one-stage test of Quick remains a satisfactory method of control in the great majority of cases on coumarin therapy. It is well to bear in mind, however, that occasionally such severe prothrombin deficiency may exist, together with bleeding or the imminent danger of it, when the Quick test, measuring as it does factor VII and not prothrombin, is reassuringly near or even within the therapeutic range.

In the cases of liver disease described here the situation is different. Neither of them showed more than slight prolongation of the clotting-time in the one-stage test, and on the classical interpretation of this test the hypoprothrombinaemia would be slight. Yet these patients showed haemorrhage and true prothrombin levels in the region of 10%. In such cases the Quick test may give a quite misleading indication of the tendency to bleed, showing as it does evidence only of moderate factor VII depression and no indication of the severe hypoprothrombinaemia.

In neither of these two groups can it be assumed that this deficiency in prothrombin is the necessary or only cause of the haemorrhage, but in these cases it is the one constant and common factor, suggesting a possible aetiological relationship. It should be stated, however, that other patients have been studied in whom the prothrombin measured by the two-stage area method was below 10% of normal and yet no bleeding occurred, so that other factors are probably concerned in the onset of haemorrhage.

It is common practice to measure the effect of vitamin K preparations by the changes in the one-stage Quick test. Cases 2 and 3 illustrate how fallacious this may be. The efficacy of vitamin K₁ in stopping bleeding is probably more closely related to its effect on prothrombin than on the one-stage test (factor VII).

Summary

Four cases of haemorrhage due to coumarin anticoagulants, one due to hepatocellular disease, and one to obstructive jaundice are described.

In all four coumarin-treated patients the haemorrhage was associated with very low prothrombin levels rather than with undue prolongation of the clotting-time in the one-stage test of Quick.

Neither of the patients with hepatic disease had more than moderate prolongation of the one-stage clotting-time, and this was due to factor VII deficiency. Both had very low levels of prothrombin.

The Quick test is not a good measure of hypoprothrombinaemia, which, however, may play an important part in the initiation of haemorrhage in coumarin overdosage and liver disease.

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RECURRENT RENAL STONE*

BY

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Stone in the kidney has a high recurrence rate after operation. Table I shows the incidence of recurrence on the operated side in various series, following the operations of pyelolithotomy, nephrolithotomy, and ureterolithotomy (the recurrence in that case being in the kidney and not in the ureter). The figures shown in the table under my name include cases operated on by various Leeds surgeons which were followed up from two to twenty years, the recurrence being confirmed by radiography. It has unfortunately been impossible to obtain an accurate follow-up in more than a small proportion of the total cases treated. Table II shows the incidence of contralateral recurrence after operations for renal stone.

TABLE I.—Recurrence of Renal Stone after Operation in Various Series

	Pyelolithotomy			Nephrolithotomy			Ureterolithotomy		
	Total	Recur.	%	Total	Recur.	%	Total	Recur.	%
Cabot and Crabtree (1915) ..	33	17	51	30	17	56			
Barney (1922a, 1922b) ..	—	—	32.8	—	—	52.9			
Braasch and Foulds (1923) ..	371	44	11.85	104	25	24.0			
Brongersma <i>et al.</i> (1924) ..	38	9	23.6	62	22	35.5			
Twinem (1940) ..	102	21	20.9	100	28	28			
Sutherland (1954) ..	100	47	47	40	25	62.5	49	18	37
Pyrah ..	63	22	34.9	50	30	60	43	9	20.9

TABLE II.—Contralateral Recurrence of Renal Stone after Operation in Various Series

	Contralateral Recurrence	
	After Pyelo- or Ureterolithotomy	After Nephrectomy
Twinem (1937) ..		4.2%
Oppenheimer (1937) ..	15.1%	14.8%
Sutherland (1954) ..	12.3% (195 cases)	11.1% (45 cases)
Pyrah ..	15.4% (136 ")	15.9% (44 ")

The factors most commonly responsible for recurrent stone are, first, the small pieces of grit or tiny calculi left behind at operation; and, secondly, infection. In the remaining cases it is sometimes possible to discover a persisting cause of stone formation, which it may or may not be possible to correct, and which determines recurrence after operation; some of these causes are well understood, other less so. The factors which may lead to recurrence of calculus formation are considered below.

Extrarenal Causes

Extrarenal causes of stone formation, and hence of recurrence, are possible errors in oxalate metabolism and hyperparathyroidism.

