

T H E S I S

**Submitted to the University of Glasgow
for the Degree of Doctor of Medicine.**

-oOo-

**"The Plasma Cholesterol in Nephritis -
Observations on a Short Series of Cases."**

-oOo-

By

Christian M. Fleming.

-----oOo-----

Glasgow.

April 1930.

ProQuest Number: 13905311

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 13905311

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

THE PLASMA CHOLESTEROL IN NEPHRITIS - OBSERVATIONS
ON A SHORT SERIES OF CASES.

Although cholesterol was first isolated in 1775, little was known regarding it until a comparatively recent date. In the last twenty years much work has been done on the various problems connected with cholesterol as it occurs in physiological and pathological conditions. Its metabolism unfortunately is not yet fully understood and until it is so, many of these problems will remain unsolved. It is known, however, to be closely associated with fatty acids and lecithin.

Cholesterol is found in the blood in two forms:-

(a) as free cholesterol which exists mostly in the cellular elements, and

(b) as cholesterol combined with various fatty acids to form esters. This latter form predominates in the plasma, but free cholesterol is also present. The two forms together constitute the total cholesterol of the blood, and it is this combined value which is considered in the present work.

In numerous pathological conditions, variation in the cholesterol content of the blood occurs. Nephritis is one of the diseases which has excited most interest and many investigations on the subject have been made. Campbell⁽¹⁾ in a review on "Cholesterol in Health and Disease", comments on the discrepancy in the various results recorded, especially by the earlier workers. He concludes that, on the whole, high values are likely to be found in chronic parenchymatous nephritis, and to a less degree in chronic interstitial nephritis, and that in the latter, a fall occurs with the onset of uraemia. He adds, however, that more work is necessary/

necessary to determine the exact conditions in nephritis under which an increase takes place. It seemed therefore worth while, to investigate a series of cases, not only to confirm results already obtained but to ascertain the diagnostic and prognostic significance of the Cholesterol Content of the blood in the various types of nephritis.

Present Investigation.

To elucidate these points estimations were carried out on I. A series of healthy control cases.

II. A series of patients suffering from nephritis.

III. A series of patients with renal conditions other than nephritis.

IV. A series of cardiac cases with oedema.

Method of Investigation.

In all the nephritic, and in most of the other cases, specimens of blood were taken, for convenience' sake, just before the beginning of a urea concentration test, so that the same sample served for the estimation of both cholesterol and other substances. In the few remaining cases, where this procedure was not adopted, specimens of blood were collected three to four hours after a light breakfast.

The cholesterol estimations were made on the plasma after the technique of Myers and Wardell, as modified by McAdam and Shiskin⁽²⁾ and each estimation was done in duplicate. Extraction with chloroform in a Soxhlet apparatus was allowed to proceed for three hours. The standard solution used was of cholesterol in chloroform. This was found to be much more satisfactory than the solution of naphthol green B, which it had been suggested might replace the chloroform standard. Nevertheless, difficulty was often experienced in matching the two solutions owing to a difference in the shades of green of the standard and the unknown/

unknown. The fact that this difference occurred in some estimations and not in others, while the same chloroform and reagents were in use, suggests that it is due to some difference in the plasmas. It was noted that overheating at any point in the procedure, or the presence of moisture lowered the readings. Where the duplicate readings were not in close agreement, the estimation was discarded.

Results obtained. I. Control Cases.

A series of seventeen control estimations were made, ten on students, and seven on patients who had been in hospital for various conditions not known to be or likely to be associated with any change in the cholesterol content of the plasma. The maximum, minimum and mean readings were respectively 227, 138 and 170 mgs. per 100 ccs. These figures are slightly higher than those found by other workers using the same method. McAdam and Shiskin⁽²⁾ found the range to lie between 191 and 133 mgs., while Maxwell⁽³⁾ gives maximum and minimum figures of 200 and 130 mgs. Campbell⁽¹⁾ takes the normal range to be 150 to 200 mgs. with an average of 180 mgs.⁽⁴⁾ Bloor at an earlier date, using a different method found the average value to be much higher and gives 220 mgs. as a mean cholesterol value.

On the whole, the impression gained in this investigation is that the upper normal limit is frequently higher than the commonly accepted value of 200 mgms.

