|
| Normal | 35 | |
| 1st Stage Biochemical Osteomalacia | 9 | |
| Hyperglobulinaemia | 8 | |
| Hyperparathyroidism | 1 | (Not yet proven histologically) |

(b) URINARY CALCIUM OUTPUT (19 CASES)

| | |
|---|---|
| Normal | 9 |
| High Normal | 3 |
| Raised | 7 |

(c) STONE ANALYSIS (33 CASES)

| | |
|---|---|
| Calcium Oxalate | 16 |
| Calcium Oxalate + Calcium Phosphate | 4 |
| Calcium Phosphate | 11 |
| Ammonium Magnesium Phosphate | 2 |

TABLE 49. COURSE OF 47 CASES OF BILATERAL UNBRANCHED CALCULI TREATED BY OPERATION

| Present Condition | Symptoms Present | Symptoms None | Total | TREATMENT: Unilateral Conservative | TREATMENT: Unilateral Conservative + Nephrectomy | TREATMENT: Nephrectomy | TREATMENT: Bilateral Conservative |
|---|---|---|---|---|---|---|---|
| Died – other causes | – | – | 2 | 2 | – | – | – |
| Clear | – | 16 | 16 | 8 | 2 | 2 | 4 |
| Leaving | | | 29 | | | | |
| Original stone remains untreated | 1 | 8 | 9 | 9 | – | – | – |
| Mild recurrence | 3 | 10 | 13 | 11 | – | – | 2 |
| Severe recurrence | 7 | – | 7 | 4 | 1 | – | 2 |
| Totals | 11 | 18 | 47 | 34 | 3 | 2 | 8 |

SUMMARY

Died or clear 18

Stones present 29 – Symptoms 11; No symptoms 18

| | |
|---|---|
| Original untreated | 9 |
| Mild recurrence | 13 |
| Severe recurrence | 7 |

TABLE 50

## BILATERAL STONE

## UNILATERAL BRANCHED, UNILATERAL UNBRANCHED

## RESULTS OF OPERATION - 26 CASES

| No. | Operation (See Code) | Followed (Years) | Alive or Dead | Symptoms Now | Recurrence Now | Result or Present Condition. |
|---|---|---|---|---|---|---|
| 1. | N.+ S.U.C. | Nil | Dead | - | - | Post-Op. death. |
| 2. | M.U.C.(2) | 5 | Dead | Yes | Yes | Uraemia. |
| 3. | S.U.C. | 6 | Dead | Unknown | Yes | Other causes. |
| 4. | N. | 25 | Dead | Yes | Yes | Other causes. |
| 5. | N. | 14 | Dead | No | Yes | Other causes. |
| 6. | S.B.C. | 11 | Dead | Yes | Yes | Other causes. |
| 7. | S.U.C. | 3 | Dead | No | No | Other causes. |
| 8. | S.U.C. | Nil | Unknown | - | - | Untraced. |
| 9. | M.B.C.(4) | Nil | Unknown | - | - | Untraced. |
| 10. | M.U.C.(3) | 19 | Alive | No | No | Good. |
| 11. | M.B.C.(4) + N. | 12 | Alive | No | No | Fair. |
| 12. | M.B.C.(3) + N. | 25 | Alive | No | No | Good. |
| 13. | S.U.C. + N. | 9 | Alive | No | No | Good. |
| 14. | S.U.C. + N. | 7 | Alive | No | No | Good. |
| 15. | S.U.C. + N. | 6 | Alive | No | No | Good. |
| 16. | S.U.C. | 16 | Alive | Yes | Yes | Orig.untreated stone I.S.Q. |
| 17. | M.U.C.(2) | 3 | Alive | No | Yes | Orig.untreated stone I.S.Q. |
| 18. | N. | 1 | Alive | No | No | Orig.untreated stone I.S.Q. |
| 19. | S.U.C. | 1 | Alive | No | No | Orig.untreated stone I.S.Q. |
| 20. | S.U.C. | 1 | Alive | No | No | Orig.untreated stone I.S.Q. |
| 21. | N. + S.U.C. | 7 | Alive | No | Yes | Good. |
| 22. | N. + S.U.C. | 7 | Alive | No | Yes | Poor. |
| 23. | M.U.C.(3) + N. | 42 | Alive | Yes | Yes | Good. |
| 24. | M.U.C.(2) | 6 | Alive | Yes | Yes | Poor. |
| 25. | M.B.C.(2) + N. | 11 | Alive | Yes | Yes | Poor. |
| 26. | S.U.C. | 24 | Alive | No | Yes | Good. |

CODE:

S.U.C. = Single Unilateral Conservative.
M.U.C. = Multiple Unilateral Conservative.
S.B.C. = Single Bilateral Conservative.
M.B.C. = Multiple Bilateral Conservative.
N. = Nephrectomy.

TABLE 51

UNILATERAL BRANCHED, UNILATERAL UNBRANCHED - 26 CASES

TREATED BY OPERATION

SUMMARY OF PROGRESS

| | | |
|---|---|---|
| Total cases | | 26 |
| Untraced | | 2 |
| Died | | 7 |
| Urinary causes | 2 | |
| Other causes | 5 | |

Information available about 22 (followed 1 to 42 years).

| | | |
|---|---|---|
| Clear - No symptoms | 7 | (followed 6,7,9,2,1,5, and 7 years) |
| Large original stone | 5 | (symptoms 1, no symptoms 4) |
| Mild recurrence | 4 | (symptoms 1, no symptoms 3) |
| Severe recurrence | 6 | (symptoms 5, no symptoms 1) |
| Total | 22 | |

Hence of 22, 15 are symptom-free and 7 have symptoms.

