

RENAL STONE

A STUDY OF 520 PATIENTS WITH SPECIAL REFERENCE TO THE PATTERN OF RECURRENCE

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This study has been carried out on a group of 520 patients with renal stone. The cases were seen in the Department of Urology, Leeds, during a period of 2 years 1955-56. No selection was made in relation to duration of attendance. All the cases were seen regularly for follow-up after their first attendance.

The first impression gained on studying these cases was that they could be divided into 2 main groups viz:

1. *Cases presenting with their first renal stone.* The number of cases falling into this group was 419 (80%). Of these, 365 cases (87%) presented with a unilateral stone and 54 cases (13%) presented with bilateral stone.

2. *Cases presenting as recurrent renal stone.* The cases in this group numbered 101 (20%).

The term 'renal stone' is used in this paper to indicate either a single calculus or multiple calculi, unilateral or bilateral. The term 'recurrence' is used to indicate the development—isolated or repeated—of further stone, after removal or spontaneous passage of a previous stone, or in the presence of a previous stone.

RENAL CALCULOUS DISEASE

The term renal calculous disease is here used to denote the presence of renal stone as the clinical manifestation of a disease process affecting the renal tissue. Certain cases have an established etiological agent, such as hyperparathyroidism, primary renal acidosis, cystinuria, or recumbency. The vast majority of cases, however, have no proven etiological agent, although in some there are associated conditions suspected as etiological and as yet under investigation. For the group as a whole the term 'renal calculous disease' is suggested until more precise knowledge of the various etiological agents is available. Renal calculous disease may present clinically as a unilateral or a bilateral condition.

Unilateral Calculous Disease

Here the disease process appears to affect only one kidney. In this series there were 399 cases (76%) in which the disease has remained unilateral up to the present date. This group can be further divided into:

1. *Cases with no recurrence.* There were 342 such cases (86%), of which 153 (45%) presented as a ureteric stone.
2. *Cases with ipsilateral recurrence,* numbering 57 (14%).

Bilateral Calculous Disease

Clinically there are two distinct groups of cases in which both kidneys are affected by the disease process: (1) Cases presenting initially with bilateral stone, and (2) cases where both kidneys become affected at an interval of time, i.e. initially unilateral cases developing a contralateral recurrence. Both must be taken into account in assessing the incidence of bilateral calculous disease.

1. *Cases presenting initially with bilateral stone.* There were 54 such cases among the 419 seen with their first stone (13%). Among those which had recurred when first seen, 10 cases were known to be bilateral originally. A survey

TABLE I. INCIDENCE OF BILATERAL STONE

Year	Series	Incidence %
1917..	Kummel	16.0
1918..	Braasch	12.3
1924..	Chute	18.0
1925..	Thomas	12.0
1934..	Winsbury-White	13.0
1938..	Andres	16.4
1939..	Parmenter	8.0
1956..	Modlin	13.0

of the literature reporting the incidence of bilateral stone is presented in Table I. The reported incidence has been fairly constant.

2. *Cases with contralateral recurrence,* i.e. those where the second kidney became involved at a later stage. In the series of 520 cases there were 57 such cases.

Bilateral renal involvement by stone at some stage thus occurred in a total of 121 cases i.e. 24%, as compared with

13% presenting initially with bilateral stone. Correctly assessed in this way, there is thus a higher incidence of bilateral renal involvement than is generally stated.

PATTERNS OF RECURRENCE

Total Recurrence Rate

In the whole series there have been 48 cases that have developed recurrence since first attending the department, i.e. a 9% recurrence rate. This figure is not related to time; it is the figure at the time of studying the series. A survey

TABLE II. INCIDENCE OF RECURRENCE OF RENAL STONE

Year	Series	Recurrence Rate %
1924..	Chute	32.0
1924..	Braasch and Foulds	10.79
1925..	Thomas	33.0
1931..	Herbst	15.0
1933..	Higgins	16.4
1940..	Twinem	8.0
1956..	Modlin	9.0

of recurrence rates as reported by various observers is given in Table II. It will be seen that the last two figures in the table almost correspond. As Twinem's survey¹ was carried out in the USA, the recurrence rate would not seem to be influenced geographically, nor has it altered in the past decade.