Oxalate Metabolism.—The commonest renal stone seen in the surgical out-patient department is the calcium oxalate stone; it usually occurs in non-infected kidneys, and it not uncommonly recurs. Twinem (1937, 1940) reported recurrence in 11 out of 74 cases of proved oxalate calculi. While local renal factors may play a part, it is possible that recurrence is the result of metabolic causes. The source of the

* An abridged version of a paper read at the opening of a discussion on recurrent urinary stone at the Medical Society of London on February 8, 1954.

oxalic acid in the blood is largely the soluble oxalate salts in the food and is therefore exogenous. It has been suggested that, in addition, oxalate acid may be formed endogenously in the body by the breakdown of glucose, creatine, purines, and some amino-acids, such as glycine. Feeding with ethylene glycol, glycolic acid, and glyoxylic acid results in the production of oxalic acid in the body (Dakin, 1907). The theory of the endogenous formation of oxalic acid receives further support from the fact that even on an oxalate-free diet humans still excrete oxalate in the urine, and the blood-oxalate level is not reduced to zero. It seems possible that, by a metabolic error, some patients may form and excrete greater amounts of oxalate than others, and that a proportion of them may produce oxalate stones.

The stress which has been laid by some workers upon the maintenance of an acid urine to prevent the recurrence of oxalate calculi has probably been exaggerated, since calcium oxalate may be precipitated in either an acid or an alkaline medium; a low urinary pH resulting from such measures would, moreover, increase the urinary calcium.

Hyperparathyroidism.—Overactivity of the parathyroid glands, resulting either from a hyperplasia of all four glands or more often from an adenoma of one or two glands, is commonly associated with renal stone formation, the incidence of which in various series is recorded in Table III.

TABLE III.—Incidence of Renal Stone in Hyperparathyroidism

	No. of Cases	No. with Renal Calculi
Albright <i>et al.</i> (1934)	83	42
Cope (1942)	67	47
Cook and Keating (1945)	18	14
Norris (1947) (collected cases)	322	118
Pyrh	12	5

Most of the recorded cases of hyperparathyroidism with stone formation have been associated with recognizable bone disease (osteoporosis), cysts, or spontaneous fracture. When the adenoma is surgically removed the abnormal blood chemistry is corrected and the basic cause of the stone formation disappears. In many cases (in four of my personal series) the calculi, being usually composed of calcium phosphate, disintegrate and disappear spontaneously two or three months after operation. In only one of my cases, in which there was a large calculus composed of calcium phosphate and oxalate, was operation necessary. In none of these cases has there been recurrence. It has been increasingly recognized, however, that there is a group of cases of hyperparathyroidism in which renal calculi occur but in which bone disease is absent or scarcely recognizable. In such cases stones will recur after surgical removal if the primary disease, the hyperparathyroidism, is not dealt with surgically. Although these cases are probably uncommon, if they are to be diagnosed the blood calcium, phosphorus, and phosphatase should be examined, and calcium balance investigations done in all cases of recurrent stone.

Intrarenal Causes

Some intrarenal causes of calculus formation and recurrence are papillary calcification, idiopathic hypercalciuria, and renal acidosis.

Papillary Calcific Deposits.—The renal papillae, which are at the apices of the pyramids, are commonly the seat of tiny calcific deposits. Randall (1937) first described multiple cream-coloured spots or plaques on the sides of the renal papillae in 17% of a large series of kidneys examined at necropsy which did not show gross disease. Microscopically these plaques were shown to be local deposits of calcium. Randall found that some of the plaques, varying from 15 to 40% in different age groups, were associated with the beginning of a tiny calculus, firmly attached to the plaque and projecting into the minor calix. When only one caliceal stone is seen radiographically in a kidney, recurrence after operation may sometimes be explained by further stone-formation on hitherto invisible plaques; this is a possible

explanation of the recurrence in the case of a man aged 36 who, after an attack of right-sided renal colic, was found to have a stone in the lowest calix (Fig. 1, A). No other areas of calcification were noted in the remaining part of the kidney on the control radiograph. The stone was removed by nephrolithotomy. Within six months of the operation radiographs showed not only a local recurrence but crescentic calcific deposits in three other calices (Fig. 1, B). No infection was ever detected on examination of the urine, which at the present time is sterile.

FIG. 1.—(A) Intravenous pyelogram showing stone in lowest calix, October 13, 1949. (B) Recurrent stone in lowest calix, June 20, 1950. Recurrence on three other papillae possibly arising in Randall's plaques.

