a spina bifida, some decision will have to be made about the age at which it is to be performed. Some of these patients die when quite young from hydrocephalus or urinary tract infections. Those who survive sometimes develop a moderate control of bowel function during their teens, and it may be best to wait for this to occur before constructing an ileal bladder. It is not possible to lay down any hard-and-fast rule, but each case must be judged carefully, taking into account the general prognosis, family background, and possible psychological disturbances.

SUMMARY

1. The lower ileum is suitable anatomically and physiologically for incorporation in the urinary tract. Possible biochemical changes following such operations have been discussed.

2. Relatively few reports of operations of this type have been found in the literature, which is reviewed in detail.

3. A series of 13 cases is reported in which an isolated coil of lower ileum is used to enlarge a contracted bladder, to relieve at the same time a contracted bladder and a hydronephrosis of a solitary kidney, to re-anastomose ureters previously transplanted into the colon to the bladder, to replace part of a ureter excised for neoplasm, and to act as an artificial bladder.

4. The results of these operations are discussed.

We desire to thank Mr. J. Hainsworth for the photographs, Mr. C. V. G. Lyth for the drawings and paintings in *Figs.* 393, 396, 397, 401, 407, 408, and 410, and Miss C. E. Campbell for the drawings in *Figs.* 389, 390, 391, 412, and 413.

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THE MIGRATION OF SODIUM, CHLORIDE, AND POTASSIUM IONS ACROSS THE MUCOUS MEMBRANE OF THE ILEUM

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INTRODUCTION

AN isolated loop of lower ileum has been used for various urological procedures, intestinal continuity having been restored by lateral anastomosis. A series of cases has been reported in this issue by Pyrah and Raper (p. 337) in which a coil of ileum was used to enlarge a contracted bladder, to replace an excised portion of ureter, to relieve simultaneously a contracted bladder and an associated hydronephrosis of a solitary kidney, to re-implant previously transplanted ureters into the bladder, and also to

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act as an artificial bladder. The clinical results of these operations have been satisfactory. In no case has any electrolyte imbalance been noted.

Following uretero-colic anastomosis, biochemical changes are known to occur and these include a differential absorption of sodium and chloride ions across the colonic mucosa; such absorption may result in a hyperchloræmic acidosis if the kidneys have been damaged by infection. These changes have been described in earlier papers from this clinic and views have been put forward concerning their mechanisms (Parsons, Powell, and Pyrah, 1952; Parsons, Pyrah, Powell, Reed, and Spiers, 1952; Pyrah, 1954). It is clearly desirable to determine if any such changes occur following the contact of urine with the mucosa of an ileal loop in the operations referred to above.

Investigations into the ionic migration occurring across the mucous membrane of the ileum are presented in two cases. The first is devoted to a study of the possibility of chemical imbalance arising after the operation of uretero-ileocystoplasty, whilst the second centres upon the use of a perfusable loop of terminal ileum designed to act as an artificial kidney.

Visscher, Fletcher, Carr, Gregor, Bushey, and Barker (1944) have shown by the use of radio-isotopes in dogs that there is a greater absorption of sodium from perfused loops of small intestine the more distal the intestinal segment, while the secretion of sodium is diminished. They succeeded in calculating the absolute rates of movement of sodium and chloride ions and also of water in both directions across the intestinal wall and concluded that there is a forced flow of liquid across the intestinal epithelium in both directions simultaneously. Differences in the solute content of the water in the two streams and the relative rates of the streams were thought to determine the direction and magnitude of net transport. The apparent concentrations of chloride and sodium ions in the fluid moving from gut to blood are greater than those in the ingoing perfusion fluid over a large range of gut fluid concentrations, so that a net absorption of sodium and chloride ions from the gut may be expected to occur. In this connexion, Bricker (1950) and Wilson (1953) have recorded instances of hyperchloræmic acidosis after implantation of the ureters into an ileal loop. Such cases, although unusual, may indicate a differential uptake of chloride ions relative to sodium ions according to the mechanism indicated by Parsons and his co-workers (1952) for absorption by the colon. Tasker (1953) has reported a case in which death from hyperkalæmia was suspected as a result of absorption of potassium after ileocystoplasty and subsequent failure in the mechanism of potassium elimination brought about by oliguria. He has shown in dogs that an absorption of potassium takes place from a bladder enlarged in this way.

Kolff (1947) has described the operation of an artificial kidney in the form of an isolated loop of terminal ileum. He used as a perfusion fluid a solution which was approximately isotonic with the plasma of the patient calculated on the basis of the plasma water and corrected for the Donnan Equilibrium effect brought about by the indiffusible, negatively charged protein molecules in the plasma. Perfusion with this fluid resulted in the removal of both urea and calcium from the patient but by a suitable adjustment of the calcium level in the fluid this loss of calcium by the body was prevented.

Twiss and Kolff (1951) later used an isolated loop of midgut and found that at this higher intestinal level the sodium and potassium blood and loop changes were similar to those of the terminal ileum. A perfusion fluid similar to that devised by Kolff was used at the fast flow rate of about 23 ml./min. by Thompson, Lewis, and Alving (1952) for the treatment of chronic uræmia. They verified Kolff's observation that the concentration of urea removed by the loop was greater the slower the rate of perfusion. A comparison is given between our results and those they obtained (*Table XI*).

I. CHEMICAL IMBALANCE AS A RESULT OF URETERO-ILEO-CYSTOPLASTY

CASE REPORT

This case is *Case* 6 in the paper by Pyrah and Raper in this journal (p. 345) where it is described in full. Briefly, the patient, a woman aged 42, had had bilateral uretero-sigmoidostomy following a large vesicovaginal fistula. Following the transplant she had several severe attacks of recurrent ascending renal infection with electrolyte imbalance which threatened to inflict permanent damage upon the kidneys. The fistula in the disused bladder, now much smaller, was repaired and the ureters were reconnected to the bladder using a loop of ileum, the middle of which was anastomosed to the bladder; the ureters were attached to the ends of the loop. Clinically the patient has been well and no further electrolyte imbalance has been noted.

Method of Investigation.—In view of the findings reported by Bricker (1950) and by Wilson (1953), interest was centred upon the possibility of a differential absorption of chloride relative to sodium ions. It was first necessary to determine if there was any differential migration of sodium and chloride ions across the mucosa of the excluded bladder, before determining the effect in this respect of the addition of a coil of ileum to the bladder. The difference between the results obtained in the two experiments may then be attributed to the presence of the loop of ileum.

