STUDIES IN NEPHRITIS IN CHILDREN.

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Foreword.

The investigations which form the basis for this thesis were carried out in the medical wards and the biochemical laboratory of the Royal Hospital for Sick Children, Glasgow. The work was commenced at the suggestion of Professor Findlay, to whom and to Doctors Morris and Graham I am deeply indebted and very grateful for many kindly suggestions and criticisms. Unless where otherwise stated, I am personally responsible for the investigations and the deductions drawn therefrom.

The thesis naturally falls into two parts:-

Part I - An analysis of the results of decapsulation in a series of cases of subacute Nephritis.

Part II- A study of Nephritis in children, with special reference to the correlation of Clinical and Biochemical findings, and suggesting an original conception of the disease.

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Part I - An analysis of the Results of Decapsulation in a series of cases of subacute Nephritis.

Historical:- The twentieth century opened to a period of activity in experimental renal surgery. Occasional successful results accruing in cases which turned out to be Nephritis led certain surgeons, notably Harrison and Edebohls, to operate deliberately in this disease.

The earliest technique consisted of simple puncture, then incision, and later decapsulation. At first, only one kidney was decapsulated, then both kidneys at different times, and finally both together. The early operations were carried out in cases of acute nephritis, but further experience seemed to show that any results to be hoped for were to be obtained in subacute cases, in which oedema was a marked feature. One explanation offered in support of the claims for success was that the operation relieved the oedematous tension to which the kidneys in common with the tissues generally were being subjected, established a collateral circulation, and so encouraged a renewal of renal function. Since the publication of Harrison's first three cases in 1896,(1) and of Edebohls' paper in 1904,(2) the operation has undergone an extensive trial. Among others, Sir T Horder (4 cases)(3), J.Tyson (3 cases)(4), H.Koplik (5 cases)(5), T.Kidd (4 cases)(6), F.D.Boyd (2 cases)(7), J.S.Fowler (3 cases)(8), J.W.Simpson (4 cases)(9), and J Fawcett (2 cases)(10) have reported favourably on the results of the operation in selected cases. Rovsing(11) in a review of urologic surgery, has recorded the results of a large series of operations over a period of thirteen years. He divides the cases into groups, and finds, on the whole, very favourable results in the diffuse parenchymatous type.

In spite of the successes claimed for it, however, the operation in more recent times has been falling into disfavour in the general opinion. In his address on nephritis at the

British/

TABLE. 1.

CASE:-	B/P. mm.	URINE. Blood.	Alb.	Biochemical Tests before operation. Urea Concentration Test. 2nd. Hour sample.	Pigment. %	Bl.Urea. mg.per 100 c.c.	Duration of illness before operation.	Biochemical Test after operation. Urea. Conc. Test. 2nd. Hour Sample.	Pigment. %	Blood Urea mg. per 100 cc.	Summary of Pathologist's Report.	REPORT.
1.J.S. 2.	115/85	+	+++	No records			19.4/7 wks.	No records.			No records.	Died of Nephritis. 2/2/1918.
2.M.C.	110/70	+	++	No records			17 weeks.	No records.			No record	Died.
3. W.B.	110/68	-	+++		44%		22 weeks.	No records			Acute catarr-:hal nephritis.	No trace since dismissal.
4.I.McA.		-	+++		14		12.4/7 wks.	No records			No record.	Died following operation.
5.A.W.	100/65	±	+++	1.8%	48 to 64		19 weeks	3.5%	44 to 56		No record.	Complete recovery.
6.F.M.		±	++	No records			11.4/7 wks.	No records.			No record.	Seen May 1925 "Perfectly well"
7.J.D.	100/80	-	+++	2.6%	63	30	15 months.	2.7%	62		"Mixed Nephritis"	Complete recovery.
8.C.McL.	128/100	-	±	2.3%	20	27	24 weeks	2.8%	60		do do	Ultimately died of nephritis
9.G.W.		+	++	No records			28 weeks	No records			Interstitial Nephritis.	Seen 1.9/12 years after dis-:missal "Greatly improved; trace of albumin"
10.R.L.	90/60	-	++	3%	46		22 weeks	No records			Diffuse glomer-ulo-tubular nephritis.	Died 12 days after operation.
11.J.F.	95/70	-	+++	Norecords			15 months	No records			Mixed nephritis. chiefly glomerular.	Now in Eastpark Homes. Evidence of Chronic inters-:titial changes.
12.J.W.S.	104/68	-	++	1.4%	58	27.9	29.5/7 wks.	3%	58	28.3	Mixed nephritis. chiefly tubular and interstitial.	Now in Eastpark Homes. Seems almost cured.
13.B.A.		-	+++	1.5%	19		20 weeks.	No records			Glomerulo- tubul-ar nephritis.	Complete recovery.
14.D.C.	110/80	-	++	2%	45		19 weeks.	22%	50		Glomerulo tubul-:ar nephritis.	Complete recovery.
15.W.F.	118/80	+	+++	2.3%	47		18 weeks.	No records			Glomerulo-tubul-:ar.	Seen Jany. 1928. "Well but trace of albumin in urine"
16.A.L.	80/56	-	++	3.4%	18.8		9.3/7 wks.	2.5%	18		Subacute Paren-chymatous neph-:ritis.	Complete recovery.
17.J.L.	95/70	-	+++	2.6%	35		16 weeks	No records			Glomerulo - Tubular.	Died of nephritis 5/2/26.
18.N.T.	106/50	-	++	2.4%	25		7½ months.	2%	33		Glomerular nephritis be-coming chronic.	Now chronic interstitial nephritis.
19.J.J.	88/50	±	++	No records.			17 months		52		Mixed nephritis	Lost sight of since dismissal
20.J.C.	118/80	++	+++	,	24		10 weeks	2.9%	86		Acute glomeru-:lar nephritis.	Still oedema and albuminuria present.
21.J.M.	90/60	+	+++	3%	56		7½ months	1.8%	30		Glomerular Mixed nephritis	Child slowly improving .Still albuminuria and occasional oedema.
22.J.R.	112/85	-	+++	2.4%	36	N.P.N.70	11 weeks	2.7%	56	N.P.N.92	Mixed nephritis mostly interstitial.	Seems completely free from signs of disease.
23.F.McA.	110/90	-	+++	0.8%		N.P.N.66	21 weeks	No records.			Mixed nephritis.	Child died of pneumonia 13/2/29.

British Medical Association meeting in 1928, T.G.Moorhead expressed the view that the operation is uncalled for, while in the recent edition of Garrod, Batten, Thursfield, and Paterson's "Diseases of Children", J.C.Spence[13] makes the statement that decapsulation has fallen into disrepute in the light of the newer knowledge of the disease.

Details of Present Investigation:- The series on which our analysis is based consists of twenty three cases; the first was operated on in June 1917, and the last as recently as January of this year. Operation was decided on in each case primarily because of failure to respond to medical treatment. The presence of oedema was the consideration next in importance. In other words, all the cases would come under the clinical heading of subacute nephritis of parenchymatous or mixed type. No frank case of chronic interstitial nephritis was subjected to surgical treatment.

Our object in this investigation was to discover if any of our cases could be found to have shown definite improvement as the result of decapsulation, and, if so, whether we could find a feature or features common to the cases which improved, which might help in the future selection of cases suitable for operation. We propose first to examine the effect of the operation on the ultimate outcome of the case; we will follow this with an examination of any immediate results of the treatment. Our series consists of twenty three cases. We append a complete list of these cases, with a short summary of the history of each. All the cases had received medical and surgical treatment at the Royal Hospital for Sick Children, Glasgow.

In Table I we present the clinical and biochemical findings from the case sheets; these records are incomplete.

Of the twenty three cases, seven had died. An endeavour was made to have all the surviving cases come up for examination.

TABLE 11.

CASES:-	Interval. Since operation	Blood pressure	Urine Bl.	Alb.	casts.	Kidney function tests. U. C. T. B.	1.	2.	Pigment	N.P.
Case V.A.W.	2 6.3 years	119/70 mm	-	-	-	—	0.9%	1.8%	66%	25
Case VII.J.D.	6 years	106/66	-	-	-	—	1.5%	2.5%	77%	45
Case XI. J.F.	2¼ years	132/88	-	++	+	—	0.9%	1.2%	25%	
Case XII.JWS.	3½ years	120/60	-	+	-	—	2.1%	2.5%	77%	48
Case XIII.B.A	3 years	104/60	-	-	-					
Case XIV.P.C.	10 2.12years	110/75	-	-	-	—	1.8%	2.2%	64.5%	44
Case XVI.A.L.	11 2.12years	100/66	-	-	-	—	2.1%	2%	58%	47
Case XVIII.WJ	11 2.12years	158/100	-	++	+	—	0.6%	1%	8%	86
Case XX.J.C.	7 1.12years	124/80	-	++	±	—	2.2%	2.4%	61%	
Case XXI.J.M.	4 1.12years	90/62	-	+	±					
Case XXII.J.R	6 months.	100/56	-	-	-	—	0.8%	1.9%	60%	30

Contractions:-

Bl. - Blood.
Alb. - Albumin.
U.C.T. Urea Concentration Test.
B. - Before.
1. - 1st. Hour,
2. - 2nd. Hour.
N.P.N. Blood Non-protein-nitrogen.

Two cases (Nos.III and XIX) have been lost sight of since their dismissal from hospital. Three others (Nos.VI, IX and XV) could not be found for our examination but they had been seen $1\frac{1}{2}$, $1\frac{2}{3}$, and 2 years respectively after their dismissal and the records then made seem definite enough for use in our analysis. The eleven remaining cases were subjected to a clinical examination, and, where possible, to a urea concentration and pigment excretion test and to a blood non-protein-nitrogen estimation. The urea concentration test was carried out by the MacLean hypobromite method(14) the pigment excretion test by the intra muscular injection of 6 mg of phenolsulphone phthalein and colorimetric estimation of the two-hours' excretion in the urine; the blood N.P.N. was estimated by the Folin Wu method.(15) The results are set out in table III.

Analysis of Tables I and II:- A primary analysis of tables I and II, as to the ultimate outcome of the case, yields the following figures:-

No. of cases operated on - - - - - - -	23
No. of cases in which result is unknown -	2
No. of cases seemingly cured or almost so-	10
No. of chronic cases - - - - - - - - -	4
No. of deaths - - - - - - - - - - - -	7

The number of deaths is made up from -

No. of cases failing to recover from operation -	3
No. of cases dying from nephritis - - - - - -	3
No. of cases dead, cause not specified- - - -	1

The ultimate fate of the four chronic cases is still uncertain. If one may hazard a prognosis, cases XI and XVIII look to be of the chronic interstitial type and will not get well, while cases XX and XXI seem to offer hope of recovery. Accepting this estimation, our final figures are:-

No. of cases, whose fate is known - - - - - -	21
No. of recoveries - - - - - - - - - - - -	12
No. of failures - - - - - - - - - - - - -	9

Do these figures bear any significance? In other words, is this recovery rate higher than one might expect in a similar series of unoperated cases? An endeavour to answer this question/

question leads us to a consideration of the question of prognosis in nephritis of childhood. It is generally agreed that the attack of acute nephritis in a child usually clears up within a reasonable time. Our own experiences with such cases during these investigations gave the following results:-

No.of cases admitted as acute nephritis - 25.
No.of cases dead - - - - - - - - - - - - 2.
(one following decapsulation and one from tonsillitis)
No.of cases dismissed as having recovered - 20.
No.of cases still under treatment - - - - - 3.

When the acute stage doesn't clear up and passes on to the subacute, or in those cases which seem to start insidiously as the subacute form from the beginning, the outlook is much more serious. When there are indications in the clinical picture of well marked interstitial changes in the kidneys one does not expect the patient to recover completely. The two factors which influence prognosis more than any others are the duration of the disease and the extent of the interstitial damage. These two factors are not directly related. A case, in fact the type of case we are dealing with as being suitable for operative treatment, may last a relatively long time - months or even years - without showing evidence of interstitial change, while an acute case may be interstitial from the onset. The presence or absence of oedema does not necessarily determine the type of case, the term "parenchymatous nephritis" being merely a name associated by usage with a certain clinical picture. The oedema may be the principal feature of the illness, there being no evidence of loss of kidney function, thus conforming with Muller's "nephrosis"; on the other hand, a high blood urea, a raised blood pressure, and a diminished excretion of urea by the kidney may accompany the oedema in varying degree. This seems the more common type of case.

Another difficulty we have in trying to classify cases for purposes of prognosis is that of determining how long a case should be regarded as in the acute stage, and when it should be looked on as subacute and the prognosis definitely worse.

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T A B L E. 111.

Cases:-	Hospital records. B/P	Urine. Bl.	Alb.	casts.	Biochemical finds. U.	C.	T.	Pigment	Int.since. Hospital treatment.	Latest Finding. B/P	Urine Bl.	Alb.	casts.	Biochemical findings U.	C.	T.	Pig.	N.P.N.
Case XXlV. M.B.	110/70	+	++	+	1.5%	3.3%		47%	6½ yrs.	138/80	-	±	-	2.4%	2.7%		37%	46mg%
Case XXV. N.B.	95/50	-	+++	±	1.5%	2.4%		51%	5½ yrs.	115/50	-	-	-	0.8%	2.7%		62%	57mg%
Case XXVl J.McI	100/80	-	++	+	0.5%	1.6%		30%	3¾ yrs.	119/60	-	-	±	1.8%	2.2%		67%	28mg%

We must admit that nephritis in childhood, for the purposes of prognosis, refuses to be classified under any scheme as yet suggested and our series is no exception to this statement. Case XXII offers a very good example of this difficulty.

The clinical diagnosis was one of subacute parenchymatous nephritis; biochemically this diagnosis was supported by a high blood cholesterol figure and a good urea concentration result. On the other hand, a slightly raised blood pressure and an increase in the blood non-protein-nitrogen suggested glomerular or interstitial changes. This suggestion was corroborated by the pathologist's report on a piece of kidney tissue. He reported a mixed nephritis, mostly interstitial. Six months after the operation, the boy is practically well! Such unexpected findings make any attempt at basing prognosis on classification of our cases farcical.

The obvious way to arrive at a valuation of our results would be to compare them with those in a comparable series of unoperated cases. Such a proceeding we found impracticable. The one constant feature in all of our cases - apart, perhaps from oedema - was their failure to respond to medical treatment. Most of such cases, and they form the minority of cases of nephritis in childhood, had been operated on since the procedure was first instituted, and we found it impossible to summon a corresponding series of non-operated cases. Invitations were sent out to all such cases on the books of the hospital during the same period but only three came up for examination. Fortunately they proved very instructive for our purposes. Short summaries of their case histories are appended, (Nos.XXIV,XXV and XXVI) and their clinical and biochemical findings, both while in hospital and at our examination, are set out in Table III.

In each of these three cases, recovery from nephritis seems to have been complete or almost so. Case XXIV has many points of similarity to case XII of the operated series. In each, oedema and albuminuria were the prominent features during a long stay/

stay in hospital. In each, there had been a recurrence of symptoms some time after dismissal, but they have both been perfectly fit for some time now, though a faint haze of albumin in the urine in each case persists as a legacy from their nephritis. Case XXIV had, moreover, a slightly raised systolic blood pressure, but this seems to be of little significance in the presence of the very favourable result of the urea concentration test.