Idiopathic Hypercalciuria.—It has recently been recognized that some male patients who have had recurrent renal calculi, usually in association with a staphylococcal renal infection, consistently excrete a larger amount of urinary calcium than normal and, in fact, are in negative balance. The blood calcium is normal and the blood phosphorus slightly low. We do not yet know the incidence of this group of cases. The following case appears to be an example of this syndrome. The patient, a man aged 43, had had calculi removed from both kidneys in 1940. A recurrent stone in the left kidney and also one in the bladder were removed in 1950. The renal stone recurred, and rapidly grew to a considerable size, being removed in 1953. Once again it recurred. Calcium balance studies (Table IV) showed that he had a negative calcium balance. Biochemical blood tests excluded hyperparathyroidism.

TABLE IV.—Case of Idiopathic Hypercalciuria—Calcium Balance Studies

Day	Intake	Calcium Balance		Balance
		Urinary Excretion	Faecal Excretion	
1	384 mg. daily average	320 mg.	261 mg. daily average	-197 mg.
2		226 "		-103 "
3		116 "		+ 7 "
4		215 "		- 92 "
5		300 "		-177 "
6		224 "		-101 "
				Mean -110 "

Renal Acidosis.—This is a condition in which the renal tubules fail to excrete ammonia and in which there is also a hypercalciuria. It may, according to Albright and Reifstein (1948), occur without either nephrolithiasis or nephrocalcinosis; or it may occur with recurrent nephrolithiasis and without nephrocalcinosis. Probably, therefore, more blood examinations (carbon-dioxide-combining power and blood chlorides) should be made in order to detect the existence of hyperchloraemic acidosis in patients who pass small stones. Renal acidosis may also occur in patients with nephrocalcinosis alone. It may also occur with both renal calculi and nephrocalcinosis, and the patient may then present at a urological clinic with a history of the passage of recurrent calculi. Apart from the removal of obstructing calculi,

surgery plays no part in the treatment of this condition; it would appear that in some cases in this group the recurrent stone formation may be gradually remedied by corrective biochemical measures, using Shohl's solution (citric acid, 140 g.; sodium citrate, 98 g.; water to 1 litre; dose 50–100 ml. daily) to correct the acidosis.

Cystinuria.—This is an inborn error of metabolism probably due to the failure of the renal tubules to reabsorb cystine and some other amino-acids. A small proportion of cystinurics develop renal calculi, and in such cases recurrence after operative removal may be expected.

Pelvi-Caliceal Causes

The principal pelvi-caliceal causes of stone formation and recurrence are infection, recumbency, and pelvi-caliceal obstructions.

Infection.—If operation is done in the presence of infected urine the patient is not safe from recurrence until the urinary tract has been made sterile after operation, by the use of suitable urinary antiseptics. Since this is not always possible, infection in fact accounts for a large percentage of cases of recurrent stone. The urea-splitting organisms, of which *Proteus vulgaris* is the most important, can produce a favourable pH for the deposition of phosphates and can also provide an adequate organic nidus of organisms and inflammatory debris for the rapid formation of a stone. If such calculi are removed, recurrence is very common. Infection is usually regarded as the most important cause of bilateral calculi, which have formed 68 out of 507 cases on the files of the Urological Department in Leeds. This is true in the cases of medium-sized and large stones, and such stones commonly recur after removal. In 41 cases, or nearly two-thirds, there has been infected urine, but possibly this is often a secondary phenomenon. In early bilateral renal stone, on the other hand, the urinary tract is not necessarily infected; in these cases some of the other causes of calculus formation have operated. On the whole, however, bilateral calculi, when they are large, have a bad prognosis as regards recurrence.

Recumbency Calculi.—In any large series of cases of renal stones it is possible in a number to link the onset of the stone formation to a long period of recumbency for the treatment of fractured spine, pelvis, or femora, or tuberculosis of the spine or the hip. In my series of 507 cases, 20 were examples of recumbency calculi, and in many of these the stone recurred after removal. A patient who has been recumbent for two to three years for the treatment of tuberculosis of the spine is, unless he is turned in bed as a measure of therapy, a *temporary potential stone-former* because of the imperfect drainage of the renal pelvis and because of the hypercalciuria. A patient within this group may become a *temporary actual stone-former* if secondary causes appear, such as dehydration, an alkaline urine (allowing of phosphate precipitation), or a urinary infection. If a calculus is removed surgically and the recumbent state is allowed to continue, a recurrence of the stone may be expected. If the recumbent state is terminated, but if a urinary infection persists, calculus formation may recur after removal. If the primary cause of the calculi—namely, the recumbency—is removed, and the secondary causes do not include infection, in some cases the calculi may disintegrate and disappear spontaneously (assisted by the administration of ammonium chloride) and thereafter not recur (Pyrah and Fowweather, 1938).