Table I.—The Composition of the Artificial Urine

	Grammes/litre
Sodium	1·9
Chloride	2·8
Urea	13·4
Sulphuric acid	2·45
Ammonium bicarbonate	1·94
Potassium dihydrogen orthophosphate monohydrate	3·49
Creatinine	1·00
Hydrated magnesium sulphate	1·50
Calcium lactate	1·11

The investigation was first carried out when both ureters had been transplanted into the colon and the bladder fistula had been repaired. The technique was to introduce into the bladder 100 ml. of an artificial urine labelled with the radio-isotopes ^{24}Na and ^{38}Cl (half-lives 15 hours and 38 minutes respectively) and to observe the movement of these radio-isotopes into the blood. The chemical composition of the artificial urine is shown in *Table I*.

This fluid was retained in the bladder for 60 minutes and during this time blood samples were taken at suitable intervals. The activity of each sample and also that of a suitably diluted fraction of the original bladder solution was measured over a time scale in type M6 liquid counters: analysis of the decay curves, based on the difference in the half-lives of the two isotopes, gave the concentrations of ^{24}Na and ^{38}Cl appearing in the blood relative to their initial concentrations in the artificial urine introduced. (Allowance was made for the relative sensitivities to the two isotopes of all the Geiger counters used.)

In order to derive the relative migration rates of the two ions from the blood concentrations, it was necessary to make an allowance for the different volumes which sodium and chloride ions occupy in the body and for the different rates at which movement into these volumes takes place. This was done by an intravenous injection of sterile, buffered ^{24}Na and ^{38}Cl, followed by the measurement with time of the activities of blood samples taken at intervals up to an hour after this injection. The accurately measured volume of 5 ml. which was injected contained approximately 10 μC of ^{24}Na and not more than 70 μC of ^{38}Cl. By a comparison of the activities of the blood samples and of the injected solution, the dilution factors and hence the effective body spaces were derived over a time scale similar to that used in the ionic migration studies. Thus the true differential rate of migration into the blood of chloride and sodium ions across the membrane concerned could be determined.

This use of radio-isotopes not only gives a measure of the movement of sodium and chloride ions from the bladder into the blood but also, when combined with the chemical analysis of the artificial urine, before and after retention in the bladder, enables one to discriminate between the net movement and the flow in either direction occurring in dynamic interchange.

The same procedure was repeated when the patient had had one ureter anastomosed to an ileal loop, itself anastomosed to the bladder. In this case, 250 ml. of an artificial urine was used which contained 3·66 g. sodium chloride per litre in addition to the other constituents shown in *Table I*. This fluid was retained for 70 minutes. Any difference between the results obtained after 60 minutes and those obtained with the excluded bladder may then be attributed to the presence of the loop of ileum.

A complication arises when one ureter has been re-implanted into the bladder, from the addition of natural urine to the bladder during the investigation, but this may be resolved if the amount and composition of this urine is determined.

Results.—

a. The Excluded Bladder with Both Ureters Transplanted into the Colon.—The uptake by the blood of ^{24}Na and ^{38}Cl via the bladder wall is expressed as a function of time in *Fig.* 417. The concentration of each radio-isotope in the fluid introduced is expressed in terms of the average total concentration of that ion (in mEq./l.) in order to allow for the effect of isotopic dilution. The correction which has to be made for the difference in the effective body spaces of the two ions and in their rates of movement into these spaces is made in the following way.

By the method already outlined, curves were obtained for sodium and chloride which related their effective body spaces with time (*Fig.* 418). It was assumed that these curves are of the form $y_t = y_\infty - ce^{-\lambda t}$, where y_t is the effective body space at time t. By trial and comparison, values for the

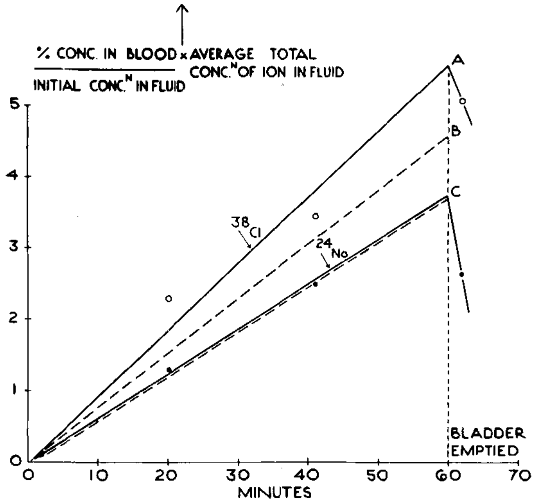

FIG. 417—The absorption of $^{24}Na^+$ and $^{38}Cl^-$ ions from an excluded bladder (the ureters having been transplanted into the colon) and the subsequent uptake of these ions by the blood. The ordinates are expressed in mEq./l. The continuous lines OC and OA represent the observed uptake by the blood of ^{24}Na and ^{38}Cl. The dotted lines OC and OB represent the absorption of $^{24}Na^+$ and $^{38}Cl^-$ ions calculated from the effective body spaces on the assumption that they are absorbed in equivalent amounts. AB represents the true differential uptake after 60 minutes of $^{38}Cl^-$ ions relative to $^{24}Na^+$.

constants y_∞, c, and λ were obtained from the curves for both ions. If next we consider the transmission of the ions contained in the bladder across the wall into the blood, we may suppose that the activity transmitted is proportional to time during the period of the investigation. If α is the number of μC transmitted in unit time, then, in an interval dt, $\alpha.dt$ μC enters a space y_t which increases with time as determined in the body space experiment. Thus the measured concentration is of the form:—

$$\int_0^t \frac{\alpha . dt}{y_t} = \int_0^t \frac{\alpha . dt}{y_\infty - ce^{-\lambda t}} = \frac{\alpha}{y_\infty}\int_0^t \left(1 - \frac{ce^{-\lambda t}}{y_\infty}\right)^{-1} . dt = \alpha . F_t$$

F_t can be evaluated for both the sodium and the chloride ions and a comparison of the calculated F_t curves with the observed concentration curves gives the relative values of the migration rates, α, for the two ions. In *Figs.* 417 and 419 the calculated curves (dotted) for sodium are fitted arbitrarily to the experimental curves at one point ($t = 50$ min.) and the dotted curves for chloride are those calculated on the basis of $\alpha_{Cl} = \alpha_{Na}$. Since the agreement with the experimental curves is reasonably close, this suggests that the migration rates for the Na^+ and Cl^- ions are in fact approximately equal in this case.