Case XXV has many features in common with case VII. The histories are somewhat similar and recovery in each case seems to have been complete except for a slightly raised blood non-protein-nitrogen, the significance of which, in the absence of all other signs, is questionable.

Case XXVI seems also to have recovered from his nephritis, his poor physical and mental condition probably not depending on renal damage.

One must admit that the unoperated series is quite inadequate to enable us to compare our recovery rates in the two series of cases, but one may conclude from a consideration of these cases that the course and ultimate result in an operated case may be very similar to those in a non-operated case and the existence of so complete a parallel between the two both in history, duration, and ultimate result seems to preclude the attributing of the recovery to the surgical treatment. Here then one may be permitted to draw one's first conclusion.

Conclusion - From the consideration of a series of operated and non-operated cases of subacute nephritis, though the latter series is very inadequate to give a complete comparison, yet it is seen that the history and ultimate result may be very similar. Consequently, it is impossible to attribute the successful results in operated cases to the operation.

It might be thought that any benefit accruing from the operation would be represented in an improvement in the results from/

from renal efficiency tests. These tests in their present stage of development are of uncertain value in nephritis in determining either the type of case, the extent of the renal mischief or the course of the disease. Moreover, our records are too incomplete to enable us to draw any definite conclusions. However, we have sufficient data to prove how inconclusive these tests have been. For instance, cases V and XII show improved results from the urea concentration test following the operation; the former is now well and the latter is almost so but with slight albuminuria. On the other hand, cases XVI and XXI gave poorer post operative results, and again the former is well and the latter improving, though still with some albumin in the urine and a slight puffiness of the face. With regard to the pigment excretion test, case VIII showed an improvement following operation and has since died of nephritis, while case XXI gave a diminished excretion and seems to be recovering. If the operation were the determining factor in the recovery, one might have expected that, in the cases which recovered at least, the kidney efficiency tests would indicate the improvement. What we do find is that these tests may show improvement or deterioration whether the case is destined to get better or not. Here we may draw our second conclusion.

Conclusion - The results of the kidney efficiency tests at our disposal do not indicate that the operation was a determining factor in the subsequent progress of the case.

One might have expected that the material supplied to the pathologist from such a series of operations would yield valuable information in helping to correlate classification and prognosis and to determine the type of case, if any, suitable for decapsulation. Here our records are fairly complete, only five of the earlier reports being missing.

Clinicians have long recognised the difficulty of correlating their clinical and post-mortem findings and it is so in our series. Pathologically, we have had only one case of the parenchymatous type/

type - case XVI - though most of our cases had been of this type clinically. In the majority of the specimens the pathologist examined, he found changes in all three kidney structures - glomeruli, tubules, and interstitial tissue, and the course of the disease seems to have been determined more by the severity of the damage, than by the particular kidney element chiefly involved. There seems to be no correlation whatever between the principal site of the mischief in the kidneys and either the clinical type of case or the course of the disease following the operation.

Conclusion - A study of the pathological findings in our series of cases of nephritis helps us neither to a classification of these cases nor to a prognosis following decapsulation.

We are left now with the case history records to seek for any result from decapsulation. In six of these histories the definite statement is made that the patient was improved immediately following the operation. We give a list of these cases with the note made in each.

Case XI - J.F. - "Oedema disappeared after the operation."

Case XII- J.W.S- "Oedema disappeared and patient was much better after operation."

Case XIV- D.C. - "Oedema and general condition improved after the operation."

Case XV - W.F. - "Marked diuresis and rapid improvement followed the operation."

Case XIX-J.T. - "After operation, oedema disappeared and child was much better."

Case XX - J.C. - "Following the operation, oedema speedily disappeared."

Each of these children had been under medical treatment for periods varying from 2½ to 17 months without any material change and in each case improvement in the clinical condition of the patient rapidly followed surgical treatment. That such improvement was a permanent one is not borne out by subsequent events for case XI is still an invalid and showing signs of chronic interstitial nephritis and case XII, though now almost completely

recovered/

recovered, had a recurrence of all his symptoms after his dismissal from hospital. However, the recent supporters of the operation have not laid claim to a cure of nephritis from the procedure, but to an improvement in the prominent symptoms. This claim seems to find support from a study of the histories of these six cases. The symptom which, in each of these cases, is primarily affected by the operation is the oedema.

The question of the relationship between renal disease and oedema has exercised the minds of physiologists and biochemists for some years now. The view formerly held was that the oedema was due to an inability of the kidney to excrete water and salts. Muller first threw doubts on the correctness of this explanation when he advanced his opinion that there existed a type of nephritis with oedema not depending on disease of the kidney but rather on some disorder of metabolism. For this type he suggested the term "Nephrosis".

Oedema of some degree is, of course, an almost constant feature of acute nephritis though never so marked as it becomes later in the subacute parenchymatous stage. Oedema is a retention of water and salts in the body tissues of sufficient severity, in the common use of the term, to be evidenced by puffiness, swelling, or pitting. Strictly speaking, it may be present without any such evidence, its presence being indicated by an increase in the patient's weight. Such a condition is found in lobar pneumonia, and in this disease, as in most cases of acute nephritis, an oliguria during the acute stage may be followed by a critical diuresis, with the passage of large quantities of water and salt.

In spite of the variety in type of nephritis in which oedema is a feature, there is no reason for believing that the underlying primary cause is different in each, though Spence (16) thinks that the oedemas of acute nephritis and of nephrosis have a different aetiology. He says - "The subcutaneous oedema of acute nephritis occurs without appreciable diffusion into the serous/

serous sacs. It is due to a decreased elimination of water by the damaged kidneys ..... The oedema of acute nephritis is to be distinguished from the oedema of parenchymatous nephritis (nephrosis) which is caused by the abnormal passage of water and chlorides from the blood to the tissue fluids." He gives no reason for this opinion and there are many facts to disprove it. Oedema does not seem to be a sign of deficient kidney function, for it is absent in the very cases in which the kidneys are most extensively diseased. Even complete anuria as may occur in enlarged prostate or experimental nephrectomy, does not give rise to oedema. T.Izod Bennett, in his second Goulstonian lecture of 1928, after a close and thorough review of the facts at his disposal came to the following conclusion - "Oedema of nephritis is at once suggestive of pathological change in tissues other than the kidney, and such pathological change is not the result of nephritis, though it is more than probable that the renal and extra-renal damage have a common cause."

Leo Loeb in his monumental monograph on oedema in "Medicine", vol.2, 1923, arrives at the conclusion that there is no relationship between the ability of the kidney to excrete salts and water and their retention in the tissues with oedema. He thinks the retention of salt by the tissues the responsible factor and that the kation Na is probably the agent. Be it noted that neither of these authors draws any distinction between different types of nephritis but each speaks of the "oedema of nephritis".

Whatever the explanation for the oedema, recent opinion seems to favour the view that it is not due to a defective excretion of salt and water by damaged kidneys but it is due to a disturbance in tissues other than the kidney.

Alongside this opinion place the fact that, in six of our cases of nephritis in each of whom decapsulation was performed, definite/

TABLE IV.

Cases:-	Duration before Operation	B/P	Oedema	Urine Alb.	Urine Bl.	Urine Casts.	Biochemical findings:- U,C.T.	Biochemical findings:- Pigment	Pathological Classification.
Case XI. J.F.	15 mos.	95/70	++	+++	-	-	no records		Mixed nephritis. Chiefly glomerular.
Case XII. J.W.S.	7 mos.	104/68	++	++	-	-	1.3%1.4%	58%	mixed nephritis, chiefly tubular & intestitial
Case XIV. D.C.	4½ mos.	110/80	++	+++	-	+	2.% 2.%	45%	Glomerulo tubular with interstitial charges.
Case XV. W.F.	41/3mos.	118/80	++	+++	+	+	1.5%2.3%	47%	Glomerular tubular nephritis.
Case XIX. J.J.	17 mos.	88/50	++	++	±	+	no records.		Mixed nephritis.
Case XXI. J.R.	2½ mos.	112/85	++	++	-	+	2.2%2.4%	36%	Mixed nephritis mostly interstitial.

definite and decided improvement was noted immediately following the operation. This improvement was general but took place only in cases where oedema was a prominent feature, and a diuresis and a lessening or disappearance of the oedema were the outward and visible signs of such improvement. It is difficult to see why an operation on the kidneys should result in an improvement only in those signs of the disease which cannot be attributed to a lesion of the kidneys. An explanation may be in the statement of Fleisher and Loeb, as quoted by Loeb in the above mentioned monograph, when, speaking of operations on the kidney, they say that "The effects of operation do not specifically depend on the interference with the function of the kidney but are due to the effect of the operation as such. Every operation as such - but not the anaesthesia - has a far reaching influence on the exchange of substances between the blood and the tissues." If this view is correct, the results are not so paradoxical as they would appear at first sight to be, though a laparotomy might have an equal curative value to a decapsulation. It would certainly seem that the usual view, that the good results from the operation are due to a relieving of the tension in the kidneys from the oedema and so to a restoration of kidney function, can not be upheld if such results are confined to a disappearance of the oedema, and no alteration in renal efficiency.

Conclusion - The operation of decapsulation effected an immediate improvement in six of our series of cases of nephritis. Such improvement was represented by a disappearance of the oedema, and did not determine the ultimate issue of the disease.

It is only left to us now to examine these cases in which improvement was recorded and find if there is a common factor or factors, by which such cases may be determined. For simplicity of analysis, we have grouped the six cases with their findings in a separate table, Table IV. A study of this table does not yield us any fresh information. The features common

to/

to all the cases are oedema and albuminuria. Pathologically, the lesion involved all three elements of the kidney in each case, if we except case XV where interstitial changes are not mentioned. Of the four cases in which efficiency tests were carried out before operation, case XII showed a poor result from the urea concentration test, case XIV showed some degree of kidney damage, while cases XV and XXII gave more or less normal results. On the other hand, case XII had a moderately good pigment excretion while that of case XXII was well below normal. Finally, the blood urea was within the upper limits of normal in case XII, while in case XXII the blood N.P.N. (which in cases of nephritis reflects the blood urea closely) shows a marked increase. Thus there seems no common feature in these six cases which improved, examined from the clinical, pathological or biochemical standpoint, which might lead to the recognition of a case suitable for operation.

Conclusion - An examination of the records of the six cases of our series showing improvement following decapsulation does not yield any information which might help us to determine beforehand which particular case is likely to benefit by the procedure.

Summary - This study is based on an analysis of twenty three cases of subacute nephritis in children, where decapsulation of the kidneys had been performed because of failure to respond to medical measures. The case histories have been studied and short summaries are appended. The pathological reports and the biochemical findings before and after operation have been examined. Our object was to determine if any benefit had been derived from the procedure; if so, what benefit, and if it were possible to determine which type of case was likely so to benefit.

We have shown that out of the twenty three cases operated on twelve are cured or almost so. We have pointed out the difficulty of assessing the value of this recovery rate and our inability to compare/

compare it with that of a similar series of non-operated cases. However, we have shown that it is possible to get a very similar course of events and ultimate result in operated and non-operated cases.

We have shown that six of the operated cases exhibited a decided improvement following operation, this improvement being represented chiefly by a lessening or disappearance of the oedema. We have shown that an examination of the records of these six cases fails to reveal any common factor or factors which might help us to the recognition of a case suitable for operation. As the result of our study the following conclusions seem justified:-

Conclusions - I That from an analysis of the data at our disposal, we are unable to conclude that the ultimate result in a case of subacute nephritis is influenced by the operation of decapsulation.

II That there is no evidence for any belief that improvement in kidney function follows the operation.

III That certain cases do show definite improvement after operation, this improvement being reflected principally in disappearance of the oedema.

IV That a study of the cases of our series which have shown improvement following the operation does not help us to arrive at any determination beforehand as to which type of case would be likely to benefit from the operation.

APPENDIX.

Case Histories.

Case I - J.S., male, aet.1 year, was admitted 16/2/17 complaining of swelling of body. He had had slight attacks of bronchitis twice, but had been otherwise well. Four weeks before admission swelling of the face was noticed; this continued and got worse till admitted. All medical measures in hospital failed. Decapsulation was carried out on 18th and 23rd June, 1917. No immediate improvement was noted. Child died of nephritis 2/2/1918.

Case II - M.C., female, aet.4 years, was admitted 9/6/19, complaining of swelling and blood in urine of 7 weeks duration. Previous health had always been good. There was well marked general oedema, with oliguria. Hospital medical treatment for 2½ months was unavailing. Decapsulation was performed 19/8/19. Child died, but no details are given.

Case III - W.B., male, aet.2 years, was admitted 23/9/20 complaining of swelling of face and legs of 14 days and of abdomen of 10 days duration. There had been no previous illness. There was general oedema and some free abdominal fluid. He was treated on medical side for 4½ months without result and was decapsulated 11/2/21. This patient was dismissed from the surgical side and has since been lost sight of.

Case IV - I.McA., male, aet.3 years was admitted 27/2/21 complaining of swelling of face and ankles of 5 weeks duration. There was no history of any previous illnesses. On admission, the oedema was general, and very marked, with pleural and abdominal fluid. He was treated on medical side for about 2 months, but the oedema, although varying in intensity, persisted. He was removed to the surgical side for decapsulation on 21/4/1921, and died on the surgical side.

Case V - A.W., female, aet.8 years was admitted 9/8/21 complaining of swelling of face and lip of 8 days duration, following a drenching. The child had always been healthy previously. On admission, the child was moderately swollen, with some dulness at the bases of both lungs, and some free abdominal fluid. At first, the oedema seemed to yield to treatment, but it recurred worse than ever, and the child became huge and bloated. Decapsulation was performed on 9/12/21. Following the operation, a slight, slow decrease was noted in the intensity of the oedema, but on dismissal to county branch there was still a fair amount of swelling. Patient spent 5 months at Drumchapel and 1½ years at East Park Home, the symptoms during this period gradually abating. Since her return home, her mother says 'she has never looked back'. She was seen 27/8/28 - table II - and seems to have made a complete recovery.

Case VI - F.McD., male, aet. 7½ years, was admitted 17/3/22 with a history of oedema of 5 months duration. Urine contained a fair amount of albumin, a few blood cells and epithelial casts. The boy improved during first 10 days in hospital, but then relapsed and for the next 3 months there was no improvement in the condition. Decapsulation of both kidneys was performed 6/6/22. No change in condition resulted for 2 months, then some improvement was noticed, though oedema of face persisted. Five months after operation child was sent to convalescent home, 3/3/22. In November, 1923, he was dismissed from convalescent home well. In May 1925, he was seen as outpatient. He was perfectly well, had been attending school regularly, and was fit for games. The blood pressure was normal, there were no cardiovascular changes, and the urine contained no albumin or casts.

Case VII - J.D., male, aet. 5½ years, was admitted 12/6/22 with a history of headaches and vomiting at intervals for one year and of pain on micturition for 6 months. Previous illnesses were - Diphtheria/

Diphtheria at 1 year, Scarlet Fever at $\frac{7}{12}$ year, chicken pox and whooping cough at 2 years. On admission, the child was found to be under average height and weight, though well nourished. There was some oedema of face but none of legs or body could be made out. There was a fair amount of albumin, red blood cells and casts in urine. Left optic disc was oedematous in appearance. For the next $2\frac{1}{2}$ months the degree of oedema varied from nil to a mild general anasarca, while the urine continued to show moderate albumin and casts. Both kidneys were decapsulated 1/9/22; on readmission to medical ward, the note was made - 'general condition unchanged'. On recovery from the operation he was dismissed home and for the next 2 years he missed a lot of schooling because of recurring headaches, and slight oedema. These symptoms gradually abated. Patient was seen outdoor, 27/8/28, table II, he is a health looking boy, with no evidence whatever, except slightly indistinct margins of the optic discs, of his having had nephritis.