Anatomical abnormalities of the renal pelvis may, if allowed to persist, favour recurrence of stone formation. If a stone in the renal pelvis is associated with an abnormality of the pelvo-ureteric junction, such as a stricture or an aberrant artery, with a resulting hydronephrosis, a plastic operation should be performed at the same time as the stone is removed, provided that the urine is sterile or can be made sterile by pre-operative measures; failure to do this may lead to a recurrence of the stone. If there is a stone in a horseshoe kidney the isthmus should be divided or a part of it excised at the same time as the stone is removed;

the ureter can then descend to the bladder without the partial obstruction or kinking which may have been caused by the isthmus.

A calculus lodging in a calix may, by causing partial obstruction or ulceration of its neck followed by contraction, result in hydrocalicosis, and this may persist after the stone has been removed; crystalline matter may continue to collect in it. The outlet of the lowest calix drains upwards, which is a disadvantage if it is unhealthy; in such cases recurrence of stone is very probable, especially if infection is present. Hence, it is argued, it is sound to excise completely the pole of the kidney containing the diseased calix, along with the calculus. Fig. 2 shows a

FIG. 2.—Calculus in lowest calix of left kidney with hydrocalicosis. Partial nephrectomy.

lower caliceal calculus which has been treated by partial nephrectomy. The dotted line shows the line of section at the operation through the lower major calix. Stewart (1952), who recently strongly advocated partial nephrectomy, reported a series of 101 cases of calcine calculi treated by partial nephrectomy; in 87 of these followed up from two to thirteen years there was a recurrence rate of 6.8%.

Clinical Importance of Recurrence

The clinical importance of recurrent renal calculus varies greatly in different patients, chiefly because of the variation in the rate of stone formation and the severity of the associated infection, if such be present.

If the basic cause of the calculus formation has a low potential persisting perhaps over many years, stone after stone may form, and may result in a series of important but temporary symptoms; the existence of such calculi may

FIG. 3.—Diagrammatic representation of history of patient who passed small stones between 1937 and 1953. Radiograph commonly negative after stone had been passed.

never threaten life, and operation may not even be needed for their removal. Fig. 3 illustrates diagrammatically the history of such a patient who passed small stones (represented by the vertical bars) spontaneously for many years between 1937 and 1953. At various times between the stone episodes the radiographs were negative. Some effective but unknown cause of stone formation must have been present for all that time; yet clinically there was intermittent morbidity but no invalidism.

If, on the other hand, the cause of stone formation has a high potential, such as a *Proteus vulgaris* infection, the surgical removal of a calculus becomes an incident, often of little permanent value, in a syndrome moving with ever-increasing momentum, which in a few years overwhelms or invalidizes the

patient. One such patient, a man aged 43, had four operations for the removal of calculi from the right kidney between 1931 and 1935; but continued urinary infection produced after a few years the enormous bilateral stones shown in Fig. 4; this patient's hold on life is very precarious.

At the other extreme is the case of a woman aged 52 who had had a stone removed from her left kidney and has had no further symptoms of any kind; ten years later,

FIG. 4.—Radiograph of man aged 43, May 20, 1953. He had had recurrent stones between 1931 and 1935, gradually forming massive calculi with *Proteus vulgaris* infection.

a routine abdominal radiograph taken for a totally unrelated condition demonstrated the existence of a medium-sized recurrent but relatively harmless caliceal stone, 1 in. (2.5 cm.) in diameter, which had formed very slowly and very quietly.

Prevention of Recurrence

Some of the measures which do or may prevent the recurrence of renal stone have already been referred to.