The analyses of the fluid used before and after retention in this excluded bladder are shown in

Table II. Except for urea, there is no appreciable net movement across the bladder wall of those ions studied. Thus, the migration of sodium and chloride ions across the bladder epithelium is a dynamic process in which movement in both directions takes place simultaneously.

Table III gives the results of the analyses of the fluid before and after its retention in the bladder.

Since the interpretation of these analyses is complicated by the gradual addition of urine via the replaced ureter during the experiment, a specimen of urine was collected at the commencement of the experiment. It was inadvertently lost, however, so that no accurate estimation of the direction and magnitude of the net movement of the ions concerned could be attempted.

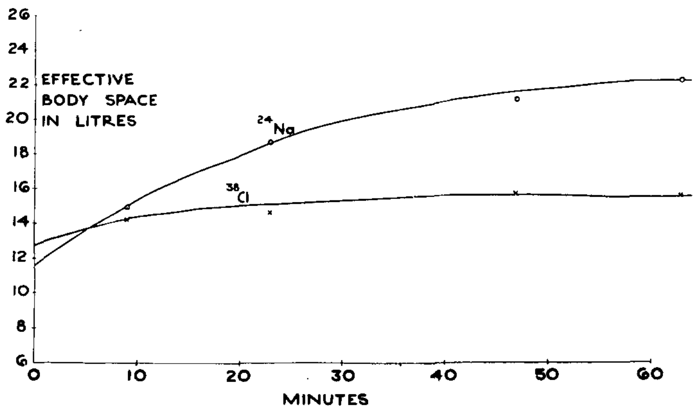

FIG. 418.—The relationship between the effective body spaces and the time after an intravenous injection of $^{24}Na^{+}$ and $^{38}Cl^{-}$ ions.

b. Bladder and Attached Ileal Loop.—The uptake by the blood of ^{24}Na and ^{38}Cl is shown as a function of time in *Fig*. 419. The effective body spaces of the sodium and chloride ions were determined by

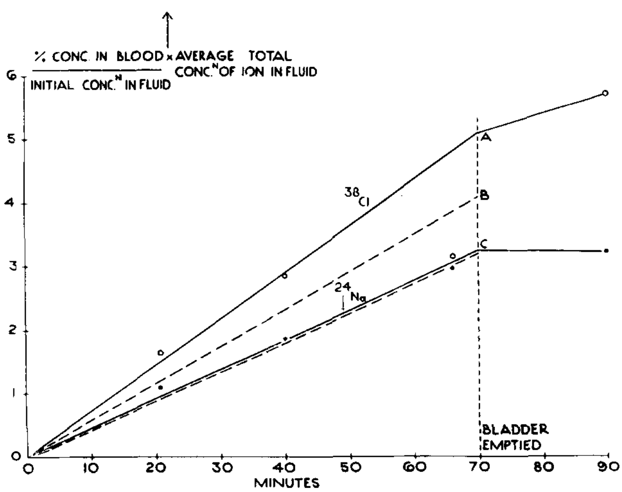

FIG. 419.—The absorption of $^{24}Na^{+}$ and $^{38}Cl^{-}$ ions from a bladder with attached ileal loop to which one ureter has been anastomosed, and the subsequent uptake of these ions by the blood. The ordinates are expressed in mEq./l. The continuous lines OC and OA represent the observed uptake by the blood of $^{24}Na^{+}$ and $^{38}Cl^{-}$ ions. The dotted lines OC and OB represent the absorption of $^{24}Na^{+}$ and $^{38}Cl^{-}$ ions calculated from the effective body spaces on the assumption that they are absorbed in equivalent amounts. AB represents the true differential uptake after 70 minutes of $^{38}Cl^{-}$ ions relative to $^{24}Na^{+}$.

the method outlined above and the resultant calculated curves are also shown. The calculated sodium curve (dotted) is fitted to the experimental curve at $t = 50$ min. The corresponding chloride curve, based on the arbitrary assumption that $\alpha_{Cl} = \alpha_{Na}$, is shown dotted.

Table II.—THE COMPOSITION OF AN ARTIFICIAL URINE BEFORE AND AFTER RETENTION IN A BLADDER ISOLATED FROM THE KIDNEYS

		BEFORE RETENTION	AFTER RETENTION
Time	min.	0	60
Volume	ml.	100	93
Cl	mEq.	7·86	7·52
Na	mEq.	8·40	8·07
K	mEq.	2·55	2·44
Urea	mg.	820	642

However, from a comparison of the curves shown in *Figs*. 417 and 419, it appears that :—

i. The addition of the ileal loop to the bladder makes no significant difference to the transmission of sodium and chloride ions from bladder to blood.

Table III.—THE COMPOSITION OF AN ARTIFICIAL URINE BEFORE AND AFTER RETENTION IN A BLADDER WITH ADDED ILEAL LOOP TO WHICH ONE URETER IS ATTACHED

		BEFORE RETENTION	AFTER RETENTION
Time	min.	0	70
Volume	ml.	250	320
Cl	mEq.	16	26·8
Na	mEq.	15·2	24·0
K	mEq.	5·76	7·38
Urea	mg.	3·25	2·72

ii. There is little or no difference in the relative migration rates of sodium and chloride ions across the ileal loop into the blood. Hyperchloræmic acidosis is therefore an unlikely consequence of uretero-ileocystoplasty. The standard errors involved, *Figs.* 417–419, are shown in *Table IV*.

2. THE USE OF AN ISOLATED LOOP OF ILEUM AS AN ARTIFICIAL KIDNEY

CASE REPORT

E. H., female, aged 48, when first seen on Sept. 14, 1950, had been in ill health for two to three years. In the last few months she had lost weight, her appetite was poor, and she had frequency of micturition usually twice at night. Shortly before admission she had a fairly severe hæmaturia lasting for ten days.