Case VIII - C.McC, male, aet.$5\frac{1}{2}$ years was admitted 28/8/22, with a history of swelling of legs, face and abdomen of 8 days' duration, vomiting and oliguria. He had had chicken pox at 10 months, measles at 3 years and whooping cough at 5 years. On admission, the child showed well marked general oedema; the urine contained a moderate amount of albumin, no blood, and some casts. During the next $5\frac{1}{2}$ months, the oedema varied but was usually severe. Both kidneys were decapsulated 13/2/25. On his return to the medical ward, child was stated to be looking well. Oedema had almost entirely disappeared, and patient was dismissed 5/6/25, much improved. He remained fairly well, though albumin persisted, till 25/3/26 when he was readmitted with a recurrence of symptoms. The nephritis was found to be complicated with peritonitis with erysipelas of left thigh. This patient ultimately died of nephritis.

Case IX - G.W., male, aet.11 years was admitted 1/3/23 with a history of headache, sore throat and oedema. These symptoms had been present some months previously but had cleared up and returned 4 days before examination. There was marked oedema of face.and legs and urine contained much albumin with blood and casts. There was no improvement in condition for 3 months and on 12/6/23 both kidneys were decapsulated. For the next 4 months there was practically no change in boy's condition and he was dismissed to East Park Home.

1 year and 9 months later he was examined as outpatient. He was found to have greatly improved, was of a good colour and looked well. There had been no oedema for a considerable time. There were no cardiovascular changes; systolic B/P 105 mms hg. Urine showed a faint trace of albumin but no casts.

Case X - R.L., male, aet.8 years was admitted 5/2/24 with a history of oedema of 8 days duration. He had whooping cough at 3 years and measles at 4 years. On admission, the oedema was confined to face, but soon became general. The urine contained a large quantity of albumin, some blood and a few casts. As the child made no progress, decapsulation was performed 12/5/24. The symptoms were unrelieved by the operation, and the boy died 12 days afterwards.

Case XI - J.F., female, aet.7 years, was admitted 23/12/24 as an acute nephritis and was dismissed 9/5/25 as a Mumps contact. She was readmitted 15/8/25 with a history of fitful health while at home, though there had been no oedema, till 5 days before readmission. The face was puffy there was some oedema over tibiae and sacrum, but no ascites. The urine showed moderate albumin urea with no blood or casts.

Child developed Empyema on left side and was operated on.

She/

She was dismissed 29/11/25 to Ruchill hospital with Scarlet fever. She was readmitted 20/3/26, looking better but with slight oedema and a large quantity of albumin in urine. The condition remained unchanged till 12/5/26 when decapsulation was performed. On her return from the surgical side, she was stated to be looking well, with no oedema, having lost about 8 kilos in weight. She was dismissed in this condition, first to the country branch and then to East Park Home, where she still remains. She was examined on 10/10/28 - Table II - child is confined to bed most of the time, with slight recurring oedema, and moderate albuminuria. The blood pressure is raised and the condition seems one of a gradually advancing chronic interstitial nephritis.

Case XII - J.W.S., male, aet.10 years was admitted 23/12/24 with a history of swelling of face and body of 7 weeks duration, and occasional vomiting. On admission, the child was found to have generalised oedema; the urine was scanty, and showed a large quantity of albumin, a few red blood cells and some casts. There was no increase in blood pressure.

Medical measures were tried for 6 months, without effecting an improvement, and decapsulation was performed 5/6/25. On readmission to medical ward, the note was made - "general condition very good; boy looks well; no oedema." He was sent home 25/8/25. On 18/8/27 he was admitted to Royal Infirmary with a recurrence of symptoms. After treatment for some weeks, he was sent to East Park Home, where he is now. He was examined there 27/8/28 and 5/9/28, and was found to be very well except for a persistence of moderate albuminuria and a slightly raised blood N.P.N.

Case XIII - B.A., female, aet. 1½ years, was admitted 18/6/25 with a history of swelling of eyelids of 2 months, and of legs of 7 days duration. On admission, there was oedema of eyelids, feet, legs and lumbar region. Rhonchi were heard all over chest. Urine showed large quantity of albumin, no blood and some epithelial granular/

granular and hyaline casts. Condition at first cleared up in hospital but later recurred with increased severity. The oedema was a prominent feature and resisted all measures to reduce it. Decapsulation was performed 5/9/25, following which no change was noted in general condition and oedema persisted. Two months later, child began to improve and was dismissed 19/12/25 much better. Albuminuria still persisted (Esbach 1.5), but there was no oedema. She was seen outdoor 30/8/28, and was found to be a healthy looking, sturdy child. There had been no recurrence of symptoms since dismissal. Urine showed no albumin, blood or casts. Table II.

Case XIV - D.C., female, aet.9 years was admitted 24/6/25 with a history of swelling of face and feet and occasional vomiting of 4 days duration. She had had Scarlet fever at 5 years but had been otherwise healthy. On admission, child did not look ill, but there was oedema of face, legs, and lumbar region and there was dulness at the bases of both lungs. There was albumin in ghe urine but no blood or casts. In hospital the child's condition got worse and decapsulation was performed 29/10/25.

Child was readmitted to medical ward 20/11/25 and note was made that child looked fairly well; there was oedema of legs and lumbar region. There was steady improvement till 28/12/25 when child was dismissed. There was still slight oedema and some albuminuria (Esbach 0.75). Patient was seen outdoor 17/8/28. Since her dismissal she had remained well except for occasional cold; she now showed no evidence of renal mischief. Table II.

Case XV - W.F., male, aet.10 years was admitted 1/7/25 with a history of swelling of face of 7 days and of feet and ankles of 3 days duration. He had had whooping cough at 2 years, pneumonia at 2½ years and measles at 6 years. On admission oedema was confined to face and ankles; the urine showed moderate albuminuria, some blood and casts. The oedema varied in intensity during/

during child's stay in hospital but was never very marked. There was no change in urine. Both kidneys were decapsulated 29/10/25; the urine immediately became more abundant and the albumin fell in quantity. On readmission to medical ward the boy looked well and had no oedema. He was dismissed 8/12/25 and was seen outdoor 8/1/28 when there was a slight trace of albumin in urine but no other indication of nephritis.

Case XVI - A.L., male, aet.3 years was admitted 3/8/25 with a history of swelling of face of 3 days and of feet of 1 day duration. There had been no previous illnesses. On admission, a mild degree of oedema was present in face, legs and lumbar region. Albuminuria was very marked but there was no blood or casts. The condition remained unchanged till 6/10/25 when decapsulation was performed. This was followed by no improvement and child was transferred to Ruchill hospital 10/11/25 with erysipelas. He was readmitted to medical ward 20/3/26 with oedema and albuminuria as before. Oedema gradually disappeared and he was sent home 12/4/26. He was seen outdoor 25/5/26 when albumin was still present in fair quantity in urine, but there was no oedema. He was again seen 27/8/28; in the interval he had remained well. He was now a bright healthy-looking boy with good colour. There was no evidence of the presence of nephritis. Table II.

Case XVII - J.L., female, aet.7 years was admitted 11/8/25 with a history of swelling of face and feet of 8 weeks duration, with occasional headaches. She had previously had whooping cough and measles. On admission swelling was confined to face, legs and lumbar region, but became more marked during stay in hospital. There was a large quantity of albumin in urine, no blood, and some casts. Decapsulation was performed 8/10/25. Child was kept on surgical side after operation, as she seemed to be getting worse. She died of nephritis 5/2/26.

Case XVIII - N.J., female, aet 10 years was admitted 15/9/25 with a history of recurring oedema of face and legs and albuminuria of 7 months duration. She had had measles and chicken pox at 2 years.

On admission, there was a little oedema; there was moderate albuminuria with casts. Decapsulation was performed 1/10/25. This was followed by no change and child was kept in hospital till 24/12/25, when condition was very similar to her previous one and she was sent home. She was seen outdoor 30/8/1928. In the interval she had had one severe recurrence of symptoms and a slight oedema and some albuminuria had persisted. The blood pressure was now 158/100 mms.hg., there were cardiovascular changes and the picture was that of chronic interstitial nephritis. Table II.

Case XIX - J.J., male, aet.3 years was admitted 9/6/26 with a history of swelling of face, limbs and body at intervals extending over one year. He had had no previous illnesses. On admission, there was general anasarca and ascites. The urine showed a moderate amount of albumin, a trace of blood and some casts. There was dulness at the basis of both lungs. During his stay in hospital, child's condition continued to come and go. Tonsillectomy was performed 27/8/26 with no evident result. Both kidneys were decapsulated 2/11/26 and the entry was made - "The general condition improved after the operation and the output of urine increased. There is no oedema".

The amount of albumin varied from a trace to 1 Esbach from this time till his dismissal 9/2/27. There was no recurrence of oedema. The boy has since been lost trace of.

Case XX - J.C., male, aet.6 years was admitted 26/12/26 with a history of swelling of face of 7 days and of abdomen and legs of 1 day duration.

He had had measles at 5 years, and there was a history of a previous/

previous attack of nephritis in Dec. 1925 for which he was treated at Stobhill hospital, being discharged "cured".
On admission, the child had very severe oedema and oliguria. The urine showed a large quantity of albumin, casts, and a few red cells. There was ascites and dulness of both lungs. Child was very pale and had a severe cough. Tonsillectomy was done 13/1/1927. The oedema and albuminuria persisted with varying intensity till 24/2/27, when both kidneys were decapsulated. The following notes appear in the surgical case sheet - 25/2/27 Esbach 4 urine 4oz. Oedema +++. 26/2/27 Esbach U+; urine 16oz; oedema of face a little less. 28/2/27 Esbach 5; urine 56oz; oedema of face and limbs much less. 1/3/27 Esbach 5; urine 60oz; no oedema.

The oedema was still gone, though albuminuria was present when he was readmitted to medical ward. Oedema returned about middle of April, but did not attain to a condition of its previous severity. The child's general condition was better and he was dismissed to East Park Home where he now is. He was examined 10/10/28 and there was slight oedema present. His systolic blood pressure was slightly increased - 124 mms. The urine contained a moderate quantity of albumin but no blood or casts (centrifuged). The kidney function tests gave fairly good results. Table II.

Case XXI - J.M., male, aet.4 years was admitted 12/3/27 with a history of a sudden attack of shivering, fever, vomiting and swelling of the face 5 months ago. The urine was said to have been red. The severe symptoms passed off and boy was allowed up but was not properly recovered. Six weeks before admission swelling of abdomen was noticed and this swelling gradually gradually increased and with an albuminuria determined his being brought to hospital. He had had no previous illness. On admission the child had general anasarca with free fluid in abdomen. Urine showed large quantity of albumin and casts, but no blood.

There was no change in the condition for the next 2 months and decapsulation/

decapsulation was performed 21/5/27. This was followed by little or no change and child was sent home 9/7/27. He was seen outdoor 10/9/28, when the following note was made - "Since dismissal child has been at home; he was confined to bed till April 1928; he now goes about a little but walks badly. He is a pale, bright boy with a little fulness of face and legs. Pulse 104; heart normal; B/P 90/62 mms.hg; O.E. nil; urine shows a slight cloud of albumin, no blood, and a few hyaline and granular casts. The mother refused to make arrangements to have kidney efficiency tests carried out." Table II.

Case XXII - J.R., male, aet.5 years was admitted 18/7/28 with a history of swelling of face and ankles of 12 days duration. He had pneumonia at 1 year, and measles and whooping cough at 2 years; he had since been well.

On admission the child was a small ill developed boy with well-marked general oedema. The urine contained a moderate quantity of albumin and casts, and no blood. The B/P was 112/85 mms. Child failed to improve under medical treatment and he was decapsulated 20/9/28. There was no perceptible change following the operation but during his stay in hospital he gradually improved. The oedema and albuminuria disappeared and he was discharged much improved. He was seen outdoor 19/3/1929, when he presented no evidence of nephritis - Table II.

Case XXIII - F.McA., male, aet.6 years was admitted 11/11/28 with a history of having had an attack of shivering, fever, vomiting and drowsiness 6 weeks before, which had passed off in 1 week. One week before admission he had a mild attack of bronchitis and 4 days before there was general swelling of body, with scanty dark brown urine.

On admission there was general oedema. The urine showed moderate amount of albumin and casts, but no blood. The condition persisted and decapsulation was performed 25/1/29. This was followed/

followed by little or no change. Pneumonia supervened and the child died 13/2/29. No post mortem was obtained.

Case XXIV -M.B., male, aet.12 years was admitted 19/5/22 with a history that child had seemed well but school doctor diagnosed nephritis 14 days before admission. After that, slight puffiness of face was observed. Boy had had measles at 5 years, chicken pox at 8 years and scarlet fever at 10 years. On admission, there was slight puffiness of face. Urine showed moderate albuminuria, some blood and casts. During 3½ months in hospital condition varied little; the albumin decreased in amount and he was dismissed 1/9/22 as having improved.

He was readmitted 17/6/23; in the interval he had been fairly well and had been seen regularly at outpatient department. Five weeks before readmission he showed recurrence of marked albuminuria and slight oedema. He was again treated for 3½ months with practically no result and was dismissed 6/10/23.

He was seen outdoor 9/10/28. After leaving hospital, he had been confined to bed for some weeks and condition gradually improved. There had been no recurrence of serious symptoms, merely an occasional puffiness under eyes. He was found to be a large healthy lad in regular employment, but urine showed a trace of albumin - Table IIII.

Case XXV - N.B., female, aet.5½ years was admitted 20/2/23 with a history of puffiness of the face of 3½ weeks duration. The following week she was admitted to Ruchill hospital with diphtheria and there was found to be suffering from nephritis. She had had measles and chicken pox at 1½ years, whooping cough at 2 years, and diphtheria at 2½ years. On admission, she was found to be a pale, spare child with very little oedema; urine showed a large quantity of albumin, no blood and occasional granular casts. While in hospital the oedema was never a feature but/

but there was well-marked albuminuria which continued till her dismissal 27/6/23. She was seen as an outpatient 9/10/28. In the interval patient had been in East Park Home, then at her own home. During this period she had diphtheria 3 times and scarlet fever.She was subject to colds and troubled with headaches. At first, eyes used to get puffy, but not lately. She was found to be a small active fairly healthy-looking child. There was no albumin in urine and no casts were found even on centrifuging. Table III.