## TABLE 52

## BILATERAL STONE

## OPERATIVE TREATMENT 23 CASES BILATERAL BRANCHED CALCULI.

| No. | Operation (See code) | Period followed (in years) | Dead or Alive | Result or Present Condition |
|---|---|---|---|---|
| 1. | S.U.C. | Nil | Dead | Post-operative death. |
| 2. | S.U.C. | Nil | Dead | Post-operative death. |
| 3. | S.U.C. | Nil | Dead | Post-operative death. |
| 4. | N. + S.U.C. | 10 | Dead | Post-operative death. |
| 5. | S.B.C. | 8 | Dead | Post-operative death. |
| 6. | M.B.C. (4) | 10 | Dead | Post-operative death. |
| 7. | S.U.C. | 10 | Dead | Uraemia - aged 40. |
| 8. | M.B.C. (4) | 19 | Dead | Uraemia - aged 65. |
| 9. | M.B.C. (3) | 12 | Dead | Uraemia - aged 62. |
| 10. | S.U.C. | 10 | Dead | Unknown - other causes. |
| 11. | S.B.C. | Nil | Unknown | Untraced - unknown. |
| 12. | S.B.C. | Nil | Unknown | Untraced - unknown. |
| 13. | S.B.C. | Nil | Unknown | Untraced - unknown. |
| 14. | S.U.C. | 10 | Alive | Still stones both sides. |
| 15. | S.U.C. | 1 | Alive | Still stones both sides. |
| 16. | N. + S.U.C. | 8 | Alive | Stone in solitary kidney. |
| 17. | M.B.C. (5) | 26 | Alive | Still stones both sides. |
| 18. | S.B.C. | 3 | Alive | Still stones both sides. |
| 19. | S.B.C. | 6 | Alive | Stone one side. |
| 20. | S.U.C. + N. | 11 | Alive | Stone in solitary kidney. |
| 21. | S.U.C. + N. | 12 | Alive | Stone in solitary kidney. |
| 22. | S.U.C. | 3 | Alive | Original untreated stone. |
| 23. | S.U.C. | 3 | Alive | Original untreated stone. |

**CODE.**

S.U.C. = Single unilateral conservative operation.

M.U.C. = Multiple unilateral conservative operation.

S.B.C. = Single bilateral conservative operation.

M.B.C. = Multiple bilateral conservative operation.

N. = Nephrectomy.

Figures in brackets refer to total operations performed.

TABLE 53.

## BILATERAL CALCULI
## POST-OPERATIVE OR LATER URINE EXAMINATION
## 90 CASES

| Findings | Total Cases | Total having no op. | Now free from stone. | Stones still present | Total Op. | Clear or no recurr. | Stone present or recurr. | Clear TOTAL | Stone present TOTAL |
|---|---|---|---|---|---|---|---|---|---|
| Sterile | 40 | 16 | 8 | 8 | 24 | 17 | 7 | 25 | 15 |
| RBC + WBC | 17 | 2 | 0 | 2 | 15 | 2 | 13 | 2 | 15 |
| B.Coli | 18 | 6 | 1 | 5 | 12 | 1 | 11 | 2 | 16 |
| B.Coli + Strep.faec. | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 |
| Strep. faecalis | 2 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 2 |
| Proteus + staph.aur. | 2 | 2 | 0 | 2 | 0 | 0 | 0 | 0 | 2 |
| Staph. albus | 2 | 1 | 0 | 1 | 1 | 0 | 1 | 0 | 2 |
| Proteus vulgaris | 4 | 1 | 0 | 1 | 3 | 0 | 3 | 0 | 4 |
| Proteus + B.Coli | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 |
| Staph. aureus | 3 | 0 | 0 | 0 | 3 | 0 | 3 | 0 | 3 |
| Totals | 90 | 29 | 9 | 20 | 61 | 20 | 41 | 29 | 61 |

TABLE 53 (Summary)

## SUMMARIES

**TOTAL SERIES (90)**

| | No stone present | Stone present | Total | % Stone present |
|---|---|---|---|---|
| Sterile | 25 | 15 | 40 | 37.5 |
| Infected | 4 | 46 | 50 | 92.0 |
| Total | 29 | 61 | 90 | |
| Per cent infected | 13.8 | 75.4 | | |

**OPERATION SERIES (61)**

| | No recurr. | Recurr. | Total | % recurr. |
|---|---|---|---|---|
| Sterile | 17 | 7 | 24 | 29.2 |
| Infected | 3 | 34 | 37 | 91.9 |
| Total | 20 | 41 | 61 | |
| Per cent infected | 15.0 | 83.0 | | |

TABLE 54

ANALYSIS OF 204 STONES IN 193 PATIENTS

174 ORIGINAL AND 30 RECURRENT STONES

| Composition | Original Stones | Recurrent Stones | Total |
|---|---|---|---|
| 1. Calcium Oxalate. | 72 | 5 | 77 |
| 2. Calcium Oxalate + calcium phosphate. | 40 | 9 | 49 |
| 3. Calcium Oxalate + apatite. | 6 | 2 | 8 |
| 4. Calcium Oxalate + Amm.magn.phosphate. | 6 | 0 | 6 |
| 5. Calcium phosphate. | 27 | 11 | 38 |
| 6. Calcium phosphate + Amm.magn.phosphate. | 10 | 0 | 10 |
| 7. Ammonium magnesium phosphate. | 3 | 2 | 5 |
| 8. Apatite. | 4 | 0 | 4 |
| 9. Calcium carbonate + Amm.mag.phos. | 2 | 0 | 2 |
| 10. Ammonium urate. | 2 | 0 | 2 |
| 11. Uric acid. | 1 | 0 | 1 |
| 12. Cystine. | 1 | 0 | 1 |
| 13. Complex polysaccharide. | 0 | 1 | 1 |
| TOTAL: | 174 | 30 | 204 |