Recurrence in cases that presented with their first renal stone

In this group of 419 cases the number of cases that have developed recurrence while under observation has been 32 (8%). The following is an analysis of the site of recurrence:

Cases developing ipsilateral recurrence ..	14
Cases developing contralateral recurrence ..	9
Cases of bilateral stone developing recurrence ..	9

Recurrence in cases that presented as recurrent renal stone

There were 101 cases in this group. The following is an analysis of their recurrence pattern up to the time of presenting at the department:

Cases with ipsilateral recurrence only ..	49
Cases with contralateral recurrence ..	28
Cases presenting with bilateral stone ..	24

The last group of 24 was further analysed as follows to determine what was the pattern of recurrence that had resulted in their presenting with bilateral stone:

Ten cases had in fact started as bilateral renal stone and had subsequently developed recurrence, with which they presented still as bilateral stone. The remaining 14 cases were originally unilateral. Of these 12 had become bilateral by developing bilateral recurrence (i.e. ipsilateral and contralateral recurrence), and the remaining 2 had become bilateral as the result of contralateral recurrence. Thus in all 14 there was contralateral recurrence.

Of the 49 cases in this group seen with ipsilateral recurrence only, 6 developed contralateral recurrence while under observation; thus the number of cases in this group remaining as pure ipsilateral recurrence was 43.

Reference to this analysis will be made again later.

Recurrence in this group while under observation. In this group of 101 patients who presented with recurrence, 16

GROUP	SITE OF PREVIOUS CALCULUS	SITE OF CALCULUS WHEN FIRST SEEN IN THE DEPARTMENT	SITE OF RECURRENCE DURING OBSERVATION	NUMBER OF CASES
I				2
II				2
III				3
IV				1
V				2
VI				3
VII				3

Fig. 1. Patterns of Recurrence. The black kidney denotes the affected side (see Table III).

developed a further recurrence (16%). This figure is double the recurrence rate in patients with first stone. The chance of recurrence after subsequent stone is thus twice as great as the chance of recurrence after first stone. An analysis of the recurrence history in these 16 cases was made by means of a series of diagrams (Fig. 1). The descriptive details are given in Table III and reference to Fig. 1 will assist in the interpretation

TABLE III. FURTHER RECURRENCES IN CASES FIRST SEEN AS RECURRENCES

Group	Description	No. of Cases
Group I	Ipsilateral recurrence in an ipsilateral recurrer	2
Group II	Contralateral recurrence in a contralateral recurrer	2
Group III	Ipsilateral recurrence in a contralateral recurrer	3
Group IV	Contralateral recurrence in an ipsilateral and contralateral recurrer	1
Group V	Ipsilateral recurrence in a bilateral recurrer	2
Group VI	Contralateral recurrence in an ipsilateral recurrer	3
Group VII	Bilateral recurrence in an ipsilateral recurrer	3
	Total	16

of the terms used. The series of diagrams clearly demonstrates the various patterns of recurrence that may occur and enables each recurrence to be correctly interpreted. Six

cases of true contralateral recurrence in this group were detected in this way.

The patterns illustrated in Fig. 1 probably occur throughout renal-stone recurrence and these 16 cases provided an excellent opportunity of studying this feature. Of importance is the demonstration that there may at any time in the natural history of the disease process be contralateral recurrence (groups VI and VII, Fig. 1).

Contralateral Recurrence

The recurrences in the various groups of cases have been analysed in the preceding paragraphs. By means of these analyses it was possible to pick out all the cases with contralateral recurrence and these have been assembled in the manner shown in Table IV. In the whole series there were 57 cases with contralateral recurrence.

The total number of cases in the series with a recurrence was 133, made up of 101 cases which had already recurred when first seen and 32 cases, seen initially with their first stone, which developed a recurrence while under observation. In the group of 101, 10 started as bilateral stone and in the group of 32, 9 were initially bilateral. Excluding these 19