Table IV.—THE RESULTS DESCRIBED GRAPHICALLY IN FIGS. 417–419 AND THEIR CORRESPONDING STANDARD ERRORS

NUMBER OF BLOOD SAMPLE	FIG. 417		FIG. 418		FIG. 419	
	Na	Cl	Na	Cl	Na	Cl
1	1·30 ± 0·03	2·29 ± 0·09	14·9 ± 0·09	14·2 ± 0·28	1·09 ± 0·04	1·64 ± 0·14
2	2·50 ± 0·03	3·46 ± 0·31	18·7 ± 0·10	14·7 ± 0·28	1·86 ± 0·04	2·85 ± 0·23
3	2·65 ± 0·04	5·09 ± 0·30	21·3 ± 0·15	15·9 ± 0·41	2·965 ± 0·05	3·16 ± 0·64
4			22·4 ± 0·15	15·85 ± 0·52	3·22 ± 0·05	5·72 ± 0·83

PHYSICAL EXAMINATION AND INVESTIGATIONS.—The right kidney was very considerably enlarged; the left kidney was slightly enlarged. She looked ill and pale. The urine gave a scanty growth of *B. coli*; there were a few pus cells. The hæmoglobin was 70 per cent and the blood-urea 134 mg. per cent. Intravenous pyelograms led to a diagnosis of congenital cystic kidney, the changes being more advanced on the right side. The patient was given general advice and was seen occasionally in the out-patient clinic.

BLOOD-CHEMICAL INVESTIGATIONS.—

Hæmatocrit	24·5	per cent		
Plasma-protein	7·25	g. per cent	1·0268	sp. g.
Urea	64	mg. N_2 per cent	134	mg. urea per cent
Chloride	91	mEq./L.	531	mg. NaCl ,, ,,
CO_2-combining power	25·5	mEq./L.	56·7	vol. per cent
Sodium	130	mEq./L.	300	mg. ,, ,,
Potassium	5·6	mEq./L.	21·8	mg. ,, ,,
Potassium R.B.C.	87	mEq./L.	340	mg. ,, ,,
Phosphorus	4·8	mEq./L.	8·25	mg. ,, ,,
Calcium	4·5	mEq./L.	9·0	mg. ,, ,,

SUBSEQUENT HISTORY.—She was re-admitted to hospital Dec. 1, 1952. She complained of aching in both loins. Her condition had become worse in recent weeks and she had been confined to bed for the previous eight weeks. She had nausea and occasional vomiting; her appetite was poor. She was unable to do any housework. She was, in fact, in a state of uræmia.

The investigations showed a sodium and chloride deficit, the CO_2-combining power was low normal, and the phosphates were considerably elevated. The patient was far more ill than the above figures would lead one to expect. It was considered that she could not live more than a short time, possibly only a matter of weeks. It was thought that it might be possible to improve the patient's condition by preparing an isolated loop of ileum, which might be irrigated by passing appropriate fluids through it.

AT OPERATION (Nov. 20).—An isolated loop, 4 ft. long, was prepared by the method described in the paper by Pyrah and Raper in this issue (p. 337). Continuity of the small intestine was restored by lateral anastomosis. The two ends of the loop were brought to the surface of the body in each iliac fossa. The seromuscular coat of the intestine was sutured to the parietes of the iliac fossa so as to lessen the chances of intestinal obstruction. The patient made a satisfactory recovery from the operation (*Fig.* 420).

The capacity of the ileum to absorb fats after the operation was estimated by measuring the proportion of unsplit fat which was present in dried fæces. A value of 10 per cent was obtained; this indicated that the absorptive capacity of the ileum for fat had not been appreciably impaired.

SUBSEQUENT COURSE.—The object was to wash out urea and possibly other toxic substances as in Kolff's case (1947); in this case the best value for urea in the irrigating fluid was 5 g. washed out in 10 hours. Difficulties in the irrigation were sometimes found, notably abdominal cramps from spasm of the intestine in the loop; these we have been able to eliminate. Although the amount of urea that we have been able to wash out has not been as great as in Kolff's case, the patient appears to have derived benefits from the periodic irrigation. She has returned willingly to hospital every few weeks for further irrigation and on each occasion there has been clinical improvement. In the last twelve months when she returned to hospital, it was frequently found that she had an electrolyte imbalance, especially an acidosis. This was usually corrected before irrigation was carried out.

It is not the purpose in this paper, however, to present the final results of treatment in this case or to attempt to assess the value of a loop of ileum as a possible artificial kidney. In using different irrigating fluids, it was soon found that it was desirable to know more about the migration of ions, notably sodium, chloride, calcium, and potassium, across the ileal mucosa into the blood. It is the methods which we have used and the results which have been obtained which are now described.

Method.—The isolated loop is perfused with a suitable fluid and transfer of urea and certain ions takes place between the blood and this fluid. Since chemical analyses of the fluid used before and after perfusion give only the net direction and magnitude of the movement of the ions involved, the use of one or more radio-isotopes was suggested as a means of labelling the movement in one direction. Preliminary experiments with the use of Kolff's solution indicated a loss of potassium by the blood during the accompanying removal of urea. In order to reduce the potassium loss to a minimum, it was decided to investigate the relationship between the movement of this ion between blood and loop and

FIG. 420.—The use of an isolated loop of ileum as an artificial kidney. The two ends of the loop can be seen in the iliac fossa.

the rate of flow and composition of the perfusion fluid. Because of the result obtained by Tasker, interest was also centred upon the direction of movement of potassium when the potassium concentration of the perfusion fluid was considerably higher than that of the corresponding plasma. ^{42}K, the radioisotope of potassium of half-life 12·4 hours, was used to label the potassium moving from the blood into the loop.

An approximate analysis of a perfusion fluid isotonic with blood indicated that, at a rate of flow of half a litre an hour, there was an excretion of potassium into the loop of about 0·1 g. per litre of fluid. On the basis of this excretion and an assumed total body content of exchangeable potassium of 125 g. the amount of ^{42}K as potassium carbonate to be injected intravenously was calculated. This injection took place at least 14 hours before the commencement of radio-activity measurement, this period being considered sufficient for equilibration of the injected ^{42}K with most of the potassium of the body. Two series of experiments were carried out; for the first we injected 660 μC in 5 ml. sterile solution containing 0·08 g. potassium carbonate, and for the second, half this activity. The counting rates obtained were sufficient to enable us to continue the investigations over two or three days.