TABLE 55. ANALYSIS OF 174 ORIGINAL STONES

RELATIONSHIP TO RECURRENCE AND URINARY INFECTION

| Constituents | Total Oper. + No Op | STONE ANALYSIS: OPERATION | | | URINE EXAMINED: URINE | |
|---|---|---|---|---|---|---|
| | | No Recurrence | Recurrence | No Operation | Sterile | Infected |
| 1. Calcium oxalate. | 72 | 34 | 10 | 28 | 36 | 22 |
| 2. Calcium oxalate + calcium phosphate. | 40 | 26 | 5 | 9 | 19 | 16 |
| 3. Calcium oxalate + apatite. | 6 | 4 | 1 | 1 | 1 | 5 |
| 4. Calcium oxalate + "triple" phosphate. | 6 | 4 | 0 | 2 | 2 | 4 |
| 5. Calcium phosphate. | 27 | 14 | 6 | 7 | 6 | 17 |
| 6. Ammonium magnesium phosphate + calcium phosphate. | 10 | 6 | 2 | 2 | 0 | 8 |
| 7. Ammonium magnesium phosphate. | 3 | 2 | 0 | 1 | 1 | 2 |
| 8. Ammonium magnesium phosphate + calcium carbonate. | 2 | 1 | 0 | 1 | 1 | 0 |
| 9. Apatite. | 4 | 2 | 2 | 0 | 3 | 1 |
| 10. Ammonium urate. | 2 | 1 | 0 | 1 | 1 | 1 |
| 11. Uric acid. | 1 | 1 | 0 | 0 | 0 | 0 |
| 12. Cystine. | 1 | 1 | 0 | 0 | 1 | 0 |
| Total | 174 | 96 | 26 | 52 | 71 | 76 |

TABLE 56

Quantitative Analysis of 90 Upper Urinary Tract Stones for Principal Constituents. 10.1.1951 to 13.5.1955

| No. | Sex. | Calcium % in ash. | $PO_4$% in ash. | Mg.% in ash. | Oxal.% in stone. | Calcium % in stone. | $NH_3$ | Ash % |
|---|---|---|---|---|---|---|---|---|
| 1. | M. | 63.5 | - | - | - | 26.5 | - | 41.6 |
| 2. | M. | 54.9 | 0.98 | - | 62.4 | 24.6 | Tr. | 44.8 |
| 3. | M. | 60.2 | 0.62 | - | 63.5 | 29.6 | Tr. | 45.4 |
| 4. | M. | 69.4 | 4.74 | - | 78.9 | 29.3 | - | 42.2 |
| 5. | M. | 63.2 | 23.5 | - | - | 40.0 | - | 63.2 |
| 6. | F. | 66.0 | - | - | - | 26.1 | - | 39.4 |
| 7. | M. | 40.7 | 14.5 | - | 72.3 | 28.7 | - | 70.6 |
| 8. | M. | 59.6 | 7.7 | - | 82.2 | 26.0 | - | 43.6 |
| 9. | F. | 40.4 | 18.1 | - | 28.0 | 27.4 | + | 68.0 |
| 10. | M. | 55.4 | 15.8 | - | 51.7 | 26.0 | - | 47.0 |
| 11. | M. | 71.0 | 17.1 | 4.08 | - | 23.6 | - | 53.2 |
| 12. | M. | 43.6 | 17.2 | 0.6 | - | 31.7 | - | 72.8 |
| 13. | M. | 42.2 | 17.1 | 0.25 | 16.9 | 33.5 | + | 79.4 |
| 14. | M. | 42.5 | 17.5 | 1.43 | 23.0 | 31.3 | - | 73.6 |
| 15. | M. | 47.5 | 9.1 | - | 80.2 | 27.3 | - | 58.0 |
| 16. | M. | 39.5 | 13.6 | 0.25 | 35.3 | 29.0 | - | 73.4 |
| 17. | F. | 36.8 | 20.4 | 0.97 | 7.0 | 24.3 | - | 66.2 |
| 18. | M. | 49.2 | 14.1 | 1.03 | 63.4 | 30.0 | - | 61.0 |
| 19. | F. | 52.9 | 11.1 | - | 64.0 | 26.4 | - | 49.8 |
| 20. | M. | 56.9 | 11.1 | - | 71.3 | 28.4 | - | 50.0 |
| 21. | M. | 42.7 | 16.2 | - | 40.2 | 30.0 | - | 70.4 |
| 22. | M. | 56.7 | 1.6 | - | Insuff. | - | - | - |
| 23. | F. | 42.9 | 3.36 | - | 86.6 | 21.4 | - | 44.8 |
| 24. | M. | 29.7 | 16.4 | - | 10.2 | 23.9 | - | 80.6 |
| 25. | M. | 44.9 | 3.83 | - | 88.1 | 24.3 | - | 52.0 |
| 26. | M. | 38.9 | 12.23 | - | 68.5 | 26.2 | - | 67.4 |
| 27. | M. | 40.0 | 18.05 | - | 39.2 | 26.2 | - | 65.6 |
| 28. | M. | 40.4 | 1.5 | - | 95.7 | 19.4 | - | 48.0 |
| 29. | M. | 66.7 | - | - | 96.0 | 26.0 | - | 39.0 |
| 30. | M. | 62.5 | 9.4 | - | 65.0 | 28.4 | - | 45.4 |
| 31. | M. | 65.0 | 10.8 | - | 57.0 | 19.3 | - | 29.6 |
| 32. | M. | 52.9 | 14.4 | - | 57.0 | 27.8 | - | 52.6 |
| 33. | F. | 28.0 | 15.9 | 6.21 | 5.8 | 17.0 | + | 60.8 |
| 34. | F. | 49.1 | 11.4 | - | 54.7 | 28.6 | Ins. | 58.2 |
| 35. | M. | 66.5 | 3.1 | - | 88.0 | 25.1 | Ins. | 37.8 |
| 36. | F. | 35.0 | 0.87 | 1.95 | Insuff. | - | Ins. | 10.7 |
| 37. | F. | 40.6 | 1.97 | 2.70 | 26.0 | 30.7 | - | 75.8 |
| 38. | M. | 46.0 | 0.77 | - | 85.1 | 29.7 | - | 64.6 |
| 39. | M. | 62.6 | 0.82 | - | 98.6 | 28.0 | Ins. | 44.8 |
| 40. | M. | 63.8 | 0.42 | - | 86.2 | 25.3 | Ins. | 39.6 |
| 41. | M. | 20.4 | 15.30 | - | 38.5 | 13.1 | - | 64.2 |
| 42. | M. | 38.4 | 18.10 | 0.52 | 31.4 | 28.1 | - | 73.2 |
| 43. | M. | 36.4 | 17.4 | 0.74 | 31.7 | 26.9 | - | 74.0 |
| 44. | M. | 50.1 | 11.25 | 1.07 | 71.9 | 22.0 | - | 44.0 |
| 45. | M. | 47.6 | 9.89 | 1.16 | 69.1 | 23.1 | - | 48.6 |