Case XXVI - J.McN., male, aet.7 years was admitted 19/12/24 with a history of swelling of face, feet and abdomen of 6 weeks duration which at first seemed to improve but was now getting worse. He had had no infectious disease, but had been troubled with a chronic cough and had never seemed a strong child. On admission he was found to have general oedema of severe degree. The urine contained a moderate amount of albumin and casts, but no blood, though a trace appeared occasionally while he was in hospital. Child was treated for 5 months; at first there was practically no change in the condition, but latterly the oedema diminished and finally disappeared. The child was dismissed 15/5/25 to country branch; the urine still showed a moderate degree of albuminuria and occasional casts. He was seen as an outpatient 9/10/28. He was now a small poorly developed child with evident lack of intelligence. He can neither read nor write. He had a severe chronic cough and his breath was very foul. The chest was markedly flattened at sides. There was systolic murmur heard best at pulmonic area and transmitted down left border of sternum. The blood pressure was not increased. The urine contained no albumin and an occasional hyaline cast. The results of the kidney function tests were satisfactory. The child's poor physical condition did not seem to depend on renal trouble. Table III.

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products of metabolism and play a part in regulating the osmotic pressure and the acid-base balance of the blood. Whether these functions belong to the kidney cells themselves, what part the internal secretions, particularly that of the pituitary, play, whether the kidney possesses a hormone or hormones which may activate the various processes, as seems not unlikely, are questions on which our knowledge is still deficient.

Again, it is a moot point as to whether it is possible for one separate renal function to be impaired as the result of disease of the kidneys while the others remain unaffected. One of the recent pronouncements on this subject is that of Fishberg,(1) who says - "It is widely held that disease of the kidney may injure the ability of the organ to excrete individual substances while the excretion of other substances remains unimpaired. But I have pointed out in a previous communication(2) that there is no substantial basis for this view of isolated injury to individual renal functions in diffuse renal disease; available evidence points to there being but one variety of functional injury in renal disease, namely that involving all the excretory functions of the kidney. In those cases in which there is seemingly circumscribed injury to the ability of the kidney to excrete some individual substance, the cause of the retention of this substance in the organism is not the kidney but some extra-renal factor which results in diminished supply of the substance to the kidney." If this contention is correct, and as the result of our experience we are inclined to support it, it follows that any single satisfactory test of renal efficiency is of as much practical value as a number of tests, each indicating the efficiency of a separate renal function.

The development of kidney efficiency tests opened up fresh ground for research and certainly serve in some measure to indicate when renal function is more or less grossly impaired. Many such tests have been devised but those most commonly used are the pigment excretion test and the urea concentration test, with/

with which is often combined a water excretion test. These tests, in conjunction with estimations of the blood urea or non-protein-nitrogen and the blood cholesterol constitute with the clinical examination our modern equipment in facing the question of kidney disease.

While engaged on an other aspect of nephritis, we were privileged to have at our disposal a number of cases of nephritis in children and took advantage of the opportunity to investigate these cases along the above indicated lines.

Our clinical examination took note of previous illnesses, output and pathological constituents of urine, the state of the cardiovascular system, including blood pressure, and the presence and extent of oedema. We estimated the blood non-protein-nitrogen and were privileged to use the blood cholesterol findings of Dr. Graham. We carried out the urea concentration test in various forms, and the pigment excretion test. These investigations were usually made as a routine on each case immediately after admission to hospital and at irregular intervals during their stay, always subject to special exigencies such as the age of the patient and the severity of the illness. Very young children formed unsuitable material for certain of these investigations.

The number of cases on which these observations are based is twenty six, with ages varying from fourteen months to twelve years. With one exception, a good example of renal dwarfism, they were all admitted as suffering from acute nephritis, though two of them progressed to the subacute parenchymatous stage while in hospital and were decapsulated (Part I).

For the purposes of this paper it seems unnecessary to give case histories of the twenty six cases. We propose rather to take up the essential features of the disease already enumerated and discuss them one by one in the light of our findings. Appended is a complete list of cases with these data, and from this list separate tables will be compiled under the/

under the several headings for ease in correlation. We shall deal first with the clinical findings and pass thence to the results of blood examinations and renal efficiency tests.

Previous Illnesses:- Examination of the case histories with regard to the incidence of the common ailments of childhood shows that measles, whooping cough, chicken pox, mumps, diphtheria and pneumonia occurred in the usual proportion of cases. Scarlet fever was conspicuous by its absence. One case admitted as suffering from kidney disease showed evidence of desquamation and was considered a scarlatinal nephritis; her recovery was rapid and uneventful. This was the only case of our series in which scarlet fever was said or thought to have occurred. In five of the case histories the statement was recorded that there had been an attack of "influenza" three weeks before admission, the signs of nephritis having exhibited themselves in the third week following the influenzal onset. More significant than this seem to be the notes made on the condition of the throat and nose on admission. In every case, without exception, the state of the nasopharynx was considered sufficiently abnormal to merit comment from the physician. "Red throat", "enlarged tonsils", "copious nasal discharge", and "foetid breath and enlarged cervical glands" are the descriptions as they occur in the case sheets. Two cases had had tonsillectomy performed, and one reputedly so, though the tonsils were present and diseased. To find data by which to estimate the value of these figures we examined a number of case histories of children admitted suffering from diseases other than nephritis. The case sheets were chosen at random and the diagnosis included Banti's disease, cerebral tumour, cretinism, epilepsy, etc. In this series, the note made on the condition of the throat and nose was "nil" in seventeen out of thirty three cases. The difference between 100% of diseased throats in one series and 48·5% in the other is striking. That a relationship exists between throat infections and nephritis is no new observation; our/

TABLE 1. A.

BLOOD IN URINE ++.

CASE:-	B/P.mmhg.	Oedema.	Alb.	Blood Bio Chemistry N.P.N. mg. per 100 c.c.	Cholesterol	Urea Conc. Test. Before.	1st.	2nd.	Pigment. %
7.J.C.	124/78	General	E 6.5	86	-			1.3	30
13.J.K.	94/68	Puffy eyes?	+ +	60	220			2.3	59
16.A.G.	112/65	slight general	E 4.	91	330	1.9	1.9	2.1	56
23.A.R.	136/94	Nil	+	130	190	1.5	1.5	1.7	—
24.N.C.	98/60	Puffy face	E 2.	48	---	----------			--
25.J.McD.	130/118	General	+++	36			0.9	2.5	—
26.M.E.	102/80	Puffy face	+++	57	150			2.2	—
TABLE. 1. B.			BLOOD IN URINE +.						
2.C.L.	104/65	slight of face and feet	±	61	---			1.8	24
3.W.L.	98/54	General	E.4.75	70	185		1.5	1.7	71
8.W.H.	140/100	of face and feet	+ + E.1.5	46	152.		1.9	3.	50
9.A.P.	130/?	slight	+	32	185		---	---	--
14.J.G.	110/80	Face	E.0.75	37.5	240		2.6	2.	53
4.M.R.	------	Puffy slight pitting	E.1	28	180		2.2	2.2	28
15.F.F.	100/?	General	+++	44	160		2.1	2.1	—
18.T.H.	90/?	Nil	+	96	86	3.75	3.45	3.	31
19.G.B.	105/72	Nil	E.0.75	37.5	340	2.5	2.2	2.	48
20.A.G.	136/70	slight	+	43	333	2.	2.4	2.9	55
22.J.H.	108/70	Puffy face.	+	46	---	2.8	1.3	3.	—
TABLE.1. C.			NO BLOOD IN URINE.						
1.J.R.	112/85	Severe general	E.7	70	333			2.4	36
5.FMcA.	110/40	Severe general	E6.25	40	380			2.	40
6.E.G.	104/74	Nil	±	120	150			1.3	29.
10.E.L.	92/45	slight pitting over shins	+	70	130		1.8	2.4	56
11.J.B.	100/54	of face	trace	43	180		1.1	2.	26
12.M.E.	118/85	Puffy "	E0.25	46	---			2.8	—
17.A.H.	92/50	slight of face & legs		55	---		---	---	---
21.E.McM.	100/?	mild general	+++	96	225		2.4	2.5	75

our figures serve to bring out this relationship in bold relief.

One further point we would make is that tonsillectomy does not remove the risk of a subsequent attack of nephritis, however far it may lessen it, as many observers are inclined to believe.

Urine Examination:- Most of our cases gave a history of having passed 'red', 'dirty' or 'dark' urine for some days before admission. In some cases the urine was noticed to have been diminished in quantity, in others the quantity was said to have been as usual, while in others no note was made. On admission, the volume of urine was usually small for the first two or three days but increased on the third or fourth day to well above the amount normal for the age of the patient and the fluid intake. For instance, case II passed a few ounces only for the first two days; diuresis set in on the third day and the average daily volume for the ensuing week was fifty ounces. Thereafter the daily volume fell to 30 ounces during the remainder of the child's stay in hospital. This diuresis was always accompanied by a fall in body weight. In a few of the cases, this diuresis was delayed till later in the illness. In two cases which developed pneumonia shortly after their admission, the increased urinary output took place as the temperature returned to normal, while two examples of subacute parenchymatous nephritis with marked oedema had no diuresis before decapsulation.

Blood in the Urine:- The presence of blood in large quantities in the urine in some cases of nephritis has led to the use of the term acute haemorrhagic nephritis, involving the conception of a type of the disease distinct from the parenchymatous. A case of the former type may or may not exhibit oedema but has some degree of azotaemia while one of the latter type exhibits oedema as a constant feature but not haematuria or azotaemia.

Of our twenty six cases, in seven blood was recorded as having been present in the urine in large quantity, in eleven in moderate or small quantity, while it was absent in eight. We have set out these three groups in tabular form, Tables Ia, Ib and Ic, giving the clinical and biochemical findings in each

case. As the presence of a single sign of the disease seems to be an inadequate reason for conceiving a separate type, we wanted to find whether or not haematuria should prove to be accompanied by a characteristic grouping of features which might justify its use for purposes of classification. An examination of our tables leads us to conclude that no such correlation exists. In the cases in which a large quantity of blood was present in the urine, as in the other two groups in which there was a moderate amount or none at all, there is a complete absence of uniformity in the findings under the other headings if we except albuminuria, where one would naturally expect the amount of albumin to be in proportion to the quantity of blood present, other factors being equal. It is true that the parenchymatous type is faithfully reproduced in F.McA (case 5) without blood in the urine, but J.McD. (case 25) presents a similar picture except that blood was present in large quantity, while the azotaemic features of A.R. (case 23) are presented in a minor degree but without haematuria in J.R. (case I) and J.B. (case 11).

An interesting observation was made in one case - A.C. (case 20) - of acute nephritis with a moderate degree of haematuria. When the patient was convalescent and the blood had disappeared, she was put on calcium chloride to determine the effect, if any, of an experimental acidosis on the blood and urinary findings. The experiment was carried out twice and each time we produced a diuresis and a recrudescence of the haematuria. A repetition of the experiment in other cases with calcium chloride, ammonium chloride and hydrochloric acid was invariably followed by the diuresis but failed to set up a haematuria. It is interesting to record that Morris and Paul found experimentally that intravenous injection of various acids almost invariably produced haematuria in rabbits (unpublished work).

No other constant changes were found in our cases, clinically/

TABLE 11.

SEVERE ALBUMURIA

CASE:-	B/P mm.hg.	Oedema	N.P.N. mg. per 100 c.c.	Cholesterol. mg. per 100 c.c.	Urea. B.	Conc. 1.	Test. 2	Pigment. %
1.J.R.	112/85	Severe general	70	333			2.4	36
3.W.L.	98/54	general	70	185		1.5	1.7	36
5.F.McA.	110/90	Severe general	40	380	2.2	2.	2.	40
7.J.C.	124/78	General	86	175 *			1.3	30
15.F.F.	100/?	General	44	160 *		2.1	2.1	--
16.A.G.	112/65	General	91	330	1.9	1.9	2.1	56
21.E.McM.	100/?	General	96	225		2.4	2.5	75
25.J.McD.	130/118	General	36	180 *		0.9	2.5	--
26.A.E.	102/80	Puffy face.	57	150			2.2	--

* Estimation made after Oedema had disappeared

clinically or biochemically, unless the usual signs of an acidosis.

The relationship between the administration of calcium chloride and the haematuria seemed quite definite in the one case, but whether or not this suggests that the acidosis described as occurring in nephritis has any significance in the production of haematuria we do not know.

We do think, however, from a consideration of tables Ia, Ib, and Ic, that the presence of blood in the urine in cases of acute nephritis is not of sufficient constancy in its association with other features to justify its presence being used for purposes of classification. We leave out of this discussion cases of embolic nephritis, secondary to such conditions as infective endocarditis.

Albuminuria:- The presence of this sign is the factor on which most commonly a tentative diagnosis of nephritis is made. Albumin was present to a greater or lesser degree in all of our cases. The amount of albumin was variously indicated in the case sheets by an Esbach figure or by a number of pluses, thus:- ±,+,++, and +++. For purposes of correlation we have arranged in a separate table (Table II) those of our cases (nine) in which a large amount of albumin was present in the urine.

From a study of this table it will be seen that in all of these cases but one - A.E.(case 26) - the albuminuria was accompanied by a general oedema. Moreover, in only two of these cases did the result of the urea concentration test indicate any marked lessening of the ability of the kidney to excrete urea. The pigment test and the blood non-protein-nitrogen estimations gave varied results. The blood cholesterol, which is usually found raised in oedematous cases, seems to be contradictory in our series but the explanation lies in the fact that in every case where a figure under 200 is given the estimation/

estimation had been made after the oedema had subsided.

The association of severe albuminuria with a relatively good result from the urea concentration test in most of these cases seems significant, and leads us to conclude that, whatever factor in the disease produces the albuminuria, this same factor does not interfere with the power of the kidney to excrete urea. This is in accordance with the usual conception of parenchymatous nephritis. That interference with the excretory function of the kidney and the consequent accumulation of waste products in the blood is a certain indication of renal damage is a generally accepted view about which there seems no doubt. The idea that the presence of albumin in the urine is also necessarily such an indication is sub judice, but many authorities are of the opinion that the albuminuria of certain types of nephritis ("Nephrosis"), of the toxaemia of pregnancy, of postural albuminuria and of other morbid conditions is independent of kidney function. This view has recently been confirmed by Jungman,(3) who removed a portion of kidney from an early case of nephrosis and found it to be normal. It must be remembered that the normal kidney can and will excrete protein when required to do so, as for instance injected proteins or liberated haemoglobin.

In his explanation of nephrosis, Epstein(4) suggests that the primary error is a metabolic one, whereby serum albumin can no longer perform its proper functions in the body and is therefore excreted.

Taking the analogy from sugar metabolism, he has lately named the condition "diabetes albuminuricus". Other facts pointing to the metabolic nature of the disease are the increase of lipoid bodies in the blood and tissues and the unusually high tolerance of the patient to thyroxin. The change described as occurring in the kidneys is a degeneration of the tubular epithelium, with no cellular reaction, and may be secondary to

the/

the prolonged albuminuria.

We have already indicated that with one exception - A.E. (case 26) - all cases with a severe albuminuria exhibited a general oedema. In this case - A.E. - the blood cholesterol, estimated in the early stage of the illness was well within normal limits. The existence of this case would seem to preclude our drawing a general deduction unless we can explain it on other grounds. The records of the urinary findings during the progress of this case show that the amount of blood and of albumin in the urine decreased pari passu, and that when the blood had disappeared the presence of albumin was represented by a "very faint trace". This statement is also true in certain of the oedematous cases, e.g. J.C. and J.McD. but in these cases the oedema is found to have decreased coincidently with the blood and albumin and wherever the oedema persisted after the blood had disappeared, as in W.L. (case 3), albumin was still found to be present. We seem justified in drawing the conclusion that severe albuminuria, where not explained by the presence of a severe haematuria, is, in our series of cases, always accompanied by a general oedema.