II. Nephritic Cases.

Estimations were made in 60 cases of nephritis. In some instances there was difficulty in classification, but the following grouping was eventually adopted.

Group/

Group 1. Acute Glomerular & Tubulo Glomerular Nephritis	22 cases.
Group 2. Chronic Interstitial Nephritis	11 "
Group 3. Arterio Sclerotic Cases	9 "
Group 4. Chronic Parenchymatous Nephritis	13 "
Group 5. Mixed type of Nephritis	5 "

The results in this series can be most conveniently recorded by giving the general findings in tabular form, in the first instance, and thereafter considering the general groups in greater detail.

<u>Group</u>	<u>Cholesterol Content of Plasma in</u> <u>mgms. per 100 ccs.</u>		
	Maximum	Minimum	Mean.
I. Acute Nephritis	363	131	223
II. Chronic Interstitial Nephritis	266	141	182
III. Arterio Sclerotic Cases	314	166	245
IV. Chronic Parenchymatous Nephritis	408	160	259
V. Mixed Type of Nephritis	333	195	253

We shall now consider the groups in detail, paying particular attention to the behaviour of the plasma cholesterol during the course of the disease, the significance of a rise or a fall in the amount, and the association with oedema, and with nervous disturbances.

GROUP I.

Acute Nephritis Cases No.1 - 22.

In this group there were 22 cases. The characteristic features of these were (1) albuminuria, with or without haematuria (2) raised blood pressure (3) oedema (4) headache (5) sudden onset in an apparently healthy individual. The criterion of recovery taken was the absence of albumin from the urine.

The maximum, minimum and mean readings for the group were 363, 131 and 223 mgms. per 100 ccs. respectively. Second estimations made before dismissal in 21 of the cases gave the following figures: maximum 274, minimum 114 and mean 186 mgms. There is therefore a tendency towards a decrease in the amount of cholesterol in the plasma, during recovery. The most marked example of this fall in the plasma cholesterol is seen in the case of patient No.15 who was having repeated convulsions on admission. The reading at this time was 274 mgms., while before dismissal the cholesterol content had fallen to 140 mgms., a decrease of 134 mgms.

Three cases, Nos. 7, 8 and 21 shewed an increase in cholesterol during convalescence. In cases No.7 and 8 the increase was slight and may possibly be explained by the fact that in both patients there was evidence of an infection. Case No.7 was subject to malarial attacks from one of which he had just recovered on admission to hospital, while case No.8 had a generalised slight glandular enlargement. As a reduced cholesterol content is found in acute infections, the ultimate rise in these cases might merely indicate a subsidence of the infective process. Case No.8 made a good recovery and had no albuminuria on dismissal. Two years later, she was found on examination to be in excellent condition, and had gone through/

through a pregnancy without any evidence of renal disturbance. The cholesterol content at this time - i.e. two years after dismissal from hospital, was 178 mgms. Case No.7 has unfortunately not been traced. One cannot draw conclusions from one case but in comparison with cases Nos. 47,49,54,55 and 59 of the parenchymatous group, it would suggest that a slight rise in the cholesterol content is not of serious significance provided the albuminuria is disappearing. The remaining case, No.21, which shewed a rise in cholesterol during convalescence was uraemic on admission and had nitrogen retention in the blood. The low initial reading in this case may be associated with the uraemia in which low values are common. The low readings in these cases have been ascribed to toxic influence, although direct proof is scanty. A certain increase in cholesterol was therefore to be anticipated in this case, but in point of fact, the value increased to an abnormal extent. The behaviour in this respect resembles, and is probably akin to that observed in cases of infection where a low reading in the acute stage is followed by an abnormally high reading during convalescence.⁽⁵⁾

With the exception of six cases to be mentioned later, all the patients had oedema in some degree but in none was it excessive. The four cases shewing the greatest oedema, Nos 1, 7, 16 and 20, gave cholesterol values of 177, 200, 316 and 153 mgms. respectively, so that the oedema was not apparently proportional to the amount of cholesterol present in the blood. This is not in agreement with the results of Maxwell⁽³⁾ who found that in acute nephritis with oedema, the cholesterol content is raised proportionately to the oedema. The possibility of a complication such as anaemia being responsible for the normal cholesterol content in/

in those cases shewing considerable oedema has been considered, but in none was any complication found, and the degree of anaemia present was slight.