TABLE IV. CONTRALATERAL RECURRENCES

Group	Description of Cases	No. of Cases
I	Among those seen with their first stone	9
II	Among recurrers when first seen: Unilateral stone cases which were contralateral recurrences when first seen	28
	Cases seen as bilateral stone; as a result of a bilateral recurrence in a unilateral stone (i.e. ipsilateral and contralateral recurrence)	12
	Cases seen as bilateral; as a result of a contralateral recurrence only	2
III	Among recurrences in cases which were recurrers when first seen: Contralateral recurrence in a case first seen as an ipsilateral recurrer (Group VI, Table III)	3
	Bilateral recurrence in a case first seen as an ipsilateral recurrer (Group VII, Table III)	3
	Total	57

cases of initially bilateral stone, there remain 114 cases of unilateral stone with recurrence. Of these 114 cases, as shown in Table IV, 57 were cases of contralateral recurrence i.e. 50%. Thus the chance of stone recurrence in the kidney not affected is as great as the chance of recurrence in the previously affected kidney. This is of considerable importance in studying the etiology of renal calculous disease and in the prevention of recurrence by present methods.

For the purpose of comparative study these 57 cases were divided into 2 groups:

1. The cases that had developed contralateral recurrence after investigation and treatment elsewhere. They numbered 42 (group II, Table IV).

2. The cases that developed contralateral recurrence after investigation and treatment in the department. They numbered 15 (groups I and III, Table IV).

Dealing only with unilateral calculous disease, in the first group there was a total of 91 cases with recurrence, the 42 cases with contralateral recurrence representing 46% of this total. In the second group there was a total of 37

cases with recurrence, the 15 cases with a contralateral recurrence representing 40% of this total. The small drop in percentage may possibly be accounted for by the elimination, in a specialized department, of the known etiological agents, but the difference is so small as to confirm the great extent to which the nature of the disease remains unknown.

Ipsilateral Recurrence in unilateral calculous disease

The number of cases of ipsilateral recurrence in unilateral calculous disease in this series was 57. For the purpose of comparison these were divided into 2 groups depending on whether they were treated for their previous stone elsewhere or in this unit:

1. There were 43 cases with ipsilateral recurrence after treatment elsewhere (when first seen there were 49 cases, but 6 later developed contralateral recurrence while under observation). This represents 47% of the total of 91 cases of unilateral stone with recurrence in this group.

2. There were 14 cases that developed ipsilateral recurrence after treatment on this unit. This represents 60% of the total of 23 unilateral stone cases with recurrence in this group. As the first group have had renal calculous disease for a longer period, the figure of 47% is probably more nearly correct. It can be confidently expected that in the second group more cases will ultimately develop a contralateral recurrence as the natural history of the disease process proceeds unchecked (Groups VI and VII, Fig. 1). The figure of 60% is thus an interim one and will decrease in time with an increase in contralateral recurrence rate.

Recurrence in cases presenting with bilateral stone

There were 54 cases with bilateral stone among the 419 cases seen with their first stone. Of these 54 cases, 9 have had recurrence while under observation, i.e. 17%. This is almost double the total recurrence rate.

ETIOLOGY

Certain factors are dealt with in Table V.

Sex

In the total series the ratio of male to female is 2:1. The ratio is the same in unilateral first stone cases without recurrence and is about 3:1 in cases with ipsilateral recurrence. In cases with contralateral recurrence there is a decided increase in the proportion of females affected, and in bilateral stone the sexes were almost equally affected. Thus it would seem that whatever factor operates in affecting both kidneys does so with increasing frequency in females, when compared with unilateral calculous disease, and that bilateral calculous disease affects the sexes almost equally. In searching

for causes of bilateral calculous disease, factors related to sex *per se* can apparently be eliminated.

Family History

A history of stone in father, mother, grandparents, brothers, sisters or children is surprisingly frequent in all groups. The figure is fairly constant throughout the various groups (Table V).

Further investigation is required to see whether there is a genetic or an environmental basis for this. It should be considered along with reports of geographical 'stone forming areas'.

Renal Infection

In the investigation of renal infection as an etiological agent, careful evaluation was made of the history and definite proof was demanded of renal infection prior to stone formation. Infection at the time of examination, in the presence of or following stone, was not in itself regarded as sufficient evidence. Evaluated in this manner, renal infection was found fairly consistently throughout the groups (Table V). It does not occur with significantly greater frequency in the recurrences, and in fact in the ipsilateral recurrences it operates less frequently, which is contrary to what one would expect if it were a significant etiological factor.