Such an association may be found in the presence or absence of signs of impairment of renal function as reflected by the blood non-protein-nitrogen or the result of the urea concentration or pigment excretion test.

Cardio-vascular Changes:- The only cardio-vascular change we found in our cases was an increase in blood pressure. No case exhibited any cardiac or ophthalmic disturbance which might be associated with their kidney disease.

There are difficulties in valuing blood pressure findings in children, arising partly from the technical difficulty of estimating blood pressure in small arms with a sphygmomanometer and partly in determining a normal standard. The usually accepted standards are 90 to 110 mm hg. for systolic pressure and 40 to 60 mm for diastolic. Dawson, however, found a systolic pressure/

TABLE 111.

RAISED BLOOD PRESSURE

CASE:-	Blood pressure 1st. Reading.	Later.	Oedema	Urine Blood	Alb.	N.P.N.	Cholesterol	Urea. Conc. Test. B.	1.	2.	Pl
	mm.hg					mg. per 100 c.c.					
1.J.R.	112/85	100/56	Severe General	–	+++	73	333			2.4	
5.F.McA.	110/90	90/50	Severe General	–	+++	40	380	2.2	2.	2.	
7.J.C.	124/78	90/42	General	++	+++	86	175			1.3	
8.W.H.	140/100	98/52	slight of face, shins &c.	+	+	46	152		1.9	3.	
9.A.P.	130/?	—	slight	+	+	32	185		—	—	
12.M.E.	118/85	102/60	Puffy face	–	+	46	—			2.8	
20.A.C.	136/70	104/64	slight	+	+	43	333	2.	2.4	2.9	
23.A.R.	136/94	94/60	Nil	++	+	130	190	1.5	1.5	1.7	
25.J.McD.	130/118	90/60	General	++	+++	36	180		0.9	2.4	

pressure over 130 mm in 8% of 650 school children. This possibility of an abnormally high blood pressure being normal for any individual case did not require consideration in our series as a rise in blood pressure was always indicated by the subsequent fall to normal.

In our records we found, as other observers have done, that the blood pressure is raised for some days at the commencement of an attack of nephritis, but soon returns to normal. The rise was never very high - 140 mm systolic and 118 mm diastolic being our highest readings - and always had subsided by the time the next observation came to be made. In our single case of chronic instertitial nephritis with renal dwarfism - E.G. (case 6) - the blood pressure was not increased to any extent - 104/74 mm. On the other hand, in the case which of all our series most closely resembled a true nephrosis - F.McA (case 5) - the initial blood pressure was 110/90 mm., and the extent of the rise was indicated by the subsequent reading, 90/50 mm.

To discover whether a raised blood pressure was in constant association with any other sign or signs of nephritis we have grouped those of our cases showing the most pronounced rises in pressure in a separate table, Table III. When available, we give the readings before and after the return to normal, better to indicate the extent of the rise.

A study of this table shows that no correlation seems to exist between the increase in blood pressure and the degree of albuminuria or oedema or biochemical findings. One point we may draw attention to is the fact that in all six cases when the systolic blood pressure was more than 120 mm hg. there was blood in the urine. That there is a relationship between these two signs we do not know, though they are each rather characteristic of chronic interstitial nephritis. The rise in blood pressure in acute nephritis is usually so temporary in character that our first readings on the patient's admission must have/

have been largely determined by the number of days each patient had been ill before being admitted. This reservation also applies to haematuria, for in several cases there was a history of the passage of reddish urine before admission though this was not in evidence at our examination. Moreover, in one case - N.C. (case 24) - a blood pressure of 98/60 mm was associated with a well marked haematuria, while several cases with no blood in the urine had increased pressures, evidenced by the subsequent fall of 20 mm or more.

Thus the fact that the six of our cases of acute nephritis with the highest systolic blood pressure readings should all have blood in the urine, may be purely coincidence, though we incline to the belief that this association is better explained on the existence of a common factor causing both.

Oedema:- We have discussed the oedema of nephritis in another part of this paper and have given our reasons for endorsing the opinion of those who believe that the presence of oedema is not an indication of damage to kidney function. Briefly they are:- (1) that oedema, indistinguishable from the oedema of nephritis is found in conditions other than kidney disease; (2) that in chronic interstitial nephritis, where all elements of the kidney are damaged, in anuria due to enlarged prostate, stone, etc., and in experimental nephrectomy, where there is a failure to excrete salt and water, oedema seldom if ever results; (3) that oedema is not necessarily or even typically accompanied by other indications of renal functional impairment such as high blood non-protein-nitrogen or lessened excretion of urea; and (4) that oedema is usually associated with signs which suggest some metabolic disturbance rather than a kidney lesion. Here we would add that the last argument may also be used against the idea that the oedema of acute nephritis differs in causation from that of parenchymatous nephritis in that it is due to a diminished ability of the kidneys to excrete salt and water. Our cases

show/

show that whatever the type of case, in the presence of a well marked oedema the blood cholesterol is raised. Cases 7,16,19 and 20 were cases of acute nephritis all of which cleared up in the usual way and none of which went on to merit the description of subacute parenchymatous nephritis, yet each showed a well marked increase in the blood cholesterol accompanying a general oedema, which one would not expect if the oedema were due merely to an inability of the kidney to excrete salt and water.

The presence and extent of oedema is usually gauged by the degree of puffiness or swelling evident and by the pitting on pressure. The accuracy of judgment based on these signs will depend on the build of the patient and the degree of oedema present. A much more certain estimate will be arrived at from a consideration of changes in body wieght. An increase in weight may have occurred and be quite marked though there may be no outward evidence of oedema or only a slight puffiness of the eyelids. One is seldom fortunate enough to get a case sufficiently early to be able to determine such increase but it may be presumed to have taken place from the subsequent fall which takes place, coincident with diuresis. Our series includes twenty cases of acute nephritis in which the body weight of the patient was regularly recorded. In eighteen of these cases there was a drop in weight during the early part of their stay in hospital, varying from 1.4 K to 7.4K and averaging 3.24Kilos. There are several facts which connect this fall in body weight with the disappearance of oedema. In all cases, the drop in weight occurred during the early part of their stay in hospital and was followed by a slow steady increase though the diet remained unchanged. It was always associated with an increased output of urine and with the subsidence of evident swelling or puffiness. Two of our cases, cases 16 and 17, were interesting in that they developed pneumonia shortly after their admission. There is a retention of salt and water in the body during the

active/

TABLE IV.

GENERAL OEDEMA:-

CASE:-	B/P. mm.hg.	URINE Blood	URINE Alb.	N.P.N. mg. per 100 c.c.	Cholesterol mg. per 100 c.c.	Urea. Conc. Test. B.	1.	2.	Pigment. %
1.J.R.	112/85	-	+++	70	333			2.4	36
3.W.L.	98/54	+	+++	70	185 *		1.5	1.7	36
5.F.McA.	110/90	-	+++	40	380	2.2	2.	2.	40
7.J.C.	124/78	++	+++	86	175 *			1.3	30
15.F.F.	100/?	+	+++	44	160		2.1	2.1	—
16.A.G.	112/65	++	+++	91	330	1.9	1.9	2.1	56
21.E.McM	100/?	-	+++	96	225		2.4	2.5	75
25.J.McD	130/118	++	+++	36	180 *		0.9	2.5	—

* Estimation made after oedema had disappeared.

active phase of this disease and in our two cases the drop in weight and diuresis did not take place till the temperature fell to normal.

In table IV we give a list of cases (8), in each of which there was a general oedema of moderate or marked degree noted at the clinical examination. Here again, as we found when discussing albuminuria, we seem to have a close correlation between the presence of oedema and of a large quantity of albumin in the urine. Every case with a well marked oedema also displayed a well marked albuminuria. The fact that this close association exists between the two conditions strongly points to either a common aetiological factor or a causal relationship between the two. That the presence of oedema per se should be responsible for a large quantity of albumin in the urine finds no corroboration from a consideration of other conditions in which a considerable degree of oedema may be present with little or no albuminuria. On the other hand, many authorities favour the explanation that the large loss of albumin from the blood and the consequent lowering of osmotic pressure are the cause of the attraction of fluid from the blood to the tissues. It is difficult, however, to reconcile this explanation with the fact, attested to by such a careful observer as Thomson (5) that the oedema may precede the appearance of albumin in the urine by several hours, and with the additional fact that the albuminuria may and usually does persist and be quite severe after the oedema has subsided. We prefer to believe that the close association between albuminuria and oedema depends on the existence of a common aetiological factor.

Further examination of table IV shows that no correlation seems to exist between oedema and any of the other signs of nephritis. There may or may not be haematuria and the blood pressure may be raised or normal. The blood non-protein-nitrogen may be within normal limits or markedly increased and the results of the urea concentration and pigment excretions may be good or poor/

poor.

To sum up our discussion on oedema we would state that most cases of acute nephritis, if not all, suffer from oedema at the onset, which may not be visible clinically, but be recognised by the sharp fall in body weight accompanying a diuresis. We have given our reasons for believing that this oedema can not be distinguished from that of parenchymatous nephritis, and we see no reason for postulating a different causation. We have again established a close relationship between oedema and albuminuria and in the case of each have shown that available evidence points to the primary cause being a non-renal one. From these considerations we have deduced that albuminuria and oedema are probably produced by some common factor.

Blood Non-protein-nitrogen:- A feature of kidney function being the excretion of nitrogenous waste products, one naturally looks for a retention of these in the blood when kidney impairment is suspected, as in nephritis. MacLean (6) has stated:- "Of all renal tests perhaps the most important in cases of acute nephritis is the estimation of the retained nitrogenous products in the blood. The term non-protein-nitrogen is generally used to express the total nitrogen derived from these bodies." This statement suggests, though it does not actually aver, that the increase of the nitrogenous products in the blood in such cases is due to the inability of the kidneys to get rid of them. That this is the case in chronic interstitial nephritis there is no doubt, the high N.P.N. even on a low protein diet being dependent on the renal disability. That the parallel holds in its entirety in acute nephritis we are in doubt, for it is our experience that high levels for the N.P.N. may be got in cases showing a urea concentration in the urine of over 3%. Moreover, in certain morbid conditions such as acute febrile states and prolonged severe vomiting or diarrhoea, where there is no kidney damage so far as we know, the blood N.P.N. may be raised.

It/

It seems reasonable to presume that the N.P.N. content of the blood will depend on two factors, namely (1) the rate of production, and (2) the rate of excretion, and some of our findings suggest that both factors may be operating in cases of acute nephritis. They certainly make it obvious that the level of N.P.N. in the blood is not directly proportional to the ability of the kidneys to excrete it.

In prefacing our experience of N.P.N. estimations with these remarks we in no way impugn the value of the test in acute nephritis, but merely suggest a second consideration to explain the high results. We shall refer to this question again when dealing with our own figures.

It might be argued that in estimating non-protein-nitrogen we are dealing with a number of variables any one of which may be chiefly involved in the increase, while only one of them, urea, is estimated in the urine. Experience has proved, however, that it is urea which is principally involved in the N.P.N. increase in nephritis, the percentage of urea in the blood non-protein-nitrogen normally between 40 and 50 rising in such cases to 70. It is of interest, however, that the urea fraction, in cases of eclampsia[7] shows subnormal values, suggesting an increase in the undetermined "N" fraction. Otto Folin[8] says:- "As a part of the total non-protein-nitrogen of human blood, the urea nitrogen varies under normal conditions between 35% and 55%. The proportion falls most frequently between 40% and 50%, but the variations are so large that it is not safe to assume, as is frequently done, that the urea "N" is just about one half of the total N.P.N. In nephritic nitrogen retentions the increase usually involves a greater increase of the urea than of the total "N", and the percentage of the latter represented by the urea may rise up to 70%". In spite of this, in comparing the relative of the urea and N.P.N estimations, he sums up with:- "The total N.P.N. determination represents a more valuable and a more dependable/

TABLE V.

Raised Blood Non-protein-nitrogen.

(Above 50 mg. per 100 cc.)

CASE:-	N.P.N.	B/P.	OEDEMA.	URINE.		CHOLESTEROL	UREA CONC. TEST.			PIGMENT.
	mg.per %	mm.		Bl.	Alb.	mg.per/100 cc.	B g/on.	1st Hour	2nd Hour.	%
1.J.R.	70	112/85	Severe general	—	+++	333			2.4	36.
2.C.L.	61	104/65	slight	-	±	140			1.8	24.
3.W.L.	70	98/54	general	-	+++	185			1.7	36.
6.E.G.	120	104/74	nil	-	±	150	1.2	1.3	1.3	29.
7.J.C.	86	124/78	general	++	+++	175			1.3	30.
10.E.L.	70	92/45	slight	-	+	130		1.8	2.4	56.
13.J.K.	60	94/68	nil	++	++	220			2.3	59.
16.A.G.	91	112/65	general	++	+++	330	1.9	1.9	2.1	56.
17.A.H.	55	92/50	slight	-	±	---	----	----	----	--
18.T.H.	96.	90/8	nil	+	+	86	3.75	3.45	3.	31
21.EMcM.	96	100/?	general	-	+++	225		2.4	2.5	75
23.A.R.	130	136/94	nil	++	+	190	1.5	1.5	1.7	—
26.A.E.	57	102/80	Puffy face	++ +	+++	150			2.2	—

dependable process for the study of nitrogen retention than does the urea estimation." This dictum by an authority, combined with the fact that to us the N.P.N. determination was the more practicable test, led us to use this test as a routine in our investigations.

Method:- In our estimations of blood N.P.N. we have followed the method recommended by Folin and Wu.(9) This method depends on the preparation of a protein-free filtrate from oxalated blood by precipitation of the total proteins by tungstic acid and filtration. Nitrogen is determined in a portion of the blood filtrate by a micro-kjeldahl method, using a sulphuric and phosphoric acid mixture for the digestion, the ammonia formed being estimated colorimetrically after direct Nesslerization of the digestion mixture.

Results:- Normal blood contains 25 to 35 mg per 100 cc. of non-protein-nitrogen, tending to the lower limit in children. In our series, we have had values ranging from 26 to 130 mg. In table V we have grouped those of our cases with a finding over 50 mg per 100 cc.

From a study of this table it is at once apparent that no correlation exists between the N.P.N. content of the blood and the degree of albuminuria or the presence and severity of oedema. In the presence of a high level of the former, the two latter features may vary in intensity from a slight trace to an extreme degree. This confirms our findings when we were discussing albuminuria and oedema and it seems certain that, whatever factor in acute nephritis is responsible for these two symptoms, that same factor is not the cause of the retention of nitrogenous waste products in the blood.

This same lack of correlation seems to exist when we consider the blood pressure findings in these cases. Some of our cases, it is true, with a well marked rise in pressure appear again in this table, but the majority of them don't and two of table V cases/

cases have normal readings. We have already pointed out the fugitive nature of the rise in blood pressure in acute nephritis. In chronic nephritis the association of raised blood pressure and impaired kidney function as represented by an increase in the blood N.P.N. is a common feature and we are unable to comment on this apparent lack of correlation in acute cases. Our opinion is that the difficulty of estimating slight changes and the fleeting nature of the increase even when apparent make observations on blood pressure in cases of acute nephritis in children of very little practical value.