The five non-oedematous cases, Nos. 9, 11, 12, 18 and 22, gave readings of over 200 mgms., the maximum being 333 mgms. and, as in the majority of cases in the group, a fall in cholesterol occurred with recovery.

In nine cases, the cholesterol content of the plasma at the time of dismissal from hospital was over 200 mgms. Of the nine cases, Nos. 7, 8 and 21 have already been mentioned. The remaining six, Nos. 6, 11, 12, 16, 19 and 22 all made a very slow recovery, and five of them, Nos. 6, 11, 12, 19 and 22, were eventually dismissed with slight albuminuria. Case No.6, on examination five months later, was found to be very well, and the urine free from albumin, while a similar result was got in case No.11, one year after dismissal. In case No.19, examination made fourteen weeks after the onset of nephritis, and one month after dismissal from hospital, revealed a fall of 19 mgms. in the cholesterol content, the value now being 224 mgms., but the slight albuminuria still persisted. Case No.22 was observed for a period of five months after leaving hospital and during this time the cholesterol content fell gradually to 154 mgms., a decrease of 90 mgms. The urine however did not clear entirely, but on several occasions was free from albumin. On the other hand the only case of the six, who had no albuminuria on dismissal, case No.16, was found four months later to have a faint trace of albumin in the urine and casts in the deposit. From these six cases, therefore, it would seem that a slowly falling cholesterol content is associated with slow resolution, if not indeed with a chronic lesion.

Six cases of the group had pronounced nervous disturbance/

disturbance. Five of them, cases Nos.13, 15, 16, 19 and 20 had convulsions, and their respective initial readings of cholesterol were 174, 274, 316, 363 and 153 mgms. giving an average value of 255 mgms. There was no nitrogen retention in these cases, so that they are not comparable to the sixth case, No.21, or to the uraemic cases of the chronic interstitial group. Although the average of 255 mgms. is above normal, the range of values in the five cases is wide, and suggests that there is no direct relationship between the onset of convulsions and the cholesterol content. In case No.21 on the other hand, nitrogen retention was present, and the normal value of 143 mgms. is in accord with the normal or low values found in uraemic cases of the group of chronic interstitial nephritis. This point will be discussed later.

The most gravely ill patient was case No.16, in whom the cholesterol content was 316 mgms., yet the degree of oedema, and the severity of the fits were not greater than occurred in several of the other patients of the group. A noticeable feature of this case, however, was the toxic appearance and slight cyanosis. A similar appearance was observed also in cases Nos. 19 and 22, both of whom had high cholesterol values. The significance of this is doubtful, but the association of the two phenomena seems worthy of note, and of further observation.

Conclusions.

In this group of acute cases, therefore, the main findings are:-

1. While the level of cholesterol in the plasma may or may not be unduly high, recovery is accompanied by a fall.
2. A slow or incomplete redoxery is associated with a tardy fall.

3. The degree of oedema is not proportional to the amount of cholesterol in the plasma.
4. The onset of convulsions is not closely related to an abnormal cholesterol content; where there is retention of nitrogen in such a case (1 case) the cholesterol content is normal.

It was hoped that by periodic examinations of the acute cases at regular intervals after dismissal from hospital a better idea of the prognostic value, if any, of the cholesterol estimations might be obtained. Unfortunately, this has not been found practicable except in a few cases. The subsequent histories of patients are available, therefore, in only a small proportion of the series.

I who was plasma used.

⑥ "combined value" - what with b or plasma

Deapsulation

Case 56

pg 23 - discussion in later

Accord to her fit. chol. what
count high in art-sell as she
say in summary

Summe

8 High values will not necessarily
be obtained in chron. cases in pres.
of renal lesion

accord to her it is of value in acute
cases. as high values not obtained
~~otherwise or at~~ in other conditions
than renal or in kidney cond other than
nephritis

pg 33

inclu acute wph. osam &
chol. go parallel.

GROUP 1. ACUTE NEPHRITIS.