Hypercalciuria

Hypercalciuria has been said by some investigators to play a part in renal stone formation (Flocks²). In this series the total number of cases with a urinary calcium output, on a normal diet, of over 350 mg. per 24 hours was 50 (excluding cases of hyperparathyroidism). Of these, 45 were males and 5 were females, a ratio of male to female of 9:1. In a recent review by Hodgkinson³ of the urinary calcium output in a group of 320 cases of renal stone the ratio of male to female among the hypercalciurics (i.e. with an output of over 350 mg. of calcium in 24 hours on a normal diet) was 4:1. The ratio probably lies somewhere between these two sets of figures, but what seems certain is that there is a marked preponderance of males. As can be seen in Table V, as we come to examine the cases with bilateral calculi and contralateral recurrences (i.e. the cases of bilateral calculous disease) the ratio of male to female is altered so that the number of females increases and approximates to the number of males. If hypercalciuria were causal or contributory in renal stone formation, one would expect it to act equally in relation to both kidneys and the cases with bilateral renal involvement should be predominantly male. In bilateral renal calculous disease, however, the sexes are equally affected, thus making it difficult to substantiate a claim for hypercalciuria *per se* as an etiological factor.

TABLE V. INCIDENCE OF FACTORS IN THE VARIOUS GROUPS

	Total Series	Unilateral Stone and no Recurrence	Ipsilateral Recurrence	Unilateral Calculous Disease	Contralateral Recurrence	Bilateral Stone	Bilateral Calculous Disease
No. of Cases	520	342	57	399	57	64	121
Male	65%	66%	74%	70%	58%	53%	55%
Female	35%	34%	26%	30%	42%	47%	45%
Family History	10%	10%	9%	10%	10%	16%	13%
Renal Infection	10%	9%	7%	8%	12%	11%	11%

CONCLUSIONS

The total recurrence rate of renal stone in this series was 9%. This rate has not decreased in the last decade and does not appear to be influenced by geographical factors.

The recurrence rate after first stone was 8% and recurrence rate after subsequent stones was 16%. Thus the chance of a recurrence after subsequent stones is twice as great as the chance of a recurrence after a first stone.

The contralateral recurrence rate is 50% of the recurrence rate, as compared with figures ranging from 11% to 15%

previously reported. Thus the chance of a recurrence in cases presenting with unilateral stone is the same in both kidneys.

The incidence of bilateral stone when first seen was 13%. The incidence of bilateral renal involvement by stone at any stage, however, was 24%.

The recurrence rate in cases presenting initially with unilateral stone was 6%.

The recurrence rate in cases presenting initially with bilateral stone was 17%, which is 3 times the rate of recurrence in unilateral first stone and double the total recurrence rate.

It would appear that abnormal changes occur in renal tissue, as a result of which there may be stone formation. In most instances the causative factor and its associated manifestations are unknown, renal stone being the only manifestation. Little is known regarding either the precise nature of the renal changes or the exact mechanism of stone formation.

True bilateral renal involvement by stone, as assessed above, occurred in 24% of patients in this series. It has also been demonstrated that when there is stone recurrence it is as likely to be in the unaffected as in the previously affected kidney; that it to say, 50% of recurrences are contralateral. These two features suggest that the abnormal changes in renal tissue are probably originally bilateral. The changes may exist temporarily, which is suggested by the fact that no recurrence of stone takes place in some cases; or intermittently or continuously as is suggested by the various patterns and rates of recurrence.

In bilateral calculous disease the sexes are equally affected and if bilateral involvement by stone could be regarded as

an end state in the natural history of the abnormal renal changes, then sex-determined factors do not appear to play a part in etiology. The role of infection in etiology, if correctly assessed, would seem to be of less significance than previously thought. Hypercalciuria *per se* does not appear to be an etiological factor. There does however, appear to be a family history in an appreciable number of cases and this requires further investigation.

SUMMARY

A study has been made of 520 patients with renal stone.

True bilateral involvement by stone was found to occur in 24% of these patients.

The various patterns of recurrence have been worked out. A most striking feature is a contralateral recurrence rate of 50%.

Certain conclusions have been drawn regarding the abnormal renal changes occurring in patients with renal stone.

An attempt has been made to evaluate the role in etiology of sex, family history, renal infection and hypercalciuria.

The term renal calculous disease is suggested for a group of conditions having renal stone as a clinical manifestation.

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