The perfusion fluid was run into the proximal end of the loop from a reservoir by way of a calibrated drip and a thermostat kept at body temperature. Thin-walled Foley catheters with inflated balloons inserted 12 cm. at each end of the loop provided the means of entry and exit of the perfusion fluid. Muscular contractions of the walls of the loop were prevented by increasing the flow rate slowly and by the addition at suitable intervals of 5 ml. 5 per cent procaine to the perfusion fluid. The perfusion fluid passed from the patient through a glass vessel surrounding a flow type counter, well screened from the patient. In this way, a continuous record of the counting rate was obtained. In addition, samples were taken for standardization in a type M6 liquid counter and both counters were calibrated with a diluted fraction of the initial fluid. The compositions of the fluids used are shown in *Table V*.

Before any reliable observations could be obtained, the perfusion was continued for about two hours in order to wash out any residual fluid. The rate of flow was then adjusted to some fixed value and the corresponding steady counting rate observed, correction being made for radio-active decay. When the steady rate had been established, 10-ml. samples of the efflux were collected from the flow counter and analysed chemically in order to determine the net transport of potassium across the ileal wall. In this way an accurate indication could be obtained of the movement of potassium at any one rate of flow of known initial potassium concentration. This procedure was employed for a number of different flow rates and different perfusion fluids. With each fluid used, a check was carried out on the volumes employed and the volumes recorded.

Table V.—THE COMPOSITIONS OF FLUIDS USED TO PERFUSE THE ARTIFICIAL KIDNEY

ISOTONIC		HYPERTONIC A	HYPERTONIC B	HYPERTONIC C
Sodium chloride	6·0 g./l.	The isotonic solution plus 0·4 g./l. of potassium chloride	The isotonic solution plus 0·8 g./l. of potassium chloride	The isotonic solution plus 1·2 g./l. of potassium chloride
Sodium bicarbonate	2·0 g./l.			
Potassium chloride	0·4 g./l.			
Glucose monohydrate	15·0 g./l.			
Calcium lactate	0·77 g./l.			
Hydrated magnesium sulphate	0·31 g./l.			
10 per cent CO_2, 90 per cent O_2 to saturation				
Total number of mEq./l.	340·0	350·8	361·6	372·4

Results.—Within the limits of experimental error there were no significant net changes in the volumes of any of the perfusion fluids used except at the very slow rates of flow. At 1 ml. per minute there was some absorption of fluid by the body but since the perfusion rate was so slow, this absorption was in no way dangerous.

a. Correlation between Flow Rate and Counting Rate (Flow Counter).—The counting rate given by the flow counter is a measure of that potassium concentration in the efflux which has been excreted into the loop from the blood. This neglects the ^{42}K which will return across the wall into the blood in the dynamic interchange but this effect will be very small because of isotopic dilution in the loop. The total amount of ^{42}K excreted via the urine and into the loop is regarded as too small to affect significantly its total concentration in the body during the experiment. Changes in the counting rate thus reflect changes in the movement of

Table VI.—THE CORRELATION BETWEEN FLOW RATE OF PERFUSION FLUID AND THE EXCRETION OF POTASSIUM BY AN ARTIFICIAL KIDNEY (SERIES 1)

CORRECTED COUNTS/MIN. K	DRIP RATE IN DROPS/MIN. R/0·074	DRIP RATE IN ML./MIN. R	$\frac{KR}{7 \cdot 4}$	FLUID
1350	73	5·4	987	Isotonic
880	120	8·9	1056	,,
1270	60	4·4	762	,,
1030	110	8·1	1133	,,
530	120	8·9	636	Hypertonic A
720	54	3·9	389	,,
490	155	11·3	1025	Hypertonic B

potsssium from the blood into the loop. The results of the first series of experiments are shown in *Table VI.*

Values of the drip rate, R/0·074, were plotted against corresponding values of the counting rate K (*Fig.* 421). A linear relationship was obtained for each fluid used. The equation of the curve for the isotonic fluid was:

$$R = -0 \cdot 00925\ K + 17 \cdot 25$$

The corresponding results for the second series are shown in *Table VII.*

The equation of the curve representing the use of the isotonic fluid was then

$$R = -0 \cdot 00419\ K + 15 \cdot 10$$

If allowance be made for the difference in activities and in time scales for the two series, the results are found to fit reasonably well though exact agreement would not be expected in view of the possible differences in total exchangeable potassium on the two occasions. However, the agreement is considered to be sufficiently close to justify the formulation of a general relationship, for this patient, between the flow rate and the concentration of potassium excreted into the ileal loop.

b. The Relationship between the Flow Rate, the Original Potassium Concentration in the Perfusion Fluid and the Concentration of Potassium excreted into the Ileal Loop.—It was found that reversal of the direction of net flow of potassium usually occurred when the concentration of potassium in the perfusion fluid approximated to or exceeded that of the Hypertonic B fluid.

$$\text{If } x = \frac{\text{the original potassium concentration in the perfusion fluid}}{\text{the original potassium concentration in the isotonic perfusion fluid}}$$

it was found that the results of the two series could be represented by the linear relationship:

$$\frac{K}{R} = 51 \cdot 5\ x - 158$$

Combining this with the expression relating flow rate to potassium excretion, we obtained

$$kC = K = (17 \cdot 25 - R)(158 - 51 \cdot 5x).$$

This expression gives the relationship between potassium excretion into the loop C, the potassium concentration of the perfusion fluid and its flow rate R, where k is the constant of proportionality between C and K (the observed counting rate). It is only

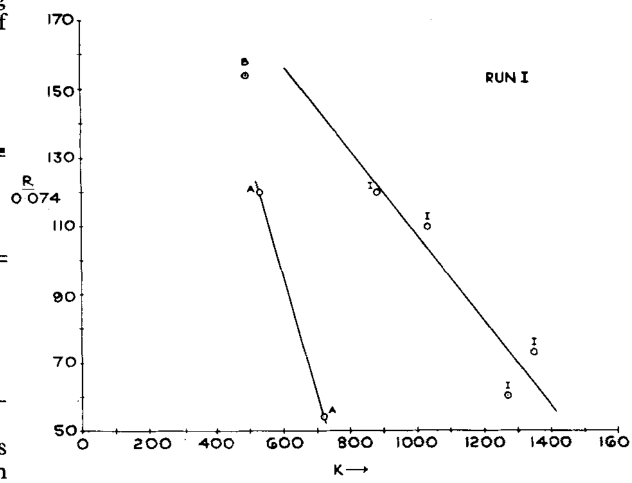

FIG. 421.—The relationship between the drip rate of the perfusion fluid, R/0·074, and the counting rate, K, where K is a measure of the excretion of ^{42}K into this fluid from the blood. I represents the use of the isotonic fluid, A represents the use of the Hypertonic A fluid, and B represents the use of the Hypertonic B fluid.