The relationship between the blood N.P.N. and the result of the urea concentration test we propose to discuss when we come to deal with the latter. Here we would draw attention to the patient T.H. (case 18) as the best though not the only illustration of the point we made with regard to the possibility of an increased production being a possible factor in the raised N.P.N. of acute nephritis. In this case we have a non-protein-nitrogen of 96 mg per 100 cc. associated with a result from the urea concentration test of 3.7% before urea, 3.4% in 1st hour and 3% in 2nd hour sample of urine. When the observation was made there was no oedema or oliguria. The two obvious explanations which occur to one are:- (1) that there has been an increased production of waste products, overtaxing slightly damaged kidneys; and (2) that the increase is due to there having been a severe interference with renal function, the accumulation in the blood being entirely due to the retention, and that when the observation was made the kidneys had resumed work and were getting rid of the excess. If the latter were the true explanation, one would expect to find a very close correlation between the height of the blood N.P.N. and the urinary excretion of urea in the very early states of the disease, before the renal function recovered. Though such a correlation exists, as we shall see later, it is not so close in the early stage as it appears to be subsequently, the time factor being of undoubted importance/

importance in the increase of the N.P.N. due to renal inefficiency. A question which occurs to us, the answer to which might throw light on this problem, is:- Is the urea fraction of the N.P.N. proportionately raised in all cases of nephritis or does the "undetermined N" play a relatively more important part in acute cases than it does in chronic cases as, we have seen, it is said to do in eclampsia, where it probably indicates an increased production of waste products from protein metabolism?

To return to table V, the results of the pigment excretion test seem to bear some relationship to the height of the blood N.P.N. for where the latter is high the former tends to be low and, where repeated observations were carried out, an improvement in the one seemed usually to be reflected in an improvement in the other. Such a correlation is expected in so far as each of these features is taken to be an index of kidney efficiency.

Blood Cholesterol:- Cholesterol as a constituent of the blood plasma has come into prominence within the last few years and has been the subject of a considerable amount of biochemical research. Unfortunately our knowledge both of its metabolism and its significance is still rudimentary. To add to our difficulty there is a marked discrepancy in the results obtained by different observers. Maxwell (10) investigated the cholesterol content of blood in a series of cases of nephritis of different types, and his findings and conclusions agree with ours very completely, and explain some of our unexpected results. Thus in dealing with cases of acute nephritis he says:- "Every case in which oedema was present at the time of the original investigation showed some degree of hypercholesteraemia." In discussing cholesterol findings in the section on oedema we made the same statement, pointing out that wherever our figures were within normal limits a reference to dates showed that the observation was made after the oedema had disappeared. Maxwell found that the cholesterol curve followed the oedema, but more slowly reaching the normal level several days after the oedema had gone/

TABLE VI.

BLOOD CHOLESTEROL:-

CASE:-	Date	Cholesterol mg.per 100cc	B/P mm.	OEDEMA	URINE Bl.	URINE Alb.	N.P.N. mg.per%	Urea. Conc. B.	Urea. Conc. 1.	Test. 2.	Pigment %
1.J.R.		333	112/85	general	-	+++	70			2.4	36
4.M.R.		205	----	slight	+	+	60		1.	2.3	--
5.F.McA.		380	110/90	severe	-	+++	40	2.2	2.	2.	40
13.J.K.		220	94/68	puffy	++	++	60			2.3	59
14.J.C.		240	110/80	puffy	+	+	37.5		2.6	2.	53
16.A.G.		330	112/65	general	++	+++	91	1.9	1.9	2.1	56
19.G.B.		340	105/72	nil	+	+	37.5	2.5	2.2	2.	48
20.A.C.		333	136/70	slight	+	+	43	2.	2.4	2.9	55
21.E.McM.		225	100/?	general	-	+++	96		2.4	2.5	75
3.W.L.	2.11.28	185		lessening			70		1.5	1.7	36
	13.11.28	145		Nil			26		1.3	2.5	53
	20.12.28	133		Nil			45	1.	2.6	2.6	50
	7.3. 28	175		Nil			30	1.2	0.8	2.5	42

gone. The decline was continued to below normal limits and remained there for one or two weeks. (He gives the normal limits of blood cholesterol in health as 0.13 to 0.2%).

We have set out in table VI the nine cases of our series in which the blood cholesterol value was over 0.20% at the time of observation. Four of these cases have appeared in tables II and IV as having had severe albuminuria and general oedema. The other five had albumin in the urine, all more than a trace, but not sufficient to warrant their being grouped with the severe cases. Moreover, all but one, J.K. (case 13), had oedema indicated by the subsequent fall in body weight. In the case of J.K. there was no such fall but there was a definite history of swelling of the face which had disappeared a day or two before his admission to hospital. If we accept Maxwell's curve as the behaviour of the blood cholesterol, this case was investigated when the oedema had disappeared but before the cholesterol had fallen. The case T.H. (case 18), on the other hand, also admitted with a history of oedema which had gone, represents the stage when the cholesterol had fallen below normal. Case 3, W.L. one of the few of our cases with repeated observations, seems to reproduce Maxwell's curve, though our figures at no time exceeded 0.20%, the first observation having been made some time after the oedema had started to decline. When the final observation was made the child was fully recovered and on a general diet, which may explain part of the final increase.

Our case M.S. recently admitted to hospital and not included in our series, though we propose to discuss it more fully in a later section, illustrated another point made by Maxwell. This child had been admitted and was under treatment for bronchiectasis, when she developed nephritis, and suddenly assumed the classical picture of uraemia. There was marked albuminuria and a general and moderately severe oedema. The blood cholesterol, estimated while the uraemia was still present was found to be 0.15%

Maxwell/

Maxwell concludes from his observations that in uraemia the cholesterol values are usually normal or low and he finds an allied condition in the toxaemia of pregnancy, "in which some similar toxic factor frequently causes lower cholesterol figures than would otherwise have been expected." From the findings in our series, interpreted in the light of Maxwell's paper, it seems we may accept it as a fact that renal oedema is almost invariably accompanied by a raised cholesterol, the exception being where uraemia has supervened.

Our figures serve to bring out a final point, in accord with Maxwell's findings, that the two conditions oedema and a raised cholesterol are not present in the same degree. The oedema may be very severe and the cholesterol value moderately increased; on the other hand, there may be a mild degree of oedema associated with a marked increase in the cholesterol. For instance, E.McM. (case 21) with at one time a cholesterol of 0.41% was not nearly so oedematous as F.McA (case 5) with 0.38% or J.R. (case 1) with 0.33% Maxwell traces this lack of perfect correlation right through the changes occurring in more chronic cases, where variations in one feature fail to be represented in changes in the other. He says:- "It seems probable that while renal oedema and cholesterol retention usually occur together, they are probably both dependent upon some underlying lesion which is the pathological basis of the disease rather than that either bears the relation of cause or effect to the other. The problem of the relationship between cholesterol retention and renal oedema will not be solved until we know more about the normal metabolism of cholesterol in the body, its synthesis and break-down products and also about the extra-renal changes which occur in nephritis."

The Urea Concentration Test.

Urinary execution of urea:- One of the renal functions being the excretion of nitrogenous waste products of which the principal constituent is urea, an obvious way to estimate the presence and extent of renal damage would seem to be to estimate the/

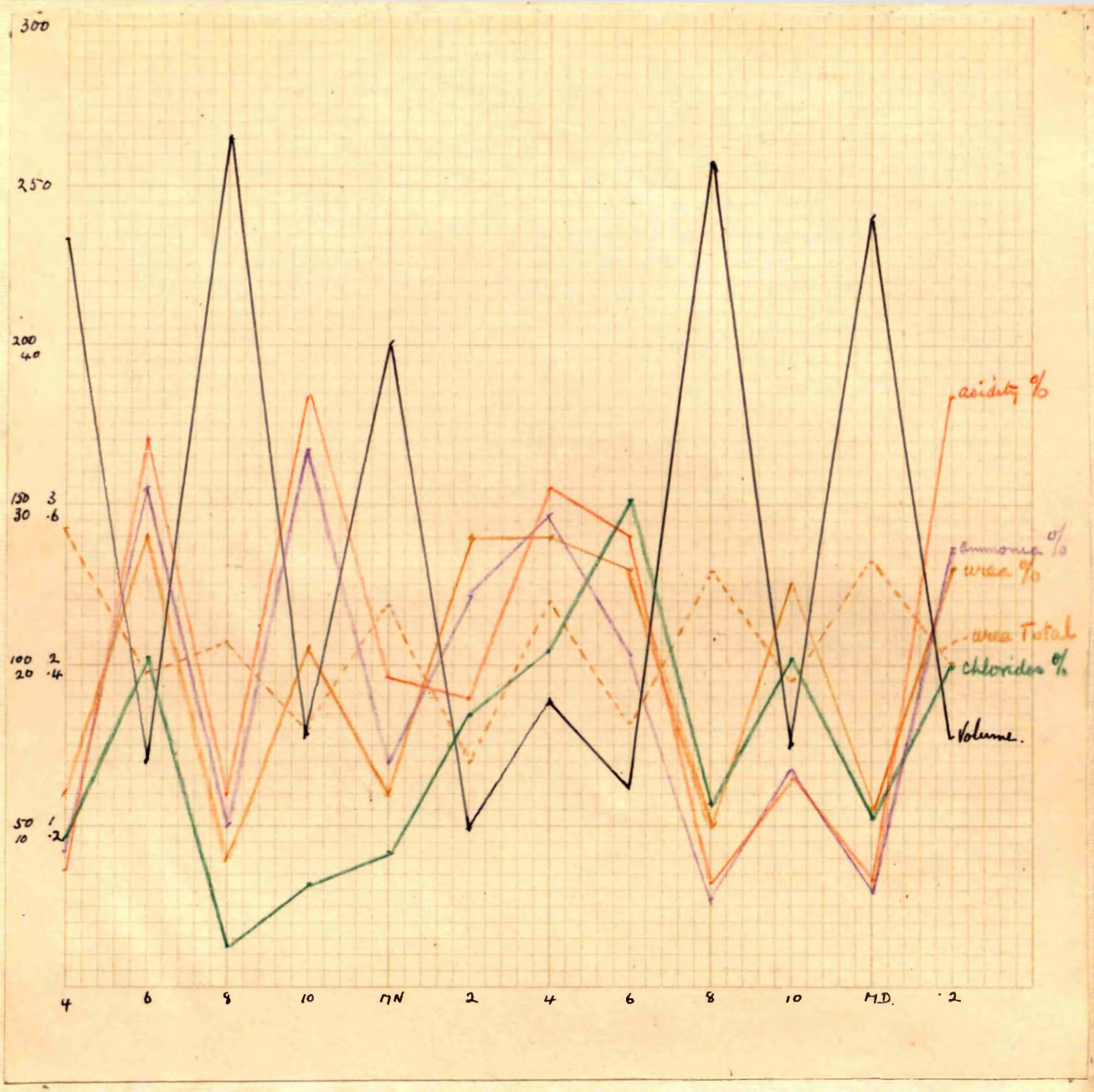

Fig. I. Normal case.

Volume of urine. unit 50cc. — Urea % unit 1%

Urea total. unit 1g — Chlorides % unit

Titratable Acidity % unit 10% — Ammonia unit 10

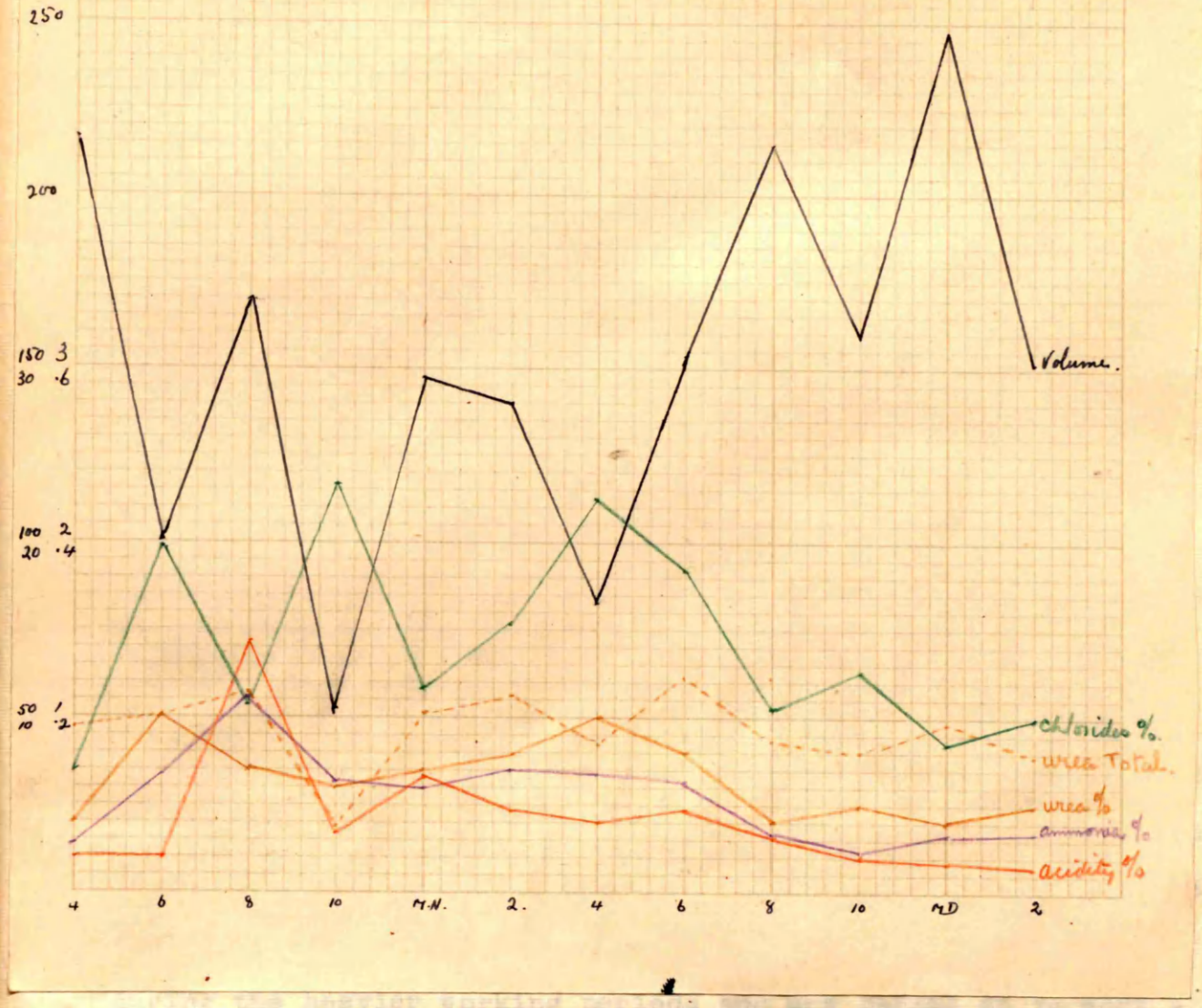

Fig. II A.E. Acute nephritis.