TABLE 56 (Continued)

| No. | Sex. | Calcium % in ash. | $Po_4$% in ash. | Mg.% in ash. | Oxal.% in stone. | Calcium % in stone. | $NH_3$ | Ash % |
|---|---|---|---|---|---|---|---|---|
| 46. | M. | 54.9 | 19.1 | 1.61 | 33.4 | 29.0 | - | 71.2 |
| 47. | M. | 38.3 | 19.0 | 2.65 | 32.8 | 26.7 | - | 70.0 |
| 48. | M. | 18.6 | 23.2 | 8.90 | 2.0 | 11.8 | - | 68.4 |
| 49. | M. | 63.2 | 3.9 | - | 69.5 | 25.8 | - | 40.8 |
| 50. | M. | 14.4 | 26.6 | 11.0 | 4.3 | 7.3 | + | 51.2 |
| 51. | M. | 44.2 | 17.3 | - | 46.1 | 26.6 | - | 60.2 |
| 52. | F. | 33.0 | 22.2 | - | 26.6 | 25.6 | - | 77.6 |
| 53. | M. | 34.1 | 7.9 | 10.5 | 76.5 | 17.4 | - | 51.0 |
| 54. | M. | 13.6 | 3.1 | - | - | - | - | *79.0 |
| 55. | M. | 40.0 | 23.6 | 1.63 | 33.5 | - | - | 63.6 |
| 56. | F. | 27.0 | 25.1 | 1.59 | 8.5 | - | - | 65.2 |
| 57. | F. | 37.0 | 17.6 | 1.34 | 50.2 | - | Tr. | 62.2 |
| 58. | F. | 1.6 | 0.5 | - | - | Not done | - | 31.6 |
| 59. | F. | 19.8 | 35.3 | 4.9 | 54.0 | Not done | + | 53.2 |
| 60. | F. | 72.0 | 10.7 | - | - | Not done | - | 22.0 |
| 61. | F. | 42.0 | 19.7 | 1.1 | 5.5 | Not done | Tr. | 69.0 |
| 62. | F. | 22.2 | 20.8 | 4.0 | 6.6 | Not done | + | 73.0 |
| 63. | M. | 38.7 | 18.0 | - | 23.4 | Not done | - | 77.6 |
| 64. | F. | 53.0 | - | - | 67.6 | Not done | - | 40.0 |
| 65. | F. | 13.0 | 12.0 | - | 2.5 | Not done | - | 6.0 |
| 66. | M. | - | - | - | - | Not done | - | **91.0 |
| 67. | F. | 30.0 | 18.4 | 3.7 | 2.2 | Not done | + | 67.4 |
| 68. | M. | 17.5 | 22.0 | 10.2 | 1.7 | Not done | + | 57.0 |
| 69. | M. | 56.0 | 6.6 | - | 69.0 | Not done | - | 43.0 |
| 70. | M. | 37.7 | 8.4 | - | 15.5 | Not done | - | 76.4 |
| 71. | F. | 34.0 | 17.7 | 1.03 | 2.0 | Not done | + | 70.0 |
| 72. | M. | 23.0 | 16.8 | 1.0 | 5.0 | Not done | + | 59.0 |
| 73. | M. | 53.0 | 11.3 | - | 44.0 | Not done | - | 54.0 |
| 74. | F. | 47.0 | 9.0 | - | 40.6 | Not done | - | 61.0 |
| 75. | F. | 53.4 | 8.0 | - | 63.5 | Not done | - | 50.2 |
| 76. | M. | 72.5 | 3.0 | - | 93.5 | Not done | - | 38.6 |
| 77. | M. | - | - | - | 66.0 | Not done | - | - |
| 78. | M. | 59.0 | 6.0 | - | 74.0 | Not done | - | 47.6 |
| 79. | F. | 34.2 | 6.7 | 0.8 | 72.0 | Not done | + | 50.4 |
| 80. | M. | 30.0 | 10.7 | - | 24.4 | Not done | - | 62.0 |
| 81. | M. | 46.0 | 7.3 | - | 74.0 | Not done | - | 47.2 |
| 82. | M. | 38.0 | 18.3 | - | 4.0 | Not done | - | 71.0 |
| 83. | M. | 28.4 | 6.8 | - | Tr. | Not done | - | 86.8 |
| 84. | M. | 28.5 | 8.1 | - | 65.5 | Not done | - | 56.8 |
| 85. | M. | 12.1 | 18.6 | 5.4 | - | Not done | + | 62.8 |
| 86. | M. | - | - | - | 46.7 | Not done | - | - |
| 87. | M. | 41.0 | - | - | 64.0 | Not done | - | 70.0 |
| 88. | F. | 81.0 | - | - | 69.0 | Not done | - | 33.0 |
| 89. | F. | 77.0 | - | - | 76.0 | Not done | - | 36.4 |
| 90. | M. | 41.0 | 54.0 | - | 35.8 | Not done | + | 35.0 |

* Pure cystine stone.
** Pure uric acid stone.

TABLE 56a.