The operation for removal of the stone must be so carried out as to minimize the chances of true and false recurrence. The stone should be removed from the renal pelvis or calix with the utmost gentleness and should be extracted intact. If there is gritty debris or fragmentation of the stone, the pelvis and calices should be washed out with a stream of sterile water. Pieces of grit left behind may lead to a false recurrence (probably a common event). If numerous calculi are present they should correspond in number to those seen on the radiograph. If there is doubt that all the stones have been removed, a radiograph of the kidney should be taken in the operating theatre. One must be careful not to leave behind, after nephrolithotomy, pieces of tissue with doubtful blood supply, which may become necrotic and form a focus for stone formation. Haemorrhage should be carefully arrested so as to avoid the retention of clot within the pelvis or calix which, if it became organized, might form a suitable nidus for further stone formation. Scrupulous care should be used to avoid the introduction of infection into the kidney either at the time of the operation or by retaining the drainage tube for too long a time. If the urine is known to be infected, suitable antibiotic cover should be given before and after the operation. Absorbable catgut should be used for suturing the kidney. If at the end of the operation there is still doubt about the complete removal of grit, the renal pelvis and calices may be irrigated for a time post-operatively with Suby's solution, though great care should be exercised to

guard against the introduction of infection from without. After operation, any residual infection should be cleared up by suitable treatment during the convalescent period.

In dealing with larger calculi it is often a matter of difficulty to decide whether the stone alone should be removed or whether nephrectomy should be performed. In the case of a kidney containing a staghorn calculus, with gross infection and some destruction of the renal parenchyma, nephrectomy is the operation of choice; whereas in the case of small and medium-sized stones in the pelvis or the calices the stone alone should be removed. Between these extremes are many intermediate cases of infected medium-sized stones in which the surgeon hesitates to sacrifice the kidney, in the hope that a conservative operation will bring permanent relief. Probably the stone alone should be removed if the surgeon thinks he can cure the infection. If he thinks the infection cannot be cured he must incline towards nephrectomy. Probably the degree and extent of the renal infection is of greater importance than the size of the stone.

General Measures.—Measures to prevent recurrence of calculi include a balanced diet, which must contain all the vitamins, especially vitamins A and D; excess of vitamin D must be avoided. There must be a liberal daily intake of fluid. Foci of infection should be corrected.

Specific Measures

Specific measures at present in use to try to prevent recurrence include the use of oestrogens, aluminium hydroxide, and hyaluronidase.

Oestrogens.—Shorr (1945) showed that the concentration of calcium ions in the urine can be reduced by the administration of oestrogens, which cause an increase in urinary citrate excretion; the calcium ions are replaced by a weakly ionized soluble calcium citrate complex. He recommended "premarin," a preparation of oestrone sulphate which is given orally in doses of 5 to 10 mg. daily for four weeks, the course being repeated after an interval.

Aluminium.—Shorr (1945) also recommended the use of aluminium hydroxide gel by mouth, to reduce urinary phosphates by precipitating aluminium phosphate in the intestine. This is given as "amphogel" in eight-hourly doses of 30 to 40 ml. after meals. The dose of the preparation is adjusted until analysis of the urine shows a reduction in its phosphate content. This can usually be achieved satisfactorily. Marshall and Green (1952) used this treatment on 37 patients suffering from recurrent urinary calculi for an average period of four years, and they found that stone formation was greatly reduced.

Hyaluronidase.—Butt *et al.* (Butt and Hauser, 1952a, 1952b, 1952c; Butt, Hauser, and Seifter, 1952a, 1952b, 1952c; Butt, Hauser, Seifter, and Perry, 1952) suggested the use of hyaluronidase to prevent the recurrence of renal calculi. Hyaluronidase is an enzyme, and is sometimes known as the spreading factor. Butt and Hauser suggested that its substrate hyaluronic acid was excreted in the urine and that this could change the surface tension of the urine by causing an increase of the protective colloids.

Work done in the Department of Urology at Leeds by Smiddy (personal communication, 1954) has shown that there is a great variation in the normal surface tension of urine, that it varies inversely with the specific gravity of the urine, and that the injection of hyaluronidase does not alter this; these findings did not support the contention of Butt and Hauser that hyaluronidase altered the urinary surface tension. Tests were then made to try out the efficacy of hyaluronidase in the prevention of vesical stones in the rat. These can be readily induced by the method of Helsby *et al.* (1953) by introducing a tiny zinc pellet into the bladder of the rat through a small incision. Forty rats were used. Half were kept as controls and half were given injections of hyaluronidase for forty to sixty days. Calculi grew equally in the bladders of both groups, so that the hyaluronidase did not appear to serve any protective function. The therapeutic efficacy of this treatment therefore appears doubtful.

Summary

The incidence of recurrent calculi in the upper urinary tract is given.

The commonest causes of recurrence after operation are infection and imperfect removal of calculi at operation. Numerous other factors, some of which are not fully understood, play a part, and these are discussed.

I wish to thank Dr. J. Dawson for the calcium balance studies in Table IV, and Mr. J. Hainsworth for the photographic work. I also wish to thank my surgical colleagues in Leeds for allowing some of their cases to be followed up.