Fig. III E.G. Chronic Interstial nephritis.

the urea output on a standard diet. The difficulties met with in following this line of research are consequent on certain features of kidney functioning. Each kidney is made up of separate units, estimated at over 2,000,000 in the human subject, and these units seldom all function together but rather in relays, a lesser or greater number being called into play as the need arises. The result is that in the healthy subject the work done by the kidney is only a fraction of its total capacity. Experimentally, two thirds of kidney substance may be removed without interfering with renal efficiency. Applied to nephritis, this means that two thirds of the total units of the kidney may be damaged without there being any reflection in the excretion of waste products, the intact units shouldering the extra burden, and their periods of rest being encroached on. As the disease progresses and more kidney elements are involved, the remainder can no longer meet the demands for excretion during the heavier working periods and are called on to work at full capacity all the time to keep the retained waste products in the blood within normal limits. As the renal function progressively fails, these products progressively mount and we have the picture of chronic interstitial nephritis with its almost inevitable final scene of uraemia.

To express the phases of kidney function, we have found it convenient to take two hourly samples of urine over twenty four hours and represent the content of various factors in the form of a graph. The cases on which these observations were made were kept on a standard diet - whole milk, 100 cc. per kilo of body weight, divided into five feeds and given 4 hourly at 6a.m., 10a.m., 2p.m., 6p.m. and 10p.m. On the graph we represent the percentages and totals of urea, and have included the volume of urine, and the chloride, ammonia and titratable acidity percentages. Fig,I represents such a graph from a control case, fig.II from A.E. (case 26), a case of acute nephritis/

nephritis, and fig.III from E.G. (case 6), our case of interstitial nephritis with renal dwarfism.

On comparing these figures, it will be observed that the variations in figure I in the graph of each of the components come to be represented by almost a straight line in fig.III; the periods of relative activity and rest of normal kidney functioning are replaced by an almost uniform activity during the twenty four hours in a case of interstitial nephritis. This same tendency to flattening is seen to a lesser degree in fig.II.

From a consideratidn of fig.I it might be argued that the determining factor is the volume of urine, the percentage of the various constituents varying inversely and their totals directly with the output of water. To a certain extent this is true but that it is not the principal factor is proved by a consideration of fig.II, where the variations in concentration of the several constituents, with perhaps the exception of chlorides, do not follow the changes in volume of the urine anything like so closely as they do in fig.I, a fact, by the way, in favour of the excretion of chlorides being controlled by a different process to, say, that of urea. Moreover, although the 24 hours output of urine is increased above the normal average, the stage of diuresis having been present, the total excretion of the various constituents, again with the exception of chlorides, is reduced. To illustrate this point, let us consider the case of urea. On our standard diet we have found the average daily excretion of urea in the urine to vary from 0.8 to 1 g. per Kilo of body weight, the average daily concentration in the 24 hours sample to range between 1.2 and 1.8%, while the volume of urine varies from about 60 to 80 cc. per Kilo. In the case of A.E. (fig.II), the corresponding figures were 0.58 g per Kilo, 0.6% and 97 cc. per Kilo, while in the case of E.G. (fig.III), they were 0.56 g. per Kilo, 0.66% and 85 cc. per Kilo. Our finding in the case of E.G. is at variance/

variance with the statement of MacLean that "a patient suffering from an advanced grade of interstitial nephritis excretes practically the same amount of urea per diem as does a healthy individual on a health diet." He explains the apparent absurdity of a high blood urea being associated with a normal urea output by postulating the necessity for a greater 'head' of urea in the chronic nephritis. Unfortunately we have had only one case on which to base our observations but it does seem simpler to assume the increase in the blood urea to be due rather to a diminished total output, an association which he admits to be present in acute nephritis, thus agreeing with our findings, (e.g. the case of A.E. fig.II). We have applied the two hourly graph method of examination to our recent cases of nephritis and it would seem that such a method would give some indication of the degree of damage to the kidneys, for the daily output was regularly lowered and there was a more or less constant tendency to a flattening of the curve. However, MacLean and de Wesselow have adopted a much more practical method in their "Urea Concentration Test". On looking at our graphs, it will be seen that the curves of the percentage and total output of urea are very similar in that both are depressed and both exhibit the same tendency to flattening in a case of nephritis. Consequently the study of either the total output or the concentration will be of equal practical value. The essence of the urea concentration test depends on the fact that by adding an extra load of urea to the work of the kidneys and estimating the response by the increase in the percentage of urea in the urine we are enabled to assess roughly their efficiency.

Methods of carrying out the test:- The authors of the test recommend that the patient, after complete voidance of urine, be immediately given a dose of urea (proportioned to age and not exceeding g.XV) in 100 cc of water, preferably on a fasting stomach. The urine is voided at hourly intervals thereafter and the concentration of urea is estimated in each of the samples

by/

by the hypobromite method, using MacLean's modification of the Gerrard apparatus. As the result of our experience with the test, we have substituted for the hypobromite method of urea estimation the urease method first suggested by Marshall.[12] The former is the easier and much quicker to perform but it loses in accuracy what it gains in simplicity in that the urine may contain several constituents to yield nitrogen on the addition of the hypobromite solution, though not by the urease method. According to Hawk:-[13] "The urease method is probably the most satisfactory of all methods for the determination of urea. Other nitrogenous constituents such as allantoin are not decomposed by urease." We have compared the two methods on several hundreds of samples of urine and find that the difference in result is in the majority of cases 0.1 to 0.3%, yet it may exceed 1% and so become a factor in the interpretation.

We now as a routine carry out the test as the authors of it suggested with the substitution of the urease for the hypobromite method of estimating urea. Calvert suggested a further modification, which he calls the "range of urea concentration test."

Calvert's Test:- The patient, who has had no liquid after noon, voids his urine at 9 p.m. and is given the urea as before. The bladder is emptied again at 10 p.m., this sample being discarded. The total urine passed from 10 p.m. till 7 a.m., when the bladder is again emptied, is collected as one sample. The patient is then given 1½ pints of water and the urine collected from 7 till 9 a.m., this sample being measured. The precentage of urea in the 10 to 7 sample represents the maximum, that in the 7 to 9 sample the minimum, the difference constituting the range of urea concentration. In addition, the volume of the 7 to 9 a.m. urine serves as a modified water excretion test.

Hunt[15] in an article approving this method, added the suggestion that an index could be arrived at on which a standard might be based by subtracting the minimum from the maximum figure and/

and expressing the result as a percentage of the former. Calvert replied to this suggestion questioning the value of such an index.

Results of the Urea Concentration Test:- To get the fullest information from the urea concentration test, the result must be considered in the light of our knowledge of renal functioning, the figures obtained constituting a miniature hourly graph.

The figure from the sample of urine before urea is given will depend on the state of kidney activity at the time, but on a fasting stomach is usually low. The first hour figure may be raised or lowered according to the degree of diuresis caused by the urea, while the 2nd hour figure will usually show the response to the urea, and be sufficient for all practical purposes, though the maximum response will not be obtained till about the fifth hour after the dose has been given. According to the authors of the test, a concentration under 2% in the 2nd hour sample indicates damaged renal function and with this we agree. However, a concentration over 2% may still suggest such damage if considered in conjunction with the other findings.

In children, healthy kidneys will concentrate urea to between 3 and 6%, as the following observations show:-

		Control	Control	W.L. convalscent from nephritis.	T.H. Acute nephriti
Before	Urea.	1.5%	1.8%	1%	1.7%
1st	Hour.	discarded	discarded	2.6%	1.6%
2nd	"	3.2%	5.1%	2.6%	1.7%
3rd	"	3.1%	4.3%	2.9%	2.3%
4th	"	3.5%	5. %	3. %	2.5%
5th	"	4.4%	5.6%	-	-

These figures will also serve to illustrate the point we wish to make, namely, that the relative lack of response, equivalent to the flattening of the graph we have already discussed, is evidence of a kidney lesion, even where the second hour finding may be over 2%. A study of our appended list of cases will yield a number of illustrations of this point. Our case M.S., whom we have already mentioned in dealing with cholesterol, serves as a particularly good example. She does not appear in our list and we now give her case history in some detail.

Case/

Case History:- M.S. female, aet. 9 years, was admitted 18.3.29, complaining of cough for 10 weeks, with fever for the past 3 weeks. She had had measles at 2 yrs., mumps at 4½yrs., and whooping cough at 7 yrs., but had otherwise been healthy. A diagnosis of bronchiectasis was made, confirmed by lipiodal and X-rays.

April 8 - Definite oedema of both legs, more marked in right. Irregular temperature.

" 11- Oedema of right leg, especially below knee. Urine - no alb.

" 18- Urine - no albumin or casts.

" 24- At 4 p.m. child drowsy. Temp. normal. Vomited twice. At 7.45 p.m. generalized convulsion. O.E. - double optic neuritis. Lumbar puncture - pandy + cells increased. N.P.N. of C.S.F. - 80 mg. per 100 cc.

" 25- Child very drowsy and still slightly convulsive. Some general oedema. B/P 120/90 mm. Urine - Alb +++. casts. Blood N.P.N. - 97 mg. per 100 cc.
Urea Concentration Test - Before urea 2.4%, 2nd hour 2.4%
Isolated observations on urine - 6 p.m. urea 2.3% Midnight, 2.7%.

" 26- General condition unchanged. Child apparently amaurotic. Blood N.P.N. 67 mg. per 100 cc.

" 28- Child seems conscious but very restless. Blood N.P.N. 60 mg %.

" 29- More restful. Sees indistinctly. Diuresis. Oedema less.

" 30- Blood N.P.N. 43 mg %. Urine vol. 2600 cc. Urea content 0.75%

From this point rapid daily recovery took place.

May 15- Urea Concentration Test - Before: 0.5% 1st Hour: 0.9% 2nd: 2.2%.

In this case, on the 25th April we have a result from the urea concentration test which, according to MacLean,(16) would put uraemia out of count entirely, yet in our opinion the absolute lack of response to the extra dose of urea gave a certain indication of renal damage, and there seems no doubt of the diagnosis of uraemia.

Some such consideration prompted Calvert to devise his "range of urea concentration test". We have carried out the Calvert test in conjunction with the MacLean test on a large number of occasions (some of the results are given in the appended/

TABLE VII.

UREA CONCENTRATION TEST:-

CASE:-	Urea. Conc. Test. B.	1.	2.	B/P mm.	Oedema	URINE Bl.	Alb.	N.P.N. mg. per 100 cc.	Cholesterol	Pigment. %
2.C.L.			1.8	104/65	slight	-	±	61	140	24
3.W.L.			1.7	98/54	general	+	+++	70	185	36
5.F.McA	2.2	2.	2.	110/90	severe	-	+++	29	400	40
	0.2	0.7	0.8					66		
6.E.G.	1.2	1. 3	1.3	104/74	Nil	-	±	120	150	29
7.J.C.			1.3	124/78	general	++	+++	86	175	30
23.A.R.	1.5	1.5	1.7	136/94	Nil	++	+	130	190	—

appended list of cases), and have come to the conclusion that any added information it might yield is fully balanced by its greater expenditure in time and care.

We would say that, if one is not content to rely slavishly on the 2nd hour reading or accept an empiric standard such as 2% but will weigh and interpret the results in the light of our knowledge of kidney function as expressed in a two hourly graph, the test will prove to give all the information the authors claim for it.

Correlation:- In table VII we have grouped the six cases of our series in which we got a result below 2% for the urea concentration in the second hour sample of urine. We have pointed out that the findings in some of our cases indicated a kidney lesion though the result was over 2%, but for purposes of correlation we prefer to take those cases in which the damage was well marked.

Of these six cases, E.G. was our case of renal dwarfism. In the case of F.McA - case V - we give two observations. This patient was admitted suffering from acute nephritis and progressed to the subacute parenchymatous type. The first observation illustrates again the flattening of the curve, with a second hour figure of 2%. At the time of this observation, the kidneys, evidently working at their full capacity, were able to keep the blood N.P.N. within normal limits. At the time of the second observation, the renal function was still further impaired and the N.P.N. had mounted.

From a study of table VII, two correlations stand out quite clearly. In every case, where the second hour figure of the urea concentration test is under 2%, (1) there is an increase in the blood N.P.N., and (2) there is a poor response to the pigment excretion test. This is what one would expect as all three serve to indicate impaired renal function.

As before, there seems to be no correlation between this impairment and the quantity of albumin or the presence of blood

in/

in the urine, the blood pressure findings or the presence of oedema.

To sum up the results of our experience with the urea concentration test, we would say that, with the substitution of the urease for the hypobromite method of estimating the urinary urea, we have found it the most satisfactory test of renal efficiency of any we have tried. To obtain the fullest information possible, it should not be used simply as a quick method of arriving at an approximately maximum concentration of urea in the urine, but rather, by considering the urea content before injection, the volume of urine excreted and the rapidity and extent of the rise, and by frequent repetition of the test, as a means of assessing the condition of the kidneys by the nature of their response to the additional work imposed by the test.

By its use we have shown the close relationship that exists between the power of the kidneys to excrete urea and the level of the blood N.P.N. and have demonstrated again the absence of correlation between these evidences of renal damage and the degree of albuminuria or the presence of oedema.

Pigment Excretion Test.

To determine the state of excretory function of the kidneys, various pigment tests have been suggested from time to time, the most widely used being that devised by Rowntree and Geraghty of America a few years ago.[17] In their method an intramuscular injection of 6 mg of phenolsulphonephthalein is made deeply into the buttock and an estimate is made by colorimetry of the percentage of the pigment passed in the urine in 2 hours. In our investigations we have used this test as a routine when practicable and we are not impressed with its value, at any rate in cases of acute nephritis. The test is useless when blood is present in the urine and must be postponed till the blood has practically disappeared. This limits its field of usefulness and for this reason the result of the test is not shown in some of our cases.

Again/

Again, in cases where the urine contains quantities of debris, particularly urates, the test seems to yield a low result, a fact we have found both in nephritis and in control cases. The usually accepted standard for normal kidneys is 60% and over for the 2 hourly excretion, but we carried out the test in a number of children suffering from diseases other than nephritis and got results varying from 40% to 80%. Where there is a lesion of the kidneys one certainly gets a lowered rate of pigment excretion, as we saw when discussing the urea concentration test. Given a low result, that one can deduce from this a lesion of the kidney is very doubtful. The rate of excretion must be modified by the rate of absorption and the individual response to a foreign substance such as pigment, and the estimation of the quantity excreted is certainly influenced by the presence of other constituents in the urine. These considerations, taken with the fact that blood in any quantity in the urine invalidates the test, serve to limit the field of usefulness of the pigment excretion test and we feel we would lose little or nothing in omitting it entirely from our routine investigation.

Conclusion:- We set out to discuss certain signs and tests associated with nephritis in the light of our own findings in the series of twenty six cases appended. We cannot go into the histological changes in the kidney as only two of the series died (one from pneumonia and one from tonsillitis) and no post mortem was allowed. Nor are we qualified to deal with the physicist's part of the subject and discuss changes in the osmotic values and acid-base balance of the body, a line along which many observers believe our next great step in the advance of our knowledge of the kidneys and kidney disease may be made. We would return, however, to the question of classification of nephritis, as we feel that our personal views have been modified considerably as the result of our investigations.

A classification of a disease can only justify itself if the great majority of cases of that disease fall naturally into the different/

different classes and do not spread themselves on the border lines. Moreover, the value of the classification is enhanced if it should help to indicate a line along which treatment might with advantage be directed in each particular type. Thus, a classification based on the aetiology or the essential pathology of a disease serves a definite purpose.

Up till now, no such classification has been possible in nephritis. The pathological changes in the different structures of the kidney have been used to determine such types as glomerular, tubular and interstitial, but in practice it is found to be impossible to correlate the clinical picture with the histological changes.