## ANALYSES OF URINARY CALCULI

### Theoretical Findings on Principal Compounds.

| Compound | Formula | % Composition | % Ash | % Composition of Ash |
|---|---|---|---|---|
| Calcium Oxalate | $Ca \begin{smallmatrix} COO \\ COO \end{smallmatrix} \cdot H_2O$ | Ca. 27.43, Ox. 61.61 | 38.4 | Ca. 71.47 |
| Calcium Phosphate | $Ca_3 (PO4)_2$ | Ca. 38.74, P. 19.99 | 100.0 | Ca. 38.74, P. 19.99 |
| Magnesium Ammonium Phosphate | $Mg.(NH_4) PO_4.6H_2O$ | Mg. 17.71, $NH_3$ 12.40, P. 22.56 | 45.5 | Mg. 21.85, P. 27.9 |
| Uric Acid | $C_5 H_4 N_4 O_3$ | - | Nil | - - |

Some Typical Results.

| Compound | % in dry Calculus | | % in Ash | | | Qual. $NH_3$ | Qual. Uric Acid | Qual. Carbonate |
|---|---|---|---|---|---|---|---|---|
| | Ash | Oxalate | Ca. | P. | Mg. | | | |
| Oxalate | 54.2<br>52.1 | 75.8 as<br>74.7 CaOx | 50.8<br>35.8 | 7.7<br>4.6 | Nil<br>Nil | Nil | Nil | Nil |
| Phosphate | 83.0<br>74.6 | 15.8<br>10.4 | 40.3<br>40.5 | 21.8<br>17.4 | Trace<br>- | Nil | Nil | Trace |
| Triple Phosphate | 57.4 | 1.82 | 4.4 | 36.3 | 9.8 | 4.1% In calculi | Nil | Nil |
| Urate | 2.0 | Uric Acid<br>73.2 | 53.0 | Nil | Nil | Nil | ++ | Nil |

TABLE 57

AVERAGE 24 HOUR URINARY EXCRETION OF CALCIUM, PHOSPHORUS AND CREATININE ON STANDARD LOW CALCIUM AND PHOSPHORUS DIET

| No. | Urinary Calcium Gms/24 hrs. | Urinary Phosphorus Gms/24 hrs. | Urinary Creatinine Gms/24 hrs. | Comments. |
|---|---|---|---|---|
| 1. | 0.158 | 0.65 | 1.18 | NR. |
| 2. | 0.213 | 0.454 | 1.24 | H. NR. |
| 3. | 0.21 | 0.36 | 0.95 | H. SR. |
| 4. | 0.313 | 0.245 | 1.03 | H. SR. |
| 5. | 0.093 | 0.153 | 0.99 | MR. |
| 6. | 0.157 | 1.39 | 0.99 | SR. |
| 7. | 0.116 | 0.621 | 1.07 | NR. |
| 8. | 0.019 | 0.084 | 0.65 | NR. |
| 9. | 0.139 | 0.355 | 1.08 | SR. |
| 10. | 0.299 | 1.00 | 1.51 | H. MR. |
| 11. | 0.258 | 1.14 | - | H. SR. |
| 12. | 0.12 | 0.83 | 1.03 | SR. |
| 13. | 0.21 | 0.365 | 0.87 | H. SR. |
| 14. | 0.38 | 0.231 | 0.86 | H. NR. |
| 15. | 0.19 | 0.17 | 1.07 | NR. |
| 16. | 0.093 | 0.495 | 1.06 | MR. |
| 17. | 0.33 | 0.405 | 0.95 | NR. |
| 18. | 0.078 | 0.394 | 1.14 | NR. |
| 19. | 0.26 | 0.46 | 0.94 | H. SR. |
| 20. | 0.452 | 2.75 | 1.16 | H. NR. |
| 21. | 0.073 | 0.30 | 0.50 | NR. |
| 22. | 0.15 | 0.34 | 1.03 | MR. |
| 23. | 0.22 | 0.63 | 1.12 | H. NR. |
| 24. | 0.185 | 0.333 | 0.456 | SR. |
| 25. | 0.17 | 0.26 | 1.04 | NR. |
| 26. | 0.122 | 0.317 | 1.00 | SR. |
| 27. | 0.367 | 1.33 | 1.94 | H. SR. |
| 28. | 0.16 | 0.41 | 0.45 | NR. |
| 29. | 0.26 | 0.72 | 1.31 | H. SR. |
| 30. | 0.114 | 0.29 | 1.80 | NR. |
| 31. | 0.356 | 0.494 | 0.88 | H. SR. |
| 32. | 0.08 | 0.15 | 0.58 | NR. |
| 33. | 0.26 | 0.62 | 1.25 | H. |
| 34. | 0.13 | 0.23 | 0.40 | NR. |
| 35. | 0.283 | 0.690 | 1.23 | H. MR. |
| 36. | 0.19 | 0.60 | 0.82 | NR. |
| 37. | 0.181 | 0.499 | 0.77 | NR. |
| 38. | 0.292 | 0.61 | 1.71 | H. NR. |
| 39. | 0.054 | 0.27 | 1.21 | |
| 40. | 0.15 | 0.56 | 2.09 | MR. |
| 41. | 0.15 | 0.424 | 1.04 | MR. |

TABLE 57 (Continued)

| No. | Urinary Calcium Gms/24 hrs. | Urinary Phosphorus Gms/24 hrs. | Urinary Creatinine Gms/24 hrs. | Comments. |
|---|---|---|---|---|
| 42. | 0.09 | 0.55 | 1.39 | NR. |
| 43. | 0.302 | 0.86 | 1.17 | H. NR. |
| 44. | 0.072 | 0.32 | 1.15 | |
| 45. | 0.206 | 0.416 | 0.824 | H. SR. |
| 46. | 0.190 | 0.665 | - | NR. |
| 47. | 0.088 | 0.38 | 0.63 | H. SR. |
| | 0.264 | 0.176 | 0.82 | H. SR. |
| 48. | 0.087 | 0.31 | 0.79 | SR. |
| 49. | 0.36 | 0.74 | 2.04 | H. NR. |
| 50. | 0.12 | 0.413 | 0.95 | NR. |
| 51. | 0.11 | 0.52 | 0.87 | NR. |
| 52. | 0.034 | 0.324 | 0.477 | NR. |
| 53. | 0.378 | 0.85 | 1.79 | H. NR. |
| 54. | 0.18 | 0.34 | 0.79 | NR. |
| 55. | 0.14 | 0.397 | 0.85 | |
| 56. | 0.23 | 0.27 | 0.68 | H. NR. |
| 57. | 0.44 | 0.803 | 1.82 | H. SR. |
| 58. | 0.231 | 0.62 | 1.4 | H. NR. |
| 59. | 0.055 | 0.44 | 0.93 | |
| 60. | 0.214 | 0.48 | 0.98 | H. NR. |
| 61. | 0.076 | 0.41 | - | SR. |
| 62. | 0.23 | 0.646 | 1.52 | H. NR. |
| 63. | 0.064 | 0.38 | 0.85 | NR. |
| 64. | 0.057 | 0.43 | 0.96 | MR. |
| 65. | 0.13 | 0.47 | 1.08 | NR. |
| 66. | 0.174 | - | - | MR. |
| 67. | 0.56 | 0.612 | - | H. MR. |

NR = No recurrence.
MR = Mild recurrence.
SR = Severe recurrence.
H = Hypercalcuria.