applicable as such when the net movement of potassium is from blood to loop and at the point of equilibrium the relationship breaks down. Beyond this point the dynamic nature of the process is demonstrated by the continued appearance of a radio-active efflux, despite the net absorption by

Table VII.—THE CORRELATION BETWEEN FLOW RATE OF PERFUSION FLUID AND THE EXCRETION OF POTASSIUM BY AN ARTIFICIAL KIDNEY (SERIES 2)

CORRECTED COUNTS/MIN. K	$\frac{K}{2}$	FLOW RATE IN DROPS/MIN. R/0·0617	FLOW RATE IN ML./MIN. R	$\frac{KR}{12.34}$	FLUID
2610	1305	66	4·07	861	Isotonic
2200	1100	91	5·61	1001	,,
1765	883	122	7·53	1077	,,
1460	730	160	9·90	1170	,,
1300	650	152	9·37	990	Hypertonic B
1620	810	66·5	4·10	538	,,
1062	531	80	4·94	424	Hypertonic C

the body of potassium. As would have been expected, this absorption of potassium from the loop appears to be greater at the slower rates of perfusion.

It should be realized that, although the use of the Hypertonic B fluid with a patient having normal potassium figures would result in little or no net movement of potassium, if the figures are subnormal then the Hypertonic B fluid is effectively more concentrated and will serve to drive potassium into the blood (*see Table XI*, example No. 3).

The fact that the direction of net potassium flow can be reversed in this way suggests the possibility of hyperkalæmia arising in a patient with oliguria, or poor kidney function, if urine be allowed to flow slowly over an area of ileal epithelium.

c. The Determination of the Efficiency of the Artificial Kidney.—

i. *The excretion of potassium into the loop as a function of time*: The curve relating K and R has the general form

$$K = -aR + c$$

where a and c are constants.

Now KR is a measure of the excretion of potassium into the loop per unit time, where $KR = -aR^2 + Rc$.

It can be shown that the maximum value of KR occurs when $R = \frac{c}{2a} = 8{\cdot}6$ ml. per minute.

This means that there is a certain rate of flow for each perfusion fluid at which the loss of potassium into the loop per unit time is a maximum. The results of Series 1 are shown in *Fig.* 422.

It should be noticed that as the original potassium content of the perfusion fluid increases, so does that rate of flow at which the loss of potassium into the loop per minute by the patient is a maximum.

ii. *The excretion of urea into the loop as a function of time*: The percentage urea concentrations in the fluid from the loop and the corresponding flow rates are shown in *Table VIII*. The inverse relationship between them does not appear to be influenced appreciably by the potassium concentration of the perfusion fluid or by the fact that the fluids used differed slightly in osmolarity. The maximum value of the percentage concentration of the excreted urea recorded was 100 mg. per cent. Since this was at a flow rate of 1 ml. per minute of the Hypertonic B fluid, the removal of urea with time was approximately 60 mg./hr.

Kolff obtained an excretion of 480 mg. of urea per hour at a flow rate of 1 litre per hour (16·6 ml./min.) during the use of a similar length of perfused ileum. Our figure of 60 mg. per hour at a flow rate of about 60 ml. per hour seems low in comparison with Kolff's result, but it should be noted that he advocates the use of the artificial kidney only when the blood-urea level of the patient rises above 340 mg. per cent. The corresponding value in our patient was only 140 to 165 mg. per cent and may well account for the smaller urea excretion which we obtained. At this very slow flow rate the movement of potassium with time is far removed from its maximum value, so that it might be concluded that the Hypertonic B fluid at a flow rate of about 1–4 ml. per minute is perhaps the best fluid to use in the perfusion of this particular ileal loop, when the blood-potassium of the patient is normal. Perfusion with the Hypertonic B fluid was tried after the blood cellular potassium of this patient had dropped below normal, this change being unaccompanied by a corresponding fall in plasma-potassium. It resulted in an absorption of potassium by the blood in such a way that the plasma-potassium remained within normal limits whilst the cellular potassium rose to nearly normal. The changes in blood-potassium associated with perfusion of the loop with different fluids are shown in *Table IX*. Throughout each perfusion period the patient was kept on an approximately constant diet, low in both protein and sodium chloride.

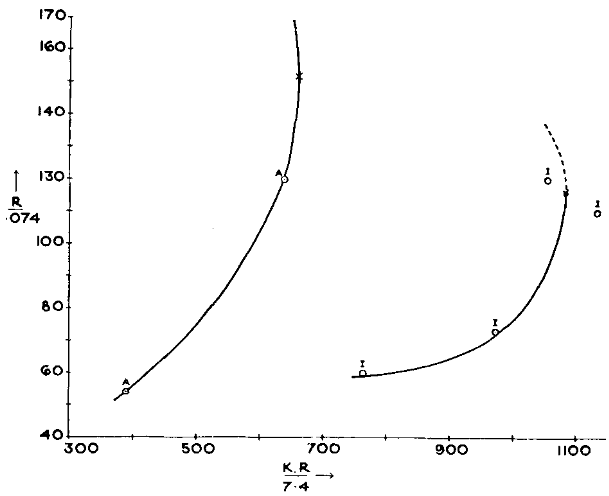

Fig. 422.—The relationship between the drip rate of the perfusion fluid, R/0·074, and the excretion of potassium into the loop with time. I represents the use of the isotonic fluid. A represents the use of the Hypertonic A fluid.