A classification dependent on the impairment of functional activity is still impossible, as our knowledge is not yet sufficiently advanced for that purpose, while a classification on a clinical basis seems to defeat its own ends in that, whatever classification one adopts, the qualification is invariably made by its originator that a great many cases in practice seem to be of mixed type. The desire for classification arises from the protean diversity of the clinical picture, but until such classification is based on something more solid than the predominence of a clinical sign or on histological changes which can be correlated neither with changes in function nor with the clinical picture, it will serve merely to confuse the issue. We have no doubt that as our knowledge advances a true classification will evolve, probably on an aetiological basis, which is the only real basis. Meanwhile, we would tentatively advance, not a classification, but a conception of nephritis, as we see it in children at any rate, which seems to offer a simple view of the disease and at the same time to indicate lines for further research and for treatment.

In our efforts at correlating the various signs of nephritis, we have found that a marked degree of albuminuria, general oedema and a high blood cholesterol are invariably associated. Of these, the/

the disturbance in cholesterol has no relationship we know of to kidney function.

Renal oedema, though formerly looked on as due to the inability of the kidney to excrete salt and water, has recently come to be regarded by most authorities as of extra-renal origin. Fischer (18) voices the opinion of most recent observers when he says:- "The oedema observed in nephritis is not secondary to the loss of kidney function. Kidney disease does not lead to the development of oedema."

The third feature of the triad, albuminuria, is also coming to be regarded in the same light as oedema, that is, as due to some lesion other than kidney damage.

On the other hand, we have found a close correlation between the level of the non-protein-nitrogen of the blood, the ability of the kidney to concentrate urea and its power to excrete pigment. Each of these features is associated with damage to kidney function, though we have suggested that such damage may not always explain all of the increase in the blood N.P.N.

The presence of blood in the urine does not seem to correlate with any of the other signs of nephritis, but one would be inclined to associate it with local damage to the kidney, for it is a common and may be the only discoverable sign of a primary interstitial nephritis while it is said to be invariably absent in the typical case of nephrosis where the lesion is thought to be extra or pre-renal.

Finally the initial rise in blood pressure also evades efforts at correlation. One consideration which might help to determine the placing of this sign is, again, the fact that it is not seem in nephrosis, while it is a common feature of interstitial nephritis.

We have now arrived at the stage in our discussion where it becomes evident that the features of nephritis we have considered seem naturally to fall into two groups - (1) those depending on a local kidney lesion or at least on interference with kidney function/

function, and (2) those not so dependent but seeming rather to arise from some extra-renal disturbance, possibly a disorder of metabolism.

Our conception of nephritis is, that it is a disease clinically not yielding to classification, whatever may divulge aetiologically, and that the diversity of type is understood at once if we conceive the disease as being due to two factors, a renal factor and an extra-renal factor, the differences in type being represented by the different proportions in which the two factors may be present in the one individual case.

At one end of the series is the case of primary interstitial nephritis, where the renal factor alone seems to be involved and there is neither severe albuminuria nor oedema. At the other end is the case of 'nephrosis', with no evidence of impaired renal function, but featuring oedema, albuminuria and a high cholesterol. Most of the cases of nephritis we meet with in practice fall into the series somewhere between the two extremes, exhibiting as they usually do some disturbance caused by each factor. If one wanted to express the conception diagrammatically, one might use some such device as this:- Let us represent the renal factor as N and the extra-renal as M (metabolic!), and let us use the figures up to 4 as indices of the degree of implication or severity. A moderately severe attack of nephritis in which a degree of oedema was accompanied by about an equal impairment of kidney function would be represented by N_2M_2, a pure nephrosis by $M_{1,2,3or4}$, a pure interstitial nephritis by $N_{1,2,3or4}$. However such a diagrammatic representation is only suggested to illustrate our meaning and is quite superfluous in practice. We admit that our conception of the disease takes no account of the separate structures of the kidney or their individual functions but this fact, with our present lack of knowledge, does not seem in any way to invalidate its usefulness.

From the pathological point of view, which we approach with diffidence, the facts do not seem to rule our conception out of count/

count. The N factor is represented by the cellular, proliferative, and finally fibrotic changes in the kidney, while the M factor is seen in the degenerative changes in the tubules, thought by many to be part of or secondary to changes in other systems of the body, and an excess of lipoids in the kidney.

In the former case, the final stage is the granular kidney, the colour of which may vary from red to almost white according to the degree to which the extra-renal factor had been involved in the course of the disease. The characteristic pathological picture of the catarrhal or nephrotic case with predominant extra-renal involvement is the "large white kidney" which may or may not go on to secondary contraction, depending on the degree of involvement of the renal factor.

(Let it be understood here that we are dealing with nephritis in the generally accepted meaning of the term, and not include such conditions as embolic nephritis or fibrotic kidney secondary to cardio-vascular changes.)

When we come to consider the disease from the point of view of treatment, it would seem that our conception might have its value in indicating the lines along which our energies should be directed. In the absence of specific treatment, our efforts are necessarily directed towards removing the outstanding disabilities imposed by the disease. Thus, in a case where the extra-renal factor is chiefly involved, our object would be to combat the cause which is upsetting the salt and water balance of the body, and so get rid of the oedema, while in the case in which kidney damage preponderates our therapeutic measures would be directed towards ensuring as much rest as possible for the damaged kidneys, in each case conbining our symptomatic treatment with an effort to locate and remove any possible primary focus of infection. To give a concrete example of how our conception might be useful, a case of parenchymatous nephritis may benefit from the use of a high protein diet, so far as the oedema and oliguria are concerned, but such a treatment would seem to be contraindicated if the renal factor/

factor were much in evidence, as any good it might do to the oedematous state would be paid for by the risk of overtaxing already damaged kidneys.

From whatever angle we view it there seems no inherent fallacy in our conception of nephritis, and we see no difficulty in accepting it as a working hypothesis to explain and group the various clinical pictures assumed by the disease. Until such time as our knowledge of the aetiology of nephritis and of the principles underlying kidney function and their relationship to kidney structure is more complete than at present, we feel that our conception, by its correlation of clinical and biochemical findings, offers a means whereby the study of nephritis may be simplified and some guidance obtained for the correct line of treatment.

------oOo------

T A B L E 1.

CASE:-	Age yrs.	Date	Weight Kilos	B/P mm.hg.	OEDEMA	Urine Blood	Urine Alb.	Blood Biochemistry N.P.N. mg. per 100 c.c.	Blood Biochemistry Cholesterol mg. per 100 c.c.
1.J.R.	5 12/12	17. 8.28		112/85	General	-	E 7		
		30. 8.28			Severe General	-	+++	77	333
		12.10.28			Still Severe	-	+ ++	92	350
		17.10.28			Decreas-:ing	-	+ +	85	305
		22.10.28				-	+ +	60	
		17. 3.29		100/56	Nil	-	-	30	190
2.C.L.	7	3. 9.28	20.24	104/55	slight of face & feet	-	±	61	
		19. 9.28	17.16		Nil	Red Cells	±	44	140
		29.10.28	18.4		Nil	-	-	41	
3.W.L.	8	3. 9.28	22.64	98/54	General	+	E4.75		
		2.11.28	18	86/44	Slight pitting	-	±	70	185
		13.11.28						26	145
		20.12.28	19.4		Nil	-	-	45	133
		7. 3.29			Nil	-	-	30	175
4.M.R.	6	22. 9.28	18		slight pitting	+	E 1.	28	180
		2.11.28	18		do	-	haze	60	205
		12.11.28			Nil	-	"	75	145
5.F.McA	6	12.10.28		110/90	General	-	E6.25		
		19.11.28		90/50	Severe"	-	+ + +	40	380
		28.11.28			" "	-	+ + +	29	400
		24. 1.29			" "	-	+ + +	66	
6.E.G.	6½	19.11.28	12.68	104/74	Nil	-	±	120	150
		19.12.28				-	±	86	
7.J.C.	4½	20.10.28	18	124/78	General	+ +	E 6.5	86	
		5.11.28	15.6	90/45	Nil	-	+	83	
		22.11.28			"	-	trace	40	175
		13. 1.29			"	-	-	37	
8.W.H.	4 8/12	25.10.28	26.8	140/100	slight of face&feet	+	E.1.5		
		8.11.28	22.4	98/52	Nil	-	-	45	
		23.11.28			"			44	152
		12.12.28			"			34	150
9.A.P.	2 1/12	27.10.28	9.64	130/?	slight	+	+	32	185
		16.11.28	8.2			-	haze		

Function Tests. Urea Concentration test. Before	1st.hour.	2nd.hour.	Pigment. %	Clinical notes &c.
		2.4	36	Decapsultation 20/9/28.
	1.9	2.7	56	
	1.3	2.7	53	Child improving clinically.
	1.2	2.9	50	
1.2	0.8	2.	50	Clinically, child seems well.
		1.8	24	
	2.2	2.2	57	
		2.5	63	Child dismissed well 2.11.28
				Note on 4.10.28 "no oedema"
	1.5	1.7	36	Weight on the 10.10.28, 15.6.K.
	1.3	2.5	53	
1.	2.6	2.6	50	
1.2	0.8	2.5	42	Child seems perfectly well.
	2.2	2.2	28	Weight on 12.10.28, 16.3 K.
	1.	2.3		
	1.	2.4	62.5	Sent to country to report later Not seen since
			40	
2.2	2.	2.		
0.2	0.7	0.8		Decapsulation 25/1/29 Died of Pneumonia 12.2.29.
C.1.9		1.1	29	Renal dwarfism.
M.1.2	1.3	1.3	20	
		1.3	30	
		2.1	45	
	1.1	2.3	33	
		3.4	63	Child dismissed well
	1.9	3.	50	
			45	
2.9	3.3	4.3	83	Child dismissed well
				Small child, test not practicable.
				Child dismissed well.

TABLE 1. (contd.)

CASE:-	Age yrs.	Date	Weight Kilos	B/P mmgh.	OEDEMA	Urine Blood	Urine Alb.	Blood Biochemistry N.P.N. mg. per 100 c.c.	Blood Biochemistry Cholesterol mg. per 100 c.c.
10.E.L.	10 6 12	9.11.28	15.4	92/45	slight pitting over shins	-	+	70	130
11.J.B.	8 9 12	14.11.28	24.9	100/54	Puffy face	-	trace	43	180
		28.11.28	20.1		Nil.			43	
12.M.E.	8½	15.11.28	22.6	118/85	Puffy face	-	E.0.25	46	—
		18.11.28				-	+		
		13. 1.29				-	-	46	
13.J.K.	5½	19.11.28	14.6	94/68	Eyes Puffy	++	+ +	60	220
		13.1 .29	15.2	78/50	Nil	-	-	41	
14.J.C.	8 5 12	23.11.28	20.2	110/80	Face puffy	+	+ E.0.75	37.5	240
15.F.F.	7 2 12	24.11.28	11.2	100/?	General	+	+ + +	44	160
		1.12.28	9.9		Nil	-	±		
16.A.G.	10 3 12	29.11.28	18.	112/65	General	++	+++ E.4	91	330
		9. 1.29	14.8		Nil	-	trace		
		25. 1.29	15.5				haze	44	
17.A.H.	4½	2.12.28	15.1	92/50	slight of face&legs	-	±	55	
		6.12.28						32	
18.T.H.	2- 3.12	8.12.28	10	90/?	Nil	+	+	96	86
		7. 1.29				-	-		
19.G.B.	10 6.12	28.12.28	15.2	105/72	Nil	+	+ E.0.75	37.5	340
		7. 1.29	15.6			-	±		

Function tests. Urea Concentration test. Before.	1st.hr.	2nd.hr.	Pigment. %	Clinical Notes &c.
	1.8	3.4	56	Irregular dismissal 12 days after admission.
	1.1	2.	26	when admitted. Scarlatinal nephritis?
				Dismissed well.
C.	2.9	0.7	62.5	
C.	2.8	1.9		wt. on 24/11/28 - 20.2 kilos. B/P 102/52
C.	3.5	1.1		
C.	4.16	0.7	51	Dismissed well
Mac.		3.4		
C.	2.4	1.2	59	No reduction in weight.
C.	3.7	0.8	53	
M.		3.6		
	2.6	2.	53	Nov.30 - "Face less puffy" - weight 17.6 kilos. Dec.10 -"No oedema" - weight 16.3 kilos" Dismissed well.
	2.1	2.1		Dismissed well
1.9	1.9	2.1	56	Developed pneumonia shortly after admission.
2.2	2.4	2.	71	Temperature fell to normal on 8.12.1928.
C.	2.5.	0.8		
C.	4.2	0.5	90	
M.1.8	2.8	2.9		Child dismissed well.
				Developed pneumonia 2 days after admission. Temperature fell to normal on 11.12.28. Weight on 21.12.28 - 12.4 kilos.
3.75	3.45	3.		
1.9	1.4	2.2	44	Dismissed well.
2.5	2.2	2.		Dismissed because of chicken pox in ward.

TABLE 1 (contd).

CASE:-	Age yrs.	Date	Weight kilos	B/p mm.hg.	OEDEMA	Urine Blood	Urine Alb.	Blood Biochemistry N.P.N. mg. per 100 c.c.	Blood Biochemistry Cholesterol mg. per 100 c.c.
20.A.C.	7 12|12	12.12.28	30.5	136/70	slight of ankles & lumbar region	+	+	43	333
		24.12.28	26.1		Nil	-	±	40	
		8. 1.29						50	
21.E.McM.	2	7. 1.29	12.4	100/?	Mild General	-	+++-	96	225
		22. 2.29			General	-	+++	37.5	410
22.J.H.	6	3. 2.29	20.5	108/70	Face puffy	+	+	46	
		11. 2.29				-	±		
23.A.R.	11 10|12	18.2. 29		136/94	Nil	++	+	130	190
		25. 2.29				+	±	40	155
		12. 3.29				±	trace	46	
24.N.C.	1½		11.4	98/60	Face Puffy	++	++ E.2	48	
25.J.McD.	6½	21. 2.29	20.2	130/118	General	++	+++	36	
		1. 3.29	13.2	96/60	Nil			43	180
26.A.E.	6	5. 3.29	19.8	102/80	Puffy face	+++	+++	57	150
		12. 3.29						48	

Contractions:-

"C" Calvert's Range of urea concentration test.
"M" MacLean's "urea concentration test."
"NPN" Blood non-protein-nitrogen.
"E" Esbach
"Alb" Albumin.

Where no letter given under Urea Concentration Test, Machin's always meant.

Function Tests. Urea Concentration Test. Before.	1st.hr.	2nd.hr.	Pigment. %	Clinical Notes &c.
2.	2.4	2.9	55	
	2.5	3.2	36	
C.	4.2	0.7		
	2.4	2.5	75	Weight fell to 10.6 kilos on 18.1.29 & oedema returned and weight increased. Still under treatment
2.8	1.3	3.		
C.	3.4	3.1		
C.	3.6	0.6		
C.	1.8	1.7		
M.1.5	1.5	1.7		
	2.7	3.	63	
C.	3.3	0.7		
				Child died of Tonsillitis.
	0.9	2.5		
C.	2.8	1.6		
		2.2		
C.	2.2	1.7		
C.	3.2	0.7	26	
M.	1.3	2.%		

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