Hyperparathyroidism cases not included.
Hence accepting 0.20 gms Ca/24 hours as the upper limit of the normal urinary calcium excretion on a standard low calcium intake, 28 of these 67 patients had an abnormally high urinary calcium excretion (41.8%).

TABLE 58

BIOCHEMISTRY

RANGE OF CALCIUM, PHOSPHORUS, PROTEINS & PHOSPHATASE
(CASES OF HYPERPARATHYROIDISM OMITTED)

| Serum Calcium | | Serum Inorganic Phosphorus | | Plasma Proteins | | Serum Alkaline Phosphatase | |
|---|---|---|---|---|---|---|---|
| Mgms. Per cent | Cases | Mgms. Per cent | Cases | Gms. Per cent | Cases | K.A. Units | Cases |
| Under 8 | 1 | 1.5-2.0 | 4 | 5.6-6.0 | 4 | Under 4 | 7 |
| 8.0- 8.5 | 5 | 2.1-2.5 | 34 | 6.1-6.5 | 16 | 4- 6 | 55 |
| 8.6- 9.0 | 11 | 2.6-3.0 | 55 | 6.6-7.0 | 68 | 6- 8 | 57 |
| 9.1- 9.5 | 33 | 3.1-3.5 | 85 | 7.1-7.5 | 75 | 8-10 | 78 |
| 9.6-10.0 | 64 | 3.6-4.0 | 66 | 7.6-8.0 | 77 | 10-12 | 29 |
| 10.1-10.5 | 76 | 4.1-4.5 | 27 | 8.1-8.5 | 20 | 12-14 | 27 |
| 10.6-11.0 | 56 | 4.6-5.0 | 11 | 8.6-9.0 | 10 | 14-16 | 5 |
| 11.1-11.5 | 25 | 5.1-5.5 | 0 | Over9.0 | 1 | 16-20 | 16 |
| 11.6-12.0 | 12 | 5.6-6.0 | 3 | | | Over 20 | 12 |
| 12.1-12.5 | 3 | Over6.0 | 4 | | | | |
| Total | 286 | Total | 289 | Total | 271 | Total | 286 |
| Average | 10.0 mgms | Average | 3.4 mgms | Average | 7.4 Gms | Average | 9.5 K.A units |

TABLE 59

PLASMA PROTEINS IN 79 CASES

ALBUMIN, GLOBULIN and A/G RATIO.

| ALBUMIN | | GLOBULIN | | A/G RATIO | |
|---|---|---|---|---|---|
| Gms. Per Cent | Number | Gms. Per Cent | Number | A/G Index | Number |
| 2.8 | 1 | 1.9 | 1 | 0.6 | 1 |
| 2.9 | 0 | 2.0 | 2 | 0.7 | 1 |
| 3.0 | 0 | 2.1 | 0 | 0.8 | 0 |
| 3.1 | 0 | 2.2 | 0 | 0.9 | 3 |
| 3.2 | 1 | 2.3 | 2 | 1.0 | 5 |
| 3.3 | 0 | 2.4 | 1 | 1.1 | 6 |
| 3.4 | 1 | 2.5 | 4 | 1.2 | 10 |
| 3.5 | 1 | 2.6 | 4 | 1.3 | 12 |
| 3.6 | 4 | 2.7 | 7 | 1.4 | 11 |
| 3.7 | 5 | 2.8 | 5 | 1.5 | 8 |
| 3.8 | 4 | 2.9 | 5 | 1.6 | 7 |
| 3.9 | 5 | 3.0 | 4 | 1.7 | 5 |
| 4.0 | 6 | 3.1 | 9 | 1.8 | 5 |
| 4.1 | 6 | 3.2 | 4 | 1.9 | 0 |
| 4.2 | 3 | 3.3 | 4 | 2.0 | 3 |
| 4.3 | 2 | 3.4 | 5 | 2.1 | 0 |
| 4.4 | 10 | 3.5 | 7 | 2.2 | 1 |
| 4.5 | 6 | 3.6 | 2 | 2.3 | 0 |
| 4.6 | 6 | 3.7 | 1 | 2.4 | 1 |
| 4.7 | 8 | 3.8 | 3 | TOTAL | 79 |
| 4.8 | 2 | 3.9 | 2 | | |
| 4.9 | 2 | 4.0 | 0 | | |
| 5.0 | 2 | 4.1 | 2 | | |
| 5.1 | 2 | 4.2 | 0 | | |
| 5.2 | 0 | 4.3 | 1 | | |
| 5.3 | 0 | 4.4 | 1 | | |
| 5.4 | 1 | 4.5 | 0 | | |
| 5.5 | 1 | 4.6 | 3 | | |
| TOTAL | 79 | TOTAL | 79 | | |