Table VIII.—The Excretion of Urea into the Loop at different Plasma Urea Concentrations and with Different Perfusion Fluids

Isotonic Fluid Plasma-urea Concentration 164 mg. per cent		Hypertonic B Fluid Plasma-urea Concentration 164 mg. per cent		Hypertonic C Fluid Plasma-urea Concentration 164 mg. per cent		Hyppertonic B Fluid Plasma-urea Concentration 151 mg. per cent		Hypertonic B Approx. Fluid Plasma-urea Concentration 140 mg. per cent	
Flow Rate ml./min.	Urea Concentration in Efflux mg. per cent	Flow Rate ml./min.	Urea Concentration in Efflux mg. per cent	Flow Rate ml./min.	Urea Concentration in Efflux mg. per cent	Flow Rate ml./min.	Urea Concentration in Efflux mg. per cent	Flow Rate ml./min.	Urea Concentration in Efflux mg. per cent
7·21	4·3	9·38	3·1	4·94	4·8	1	53·5	1	100
4·07	5·9	9·38	4·8	5·0	3·8	1	65·0	1	63
5·62	6·1	9·38	1·9	5·0	4·8	1	100·0	1	62·8
5·62	4·7	9·38	1·4	5·0	1·4	1	20·5	1	64·6
7·52	2·9	4·14	6·2			1	27·5	1	62·5
9·90	2·1					1	45·0		

d. Changes in the Composition of the Fluids used during Perfusion.—The changes which took place in the composition of the perfusion fluids after passage through the ileal loop are shown in *Table X*. The corresponding changes in the plasma-levels of these components are given in *Table XI*.

Comparison of Our Results with Those obtained by Thompson and his Co-workers.—

Chloride.—Changes in the chloride concentration of the perfusion fluids appear to depend more on the relation between the plasma chloride level and the chloride concentration of these fluids than on their rate of perfusion. Thompson and his co-workers (1952) found no significant changes in the chloride concentrations after passage through the loop.

Sodium.—There appear to be no significant changes in the sodium concentrations of the perfusion fluid used, though Thompson and his co-workers observed a decrease ranging from 2·5 to 12 mEq./l. on passage through the loop.

Potassium.—The movement of potassium between loop and blood has been shown to depend on the relative potassium concentrations in the perfusion fluid and plasma. The change in potassium concentration is greater the slower the rate of perfusion. The result obtained by Thompson and his co-workers has been verified, viz., there is an excretion of potassium by the body into an *isotonic* perfusion fluid.

Calcium.—As the calcium concentration of the perfusion fluid is increased relative to that of the plasma, the absoption of calcium by the body is enhanced. This absorption is greater at the slower rates of perfusion. Thompson and his co-workers recorded an excretion of calcium by the body in the majority of their experiments, but since in our experiments the calcium concentration in the presence of bicarbonate was maintained by saturating the perfusion fluid with carbon dioxide, the effective concentration of calcium we used was probably greater.

Table IX.—CHANGES IN BLOOD-POTASSIUM ASSOCIATED WITH THE PERFUSION OF AN ISOLATED ILEAL LOOP

BEFORE PERFUSION BLOOD K MEQ./L.		AFTER PERFUSION BLOOD K MEQ./L.		TYPES OF FLUID USED	TIME OF PERFUSION IN DAYS
Cellular	Plasma	Cellular	Plasma		
86	6·15	83	6·0	Isotonic, then Hypertonic A	2½
—	5·5	—	4·7	Isotonic, then Hypertonic B	2½
78·2	5·26	88·5	4·62	Hypertonic B	3
74·4	3·98	87·1	4·81	Hypertonic B	3

Table X.—CHANGES IN THE COMPOSITION OF THE FLUIDS USED DURING THE PERFUSION OF AN ISOLATED ILEAL LOOP

FLOW RATE	NA (MG. PER CENT)			K (MG. PER CENT)			CL (MG. PER CENT)			CA (MG. PER CENT)		
	In	Out	Diff.	In	Out	Diff.	In	Out	Diff.	In	Out	Diff.
Isotonic Fluid :—												
7·21	285	290	5	21·8	25·6	3·8	376	365	−11			
4·07	285	297	12	21·8	26·0	4·2	376	376	0			
5·62	285	312	27	21·8	25·5	3·7	376	369	−7			
5·62	285	300	15	21·8	26·0	4·2	376	364	12			
7·52	285	303	18	21·8	24·5	2·7	376	373	3			
9·90	285	295	10	21·8	23·0	1·2	376	376	0			
Hypertonic B Fluid :—												
9·38	302	295	−7	65·6	69·0	3·4	417	390	−27			
9·38	302	295	−7	65·6	67·6	2·0	417	390	−27	1·3	1·5	+0·2
9·38	302	302	0	65·6	68·0	2·4	417	418	+1			
9·38	302	300	−2	65·6	65·6	0	417	428	+11			
4·14	302	300	−2	65·6	63·2	−2·4	417	411	−6			
Hypertonic C Fluid :—												
4·94	300	310	10	86	80	−6	436	418	18			
5·00	300	305	5	86	82	−4	436	418	−18			
5·00	300	290	−10	86	84·4	−1·6	436	414	−22			
5·00	300	300	0	86	83	−3	436	421	−15			
Approximate Hypertonic B Fluid :—												
1	265	296	31·0	64	64	0	421	442	21	14	9·3	−4·7
1	265	297·6	32·6	64	49	−15	421	429	8	14	8·7	−5·3
1	265	296·4	31·4	64	44	−20	421	470	49	14	7·2	−6·8
1	265	292	27·0	64	49	−15	421	452	31	14	8·1	−5·9
1	265	284	19·0	64	60	−4	421	456	35	14	9·6	−4·4
1	265	296	21·0	64	50	−14	421	464	43	14	8·0	−6·0
Approximate Hypertonic B Fluid :—												
1	284	284	0	69	58	11	412	421	9			
1	284	276	−8	69	58	−11	412	405	−7	25·0	18·3	−6·7
1	284	272	−12	69	52	−17	412	414	2	25·0	11·6	−13·4
1	284	304	20	69	64	−5	412	450	38	25·0	14·4	−10·6
1	284	284	0	69	62	−7	412	408	−4	25·0	14·4	−10·6

Glucose.—In accordance with the results obtained by Thompson and his co-workers, glucose was found to be absorbed from the loop during the perfusion. The extent of this absorption was greater at the slower rates of perfusion.

Phosphorus.—Thompson and his co-workers demonstrated the movement of phosphorus into the loop from the blood by means of an intravenous injection of disodium hydrogen orthophosphate labelled with ^{32}P. This movement of phosphorus was verified and was found to follow approximately that of urea.