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LEVORPHAN IN ANAESTHESIA

BY

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The synthetic analgesic levorphan (methorphan; "dromoran") has been used as a supplement to nitrous oxide and oxygen anaesthesia, and the results of an investigation, in which the drug was compared with pethidine for that particular purpose, have already been reported (Brown, 1952).

It seemed desirable to explore further the possibilities of levorphan in anaesthesia, and the present paper describes its use as premedication, and as a supplement to nitrous oxide and oxygen anaesthesia when given by continuous intravenous drip. Satisfactory clinical experience with levorphan as pre-operative medication has already been reported (Stoelting *et al.*, 1951).

Levorphan for Premedication

Before using the drug for premedication it was decided to determine the time of onset of action after subcutaneous injection, the time before maximum analgesia was observed, and the total duration of action. This was studied in several patients with post-operative pain and in one patient with severe nerve-root pain due to vertebral collapse. The results were as follow: (a) the time interval between the injection and the onset of analgesia averaged 20 minutes (range 15–25 minutes); (b) the maximum analgesic effect occurred within one and a half hours of injection; (c) the duration of analgesia, after injection of one ampoule (2 mg.), was seven hours (in very severe pain).

After the period of maximum analgesia the effect of the drug gradually wore off. There appeared to be a marked cumulative action, since, once analgesia had been established by giving 4 mg. in divided doses, satisfactory freedom from pain could be maintained by use of 0.5 mg. every twelve hours. After the above points were established, levorphan was used as premedication in a series of 100 patients about to undergo a general surgical or gynaecological operation. Levorphan alone was given to 30 patients (series A), levorphan and atropine to 20 patients (series B), and levorphan and scopolamine to 50 patients (series C). All the drugs were given by subcutaneous injection. A record card was designed to give the following data: age, sex, build, and type of patient, the presence or absence of pain, the time premedication was given, and the time of induction of anaesthesia. The patient's "normal" pulse rate, the pulse rate immediately before induction, the presence or absence of drowsiness, respiratory depression, and amnesia were also noted.

Dosage.—Two mg. of levorphan was the standard premedication. In 30 patients it was the only drug used for premedication, atropine, 1/100 gr. (0.65 mg.), being given when anaesthesia was induced with thiopentone (series A). Levorphan, 2 mg., and atropine, 1/100 gr. (0.65 mg.), were given to all 20 patients in series B except three as follows: (1) a 57-year-old patient with prolapse, levorphan, 1.5 mg., and atropine, 1/100 gr. (0.65 mg.); (2) a 55-year-old patient with prolapse, levorphan, 1 mg., and atropine, 1/100 gr. (0.65 mg.); and (3) a 63-year-old patient with diverticulitis, levorphan, 1 mg., and atropine, 1/100 gr. (0.65 mg.). Levorphan, 2 mg., and scopolamine, 1/150 gr. (0.43 mg.), were given to 50 patients in series C. No attempt was made to give the drug at a constant time before induction, and in fact the interval varied from half an hour to five hours. The time lapse between premedication and induction is shown in Table XII.

Results

Before anaesthesia was induced and before the pulse rate was recorded an assessment of the result of the premedication was made. The figures resulting from this observation are given as Table I. It is concluded that there is no difference among the three series of patients with regard to

TABLE I.—Clinical Assessment of Post-premedication State

	Series A	Series B	Series C
Apprehensive	11 (37%)	3 (15%)	12 (24%)
Satisfactory	19 (63%)	17 (85%)	37 (74%)
Oversedated	—	—	1 (2%)
Total	30 (100%)	20 (100%)	50 (100%)

post-premedication state. As "omnupon" and scopolamine form the combination of drugs most often used as premedication it was decided to compare the assessment of the patients comprising series C with a control series who had been given omnupon, $\frac{1}{2}$ gr. (22 mg.), and scopolamine, 1/150 gr. (0.43 mg.). Figures for this control group are given as Table II. The 50 members of the control group were chosen by taking record cards at equal intervals from a file containing the cards of 500 patients.

TABLE II.—Clinical Assessment of Post-premedication State of Control Group

	Control Group
Apprehensive	7 (14%)
Satisfactory	43 (86%)
Oversedated	—
Total	50 (100%)

On combining the oversedated with the satisfactory, the results given in Table III are obtained. These show no evidence of difference between the two series of patients.

In addition to the above clinical assessment, specific note was taken of (a) the presence or absence of drowsiness as