TABLE 60

EXAMPLES OF "NORMAL VARIATIONS" OF BLOOD CHEMISTRY

| Patient All Males | Date | Serum Calcium Mgms % | Serum Inorganic Phosphorus Mgms % | Serum Alkaline Phosphatase K.A. Units | Plasma Proteins Gms % | Blood Urea Mgms % |
|---|---|---|---|---|---|---|
| T.A. | 16.10.52 | 11.7 | 2.04 | 6.5 | 6.4 | 46 |
| | 4.11.52 | 10.7 | 2.17 | 4.7 | - | 36 |
| | 13.11.52 | 10.3 | 2.14 | 5.5 | 6.7 | 32 |
| | 28. 9.55 | 11.1 | 2.6 | 4.9 | 7.8 | 34 |
| T.B. | 9. 6.55 | 10.8 | 3.2 | 9.0 | 6.6 | 27 |
| | 4. 7.55 | 9.2 | 3.5 | 9.2 | 6.8 | 28 |
| A.B. | 5.10.50 | 11.2 | 3.28 | 6.9 | 6.7 | 42 |
| | 9.11.55 | 10.5 | 2.5 | 9.7 | 7.3 | 35 |
| | 7.12.55 | 11.0 | 2.6 | 4.5 | 7.8 | 26 |
| W.B. | 19.10.55 | 11.9 | 2.8 | 7.4 | 7.4 | 25 |
| | 9.11.55 | 10.9 | 2.3 | 9.5 | 7.2 | 28 |
| | 16.11.55 | 10.4 | 4.0 | 5.9 | 7.0 | 30 |
| W.Br. | 10.10.49 | 12.2 | 3.43 | 4.7 | 7.4 | 26 |
| | 18.11.55 | 11.1 | 4.9 | 5.2 | 6.5 | 28 |
| | 25. 1.56 | 10.7 | 3.4 | 5.2 | 7.0 | 30 |
| | 2. 2.56 | 9.5 | 2.9 | 4.0 | 7.0 | 32 |
| D.B. | 14.10.54 | 9.9 | 3.6 | 20.0 | 7.2 | 32 |
| | 6. 3.56 | 10.3 | 2.12 | 8.8 | 7.8 | 43 |
| A.G. | 9.11.55 | 9.4 | 2.6 | 15.3 | 7.1 | 36 |
| | 29.11.55 | 11.4 | - | 6.8 | - | 25 |
| W.L. | 8. 9.55 | 9.2 | 3.4 | 4.0 | 7.1 | 20 |
| | 17. 4.56 | 11.7 | 4.0 | 5.7 | 6.9 | 33 |
| | 4. 5.56 | 11.0 | 3.4 | 6.6 | 6.7 | 27 |
| J.McN. | 13. 5.53 | 9.4 | 3.21 | 3.21 | 7.5 | 27 |
| | 22. 5.53 | 9.7 | 2.95 | 8.0 | 7.8 | 32 |
| | 20. 4.56 | 12.3 | 3.2 | 8.0 | 7.4 | 38 |

TABLE 61

SUMMARY OF BLOOD CHEMISTRY - 210 CASES

RELATIONSHIP TO RECURRENCE

| Findings | Total Oper & No Op. | Operation Total Op. | Operation No Recurrence. | Operation Recurrence. | No Operation |
|---|---|---|---|---|---|
| "Normal" | | | | | |
| 1. Normal. | 118 | 96 | 60 | 36 | 22 |
| 2. Normal blood + idiopathic hypercalcuria. | 28 | 26 | 15 | 11 | 2 |
| 3. Normal - wide variations. | 6 | 6 | 2 | 4 | 0 |
| 4. Calcium & phosphorus low normal. | 5 | 3 | 1 | 2 | 2 |
| 5. Calcium low normal Phosphorus normal. | 12 | 9 | 8 | 1 | 3 |
| 6. Calcium normal Phosphorus low normal. | 5 | 4 | 2 | 2 | 1 |
| Total "Normal" | 174 | 144 | 88 | 56 | 30 |
| "Abnormal" | | | | | |
| 1. Hyperparathyroidism. | 6 | 6 | 0 | 6 | 0 |
| 2. 1st Stage biochemical oesteomalacia. | 9 | 7 | 1 | 6 | 2 |
| 3. 2nd stage biochemical oesteomalacia. | 4 | 4 | 2 | 2 | 0 |
| 4. Increased phosphorus, phosphatase & urea. (Renal failure) | 9 | 9 | 7 | 2 | 0 |
| 5. Increased phosphatase | 8 | 7 | 3 | 4 | 1 |
| Total "Abnormal" | 36 | 33 | 13 | 20 | 3 |
| Total "Normal" + "Abnormal" | 210 | 177 | 101 | 76 | 33 |

Globulin 3.5 or more in 22/79 cases. (7 no recurrence, 11 recurrence, 4 no operation).

# CHEMICAL ANALYSIS OF URINARY CALCULI

Devised by Mr.A.J.Kenny,Biochemistry Dept.,Victoria Infirmary.
(Unpublished)

* * * * *

## Preliminary Treatment and Examination.

The sample is cleaned, dried and weighed. Its dimension and a description of the stone are recorded and, where possible, the stone should be sectioned and examined for concentric lamination and the nature of the nucleus where present. It should then be powdered in whole or in part and the following qualitative and quantitative tests performed.

1. Ash.

Ignite 50 mg. of the uniform powder in a weighed crucible over a bunsen burner. Heat gently at first and note any peculiar odour or flame colouration, then gradually increase the flame to red heat to complete combustion of all organic matter. Cool the crucible in desicator and its contents and weigh to find the percentage of ash.
Weight of ash in mg. x 2 = Ash per cent. From this finding it is possible to say whether the calculus is largely organic or inorganic. If the ash content is small, a urate, cystine or xanthine calculus may be indicated.
Cystine gives a pale blue flame. Xanthine gives no characteristic flame but the calculus should have a waxy consistency.
For cystine stones, see detailed tests in Harrison's Chemical Methods in Clinical Medicine, 3rd ed., p.69, and for xanthine stones see Hawk, Practical Physiol. Methods, 15th ed., p.805.
Dissolve the cold ash in 3 ml. 50 per cent. HCl, heat to aid solution and finally wash into a 50 ml. volumetric flask.

2. Urates and Uric Acid. (Murexide Test).

Place a small quantity of the powder in a white porcelain evaporating basin or crucible and an equal quantity of uric acid in another to act as a control, To each add sufficient concentrated nitric acid to form a thin paste and heat to dryness on a boiling water bath. It may be necessary to add a further small quantity of nitric acid and re-evaporate in order to obtain full colour development. An intense red colouration should be present in the control and may be used for comparison against the unknown.

3. Carbonate.

A small quantity of powder is taken and acidified with 25 per cent. HCl. Examine for evolution of $CO_2$ by sight and the sound of the evolving gas.