Table XI.—Changes in the Plasma Composition brought about by the Perfusion of an Isolated Ileal Loop

	Plasma Level									Perfusion Fluid	Time of Perfusion in Days
Before Perfusion					After Perfusion						
Na mEq./l	K mEq./l	Cl mEq./l	Ca mEq./l	Urea mg. per cent	Na mEq./l	K mEq./l	Cl mEq./l	Ca mEq./l	Urea mg. per cent		
No. 1											
146	5·5	103	3·15	166	141	4·7	102	3·25	164	Isotonic Hypertonic B Hypertonic C	1 1 ½
No. 2 134·5	5·26	104·9	2·5	131	137	4·62	101	2·33	151	Hypertonic B	3
No. 3 139·5	3·98	94	1·65	156	139	4·81	96	2·9	140	Hypertonic B (approx.)	3

The Effect of Reversal of the Direction of Perfusion upon the Migration of the Components of the Perfusion Fluid.—Approximately six litres of the Hypertonic B fluid were passed through the loop in the reverse direction to that described above at a overall flow rate of approximately 1 ml./min. There did not appear to be any important change in volume during perfusion. *Table XII* shows the changes in the concentrations of the components of the perfusion fluid. They do not appear to differ significantly from those results obtained by perfusion in the conventional direction (*Table X*).

Table XII.—Changes in the Composition of the Hypertonic B Fluid used to Perfuse an Isolated Ileal Loop in a Distal to Proximal Direction (mg. per cent)

	Hyp. B Fluid in	Sample of Efflux (1)	Sample of Efflux (2)	Sample of Efflux (3)	Sample of Efflux (4)	Sample of Efflux (5)
Na	280	282	271	274	267	267
K	66·0	67·8	58·9	41·0	56·0	56·9
Cl	422	453	395	395	412	401
P	0·07	1·05	0·49	2·06	0·65	0·53
Ca	12·0	9·2	11·4	6·6	11·2	10·8
Urea	<15	102	44	111	53	89
Glucose	1605	790	1390	720	1140	420
Changes in Concentration after Perfusion :—						
Na		+2	−9	−6	−13	−13
K		+1·8	−7·1	−23·0	−10·0	−9·1
Cl		+31	−27	−27	−10	−21
P		+0·98	+0·42	+1·99	+0·58	+0·46
Ca		−2·8	−0·6	−5·4	−0·8	−1·2
Urea		+100	+40	+110	+50	+90
Glucose		−615	−215	−885	−465	−1185

SUMMARY

1. The possibility of a hyperchloræmic acidosis arising from a differential uptake of chloride over sodium ions via a loop of ileum anastomosed to the bladder has been investigated by means of the radio-isotopes ^{24}Na and ^{38}Cl. No such differential uptake has been observed.

It has been shown that sodium and chloride ions migrate under the conditions of our experiment across the epithelium of the excluded bladder into the blood and also in the reverse direction from blood into the experimental fluid within the bladder. Such movement takes place simultaneously in both directions, that is, a dynamic equilibrium exists.

2. An artificial kidney in the form of a perfused loop of terminal ileum is described and a study made of the migration of several ions between blood and loop, with special emphasis laid on the movement of potassium.

Potassium ions have been shown to move simultaneously in both directions across the ileal wall and a relationship between the migration from blood to gut, flow rate, and original potassium concentration of the perfusion fluid is suggested. It has bee n shown that when the potassium concentration of this fluid is approximately three times that in the plasma of the patient, when the cellular potassium is normal, the direction of net movement of potassium is reversed and it becomes absorbed from the loop. Since the potassium concentration of the perfusion fluid at which the net movement of potassium was reversed and absorption by the blood occurred was generally about half the potassium concentration of an average urine, it seems highly probable that absorption of potassium will take place when a loop of ileum is anastomosed to the bladder. If the function of the kidneys is normal, homeostasis of the potassium could be achieved, but if kidney function is impaired, there is a real danger of hyperkalæmia.

Optimum conditions of potassium concentration and flow rate of perfusion fluid are suggested for the maximal removal with time of urea, accompanied by the minimal interference with the potassium balance. The amount of urea removed by perfusion of the loop was small at the blood-urea levels obtaining in this patient (140–165 mg. per cent), and probably it does not by itself account for the clinical improvement noticed in the patient. The larger amount of urea washed out in Kolff's case was probably related to the much higher blood-urea (340 mg. per cent).

Perfusion brought about no marked net movement of sodium and chloride ions. The direction of net movement of calcium seemed to depend on its concentration in the perfusion fluid in a similar way to that described for potassium.

We desire to thank the authorities at Harwell for their co-operation in making available supplies of radio-isotopes. We also thank Professor F. W. Spiers, of the Department of Medical Physics, University of Leeds, for his interest and advice in this research. We also thank Mr. J. Hainsworth and Miss C. E. Campbell, Department of Photography, St. James's Hospital, Leeds, for the photograph and figures. We are indebted to the members of our Departments who have assisted us with much of the routine work involved in this research.

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THE TREATMENT OF PANCREATIC CYSTS BY INTERNAL DRAINAGE

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PANCREATIC cysts large enough to need treatment are so rare that the number encountered by any one surgeon is small. For this reason the relative merits of the various methods available for handling these cysts cannot be assessed on personal experience alone.

For many years after Gussenbauer (1883) described the successful treatment of a pancreatic pseudo-cyst by marsupialization this was regarded as the treatment of choice. The method has undoubtedly been applied without regard to its limited capacity to provide permanent relief; after marsupialization recurrence of the cyst or persistence of a fistula is common, and one or other of these complications occurred in 7 out of 12 cases referred to by Cattell and Warren (1953). Although the persistence of a sinus is clearly undesirable, this disadvantage has sometimes been underestimated: thus in a review of 33 cases of marsupialized pseudocysts, Judd, Mattson, and Mahorner (1931) stated that " . . . no patients returned to the clinic with sinuses that had drained for more than two years ".

Internal drainage of cysts offers more immediate relief to the patient. Since Ombrédanne (1911) first used the method, sporadic reports of pancreatic cysts treated by anastomosis to a hollow viscus have appeared. Up to 1952, records of 82 cases thus treated have been traced in the literature, excluding cases treated by implantation of a fistula. Cysts have been anastomosed to the stomach, to the duodenum, to the jejunum, to the gall-bladder, and to the common bile-duct, the stomach having been most often selected (*Table I*). This paper records 3 cases in which cystogastrostomy has been carried out with satisfactory immediate and late results.

Table I.—SITES EMPLOYED FOR INTERNAL DRAINAGE OF PANCREATIC CYSTS*

	Cases
Stomach	41
Duodenum	7
Jejunum	24
Gall-bladder	8
Common bile-duct	2
Total	82

* This table includes cases where the pancreatic duct has been implanted into the viscus but not those in which a fistulous track has been utilized.