CASE No.	Sex	Age	Blood Pressure	Oedema	Blood Urea N. mgms. per 100 ccs.	Plasma Cholesterol mgms per 100 ccs. I.R.	F.R.	Urine on admission Albumin	Blood Casts.	Urine on Dismissal Albumin	COMMENTS.
1.	M.	11.	$\frac{160}{100}$ mm. Hg.	Consid.	18.1	177	133	++	trace	absent	
2.	M.	25.	$\frac{210}{140}$	Face	18.0	259	155	+	absent	"	
3.	F.	24.	$\frac{126}{90}$	Face	15.6	250	155	++	absent	"	
4.	F.	48.	$\frac{168}{96}$	Slight	18.3	189	154	++	absent	"	
5.	M.	28.	$\frac{142}{88}$	Slight	10.0	131	114	++	absent	"	
6.	F.	50.	$\frac{160}{120}$	Slight	17.0	245	220	++	++	trace	Albuminuria disappeared 5 mths later
7.	M.	38.	$\frac{180}{100}$	Consid.	18.5	200	220	++	++	trace	
8.	F.	30.	$\frac{180}{100}$	Slight	18.0	200	225	++	trace	absent	
9.	M.	17.	$\frac{110}{70}$	Absent	29.7	212	138	++	++	absent	
10.	M.	27.	$\frac{150}{118}$	Face	11.0	133	-	++	trace	absent	
11.	F.	16.8	$\frac{142}{80}$	Absent	10.2	228	202	++	++	trace	No albuminuria 1 year later.
12.	M.	13.	$\frac{102}{70}$	Absent	14.0	266	208	++	++	trace	
13.	M.	24.	$\frac{170}{110}$	Face	17.7	174	166	++	+	absent	Convulsions on admission.
14.	M.	18.	$\frac{172}{112}$	Face	39.0	212	196	++	absent	absent	Convulsions on admission.
15.	M.	18	$\frac{168}{70}$	Face	30.2	274	140	++	+	absent	Convulsions on admission.
16.	F.	8.	-	Consid.	25.4	316.	274	++	++	absent	Slight albuminuria. reappeared (4 mths. later)

GROUP 1. ACUTE NEPHRITIS (Contd.)

CASE No.	Sex	Age	Blood Pressure	Oedema	Blood Urea N. mgms. per 100 ccs.	Plasma Cholesterol mgms. per 100 ccs. I.R. F.R.	Urine on admission Albumin	Blood Casts	Urine on dismissal Albumin	COMMENTS
17.	M.	23.	$\frac{117}{82}$ mm. Hg	Face	19.6	232 181	++	absent	++	trace
18.	F.	21.	$\frac{102}{72}$ "	Absent	29.7	202 138	++	++	absent	trace
19.	M.	12.	$\frac{130}{100}$ "	Face	13.0	363 253	++	absent	absent	trace
20.	F.	5.	$\frac{160}{700}$ "	Consid.	30.0	153 143	++	+	absent	absent
21.	F.	12.	$\frac{160}{110}$ "	Face	52.8	143 240	++	++	++	absent
22.	F.	28.	$\frac{120}{88}$ "	Absent	20.5	333 244	++	absent	++	trace

I.R. :- Initial Reading.

F.R. :- Final Reading.

Consid. :- Considerable Oedema.

Face :- Puffiness of face

no Oedema elsewhere

GROUP 2.

Chronic Interstitial Nephritis - Cases No.23-33.

Estimations were made in eleven cases of this type, which was characterised by vascular changes, raised blood pressure, and nitrogen retention in the blood. Most of the cases shewed also albuminuric retinitis. Five of the patients had uraemia.

The maximum, minimum and mean readings were 266, 141 and 182 mgms. respectively. Four cases gave values of over 200 mgms. and of these, three, Nos. 26, 30 and 32, had pronounced vascular changes while the fourth, No.25, had generalised anasarca and was in extremis on admission. Of the cases with slight arterial degeneration, the maximum, minimum and mean readings were 194, 141 and 170 mgms. - that is to say, the values were within the normal range.