4. Ammonia.

To a small quantity of the powder in a test tube add with a pipette some 20 per cent. NaOH and test for $NH_3$ with moistened red litmus paper and by smell. Warm slightly in a water bath and continue to test. $NH_3$ evolved in the cold is due to ammonium salts. If evolved only after prolonged heating it may be due to urate or other nitrogenous compound.

5. Oxalate.

Take 10 mg. of the powder and add 5 mls. $2NH_2SO_4$. Warm at 70°C until dissolved and titrate with 0.02 N $KMnO_4$. A significant titration in the absence of * urates indicates the presence of oxalate.

Calculation: (Titration-Blank) x 14.6 = Ca (OOC) $.H_2O$ per cent in calculus.

The presence of oxalate may be confirmed by heating a small quantity of the powder for a short time at dull red heat. The dark residue should give a definite reaction for carbonate on the addition of dilute mineral acid.

* If ash negligible and (murexide test) urate positive. Calculate as uric acid.

Calculation: 14.7 x titration = % uric calcium in dry calculus.

6. Calcium.

Take 1 ml. of the ash solution in a 15 ml. centrifuge tube and add 2 ml. water and 2 ml. saturated ammonium oxalate. The reaction should then be adjusted to greenish blue with bromo cresol green as an internal indicator i.e. to pH 4.5, using a drop of 25 per cent. $NH_4OH$. Allow to stand for one hour and continue as for serum calcium. Retain supernatant for Mg. estimation. Titrate with 0.01N $KMnO_4$.

Calculation: $\frac{\text{(Titration-Blank) x 2000}}{\text{\% ash in calculus.}}$ = Ca per cent in ash.

7. Phosphorus.

Make 1 in 10 dilution of ash solution and take 1 ml. into 13 ml. water in test tube. Add 4 ml. molybdic acid reagent and 2 ml. dilute stannous chloride as used in serum phosphorus estimation.
Read off on serum phosphorus graph as mg. per 100 ml.

Calculation: $\frac{\text{mg. P found x 400}}{\text{\% ash in calculus}}$ = P per cent in ash.

8. Magnesium.

Take all the supernatant fluid from the Ca estimation into a 12 ml. finely tapered centrifuge tube. Add 0.5 ml. 5% $(NH_4)_2HPO_4$ solution and 2 drops concentrated $NH_4OH$.

Allow to stand two hours, then centrifuge. Wash three times with 5 ml. 33 per cent. $NH_4OH$ solution and finally drain. Warm until all ammonia has evaporated and dissolve in 10 ml. water.

Take 2 ml. of this solution and add 12 ml. water followed by 4 ml. molybdic acid $Sn\,Cl_2$ and 2 ml. reducing agent. Allow to stand for five minutes and read off on serum phosphorus graph as mg. P per 100 ml.

Calculation: $\frac{\text{mg. P found x 157}}{\text{\% ash in calculus}}$ = Mg. per cent in ash.

* * * * * * *

# METHODS OF ANALYSIS.

## Serum.

(1) Calcium by the method of Clark, E.P., and Collip, J.B. (1925) modified to include a standard calcium chloride solution with each batch tested. (J.Biochem.Chem.63, 461).

(2) Inorganic Phosphorus by the method of Youngburg, G.E., and Youngburg, N.V. (1930) - J.Lab.Clin.Med., 16, 158.

(3) Alkaline-Phosphatase by the method of King, E.J., and Armstrong, A.R. (1934). Canad.med.ass.J. 31, 376.

Plasma Protein, as described in Hawk, Oser and Summerson's "Practical Physiological Chemistry", Churchill, London,1947.

## Urine.

(a) The urinary calcium of patients on the low calcium diet is determined by a modification of the method for the analysis of calcium in foodstuffs (Technical Communication, No.9, Imperial Bureau of Animal Nutrition, 1937).

(b) Rough assessment of the urinary calcium content is made by the method of Silkowitch, described in"The Parathyroid Glands and Metabolic Bone Disease."

* * * * *

Table 62. Biochemical Results in Cases of Hyperparathyroidism.

| | Normal Value | Case Number 1 | 2 | 3 | 4 | 5 | 6 | Per cent with Pos. Results |
|---|---|---|---|---|---|---|---|---|
| Sex<br>Age<br>Skeleton | | M<br>57<br>+ | F<br>41<br>Nil | F<br>43<br>+ | M<br>62<br>+ | F<br>62<br>Nil | M<br>45<br>+ | |
| **Blood Chemistry** | | | | | | | | |
| Serum Calcium | 9.5 - 11.5 mgm. | 14.4 | 13.6 | 13.2 | 12.8 | 13.0 | 12.6 | -100% |
| Serum Phosphorus | 2.4 - 4.0 mg.% | 2.0 | 1.8 | 2.1 | 1.8 | 2.1 | 2.2 | |
| Serum Alkaline Phosphatase | 3-13 K.A. Units. | 21-22 | 4-7 | 13-17 | 10-13 | 16-21 | 15 | |
| **Calcium Balance** (24-hours). | | | | | | | | |
| Urinary Calcium Excretion. | Under 150 mg.Ca | 406 | 386 | 241 | 354 | 326 | ... | 100% |
| Negative Calcium Balance. | Under 130 mg.Ca | 139 | 191 | 174 | 327 | 283 | ... | 100% |
| **Induced Hyper-Calcaemia Test.** | | | | | | | | |
| (a) Rise in Serum Phosph. | 0.4 - 2.4 mgm.% | ... | 1.6 | 0.7 | 1.3 | 0.9 | ... | ? |
| (b) Per cent fall in Urinary Phosphorus. | -18 to -66 | ... | -19 | nil | -13 | -7 | ... | 75% |
| (c) Four-hour skeletal calcium retention. | 50 - 60% of dose infused. | ... | ... | ... | 29 | ... | ... | ? |
| **Renal Phosphorus Clearance.** | 4 - 14 | 38 | 28 | 22 | 33 | 18 | ... | 100% |
| **Urea Clearance.** | Over 70% | 58 | 64 | 73 | 67 | 37 | ... | |