Five of the patients, including four with uraemia, died, three of them before a second estimation could be made, and subsequent readings are available in only six cases of this group. The average cholesterol content in the five fatal cases was 195 mgms. Where a second estimation was made, the reading shewed little change from the initial value, with the exception of three cases, No.23, which will be considered later, and cases No.28 and 33. In no instance did a decrease in cholesterol accompany clinical improvement. Cases Nos. 28 and 33 were uraemic on admission and at this time gave readings of 145 and 182 mgms. of cholesterol respectively. During convalescence, a gradual rise in the cholesterol content took place, the final estimations made just prior to dismissal giving values of 196 and 210 mgms. One year later, case No.28 was in apparently good health, and had only a slight albuminuria; case No.33, two months after leaving/

leaving hospital, was well, but still excreting considerable amounts of albumin. Her subsequent history is not known. In these two cases, the rise in cholesterol should probably be interpreted as a return to the normal, from the low reading which had been found during the period of uraemia. Regarded in this way the results agree with those in the other uraemic cases of the group, and also with the observation of Maxwell, Henes⁽³⁾ and others⁽⁶⁾, who reported low values in uraemia.

It is of interest at this point to recall the fact that in Group I of acute cases, the only patient shewing nitrogen retention gave a low initial reading which gradually rose during convalescence. On the other hand, the remaining cases of Group I which shewed marked nervous symptoms but had no nitrogen retention, did not have consistently low values.

It would seem therefore that where uraemic manifestations are associated with nitrogen retention in the blood such as occurs in chronic nephritis, especially of the interstitial type, and occasionally in acute nephritis, low or normal cholesterol values are the rule. The rise occurring during convalescence (3 cases)⁽⁶⁾ is interesting in the light of Henes' work on chronic nephritis. He found that cases which were progressing favourably shewed a hypercholesterinaemia, and he suggested that cholesterol was analagous to an antitoxin.

Case No.23 is worthy of note. The patient had been in hospital eight months previously on account of chronic interstitial nephritis, and the cholesterol content, estimated on two occasions, was then 194, and 192 mgms. When readmitted, the patient was in coma and the cholesterol was found to be 173 mgms. Death occurred within 24 hours of admission/

admission, Post mortem examination shewed the kidneys to be much reduced in size, the right weighing $\frac{3}{4}$ oz. and the left $1\frac{3}{4}$ oz. while section revealed a complete absence of normal renal tissue. The findings in this case and also the course of events in case No.63 of Group 5, the mixed type of nephritis which will be discussed later, shew that the onset of uraemia in chronic nephritis is attended by a fall in the cholesterol content of the plasma. This is in agreement with the results of other workers. (3)(6)

Conclusions.

From consideration of these results it will be seen that:

1. In chronic interstitial nephritis the cholesterol content of the plasma is within normal limits unless very pronounced arterial degeneration is present.
2. The onset of uraemia is accompanied by a low cholesterol level.
3. Recovery from uraemia is attended by a rise in the cholesterol content of the plasma.

GROUP 2. CHRONIC INTERSTITIAL NEPHRITIS.

CASE NO.	Sex.	Age.	Blood Pressure	Oedema.	Blood Urea Nitrogen mgms per 100 c.cs.	Plasma Cholesterol mgms. per 100 ccs.	U R I N E. Albumin	Casts.	COMMENTS.
No. 23. Re-admission	F.	19.	$\frac{120}{90}$ mm. Hg	Absent	52.0	194	++	+	
24.	M.	57.	$\frac{135}{75}$ "	"	78.0	173	++	absent	Uraemic Coma. Death.
25.	M.	26.	$\frac{182}{124}$ "	Slight	50.0	166	++	+	Uraemia Arterio Sclerosis "
26.	M.	44.	$\frac{234}{135}$ "	Consid.	66.6	245	++	+	Uraemia "
27.	F.	25.	$\frac{230}{180}$ "	Absent	70.4	250	++	+	Art. Sclerosis, Asthma "
28.	F.	65.	$\frac{154}{105}$ "	"	125.0	141	++	+	Progressive Anaemia Death
29.	M.	62.	$\frac{100}{66}$ "	"	76.6	145. 154.	++	+	Uraemia.
30.	F.	53.	$\frac{170}{100}$ "	"	81.0	170.	++	absent	Art. Sclerosis.
31.	M.	35.	$\frac{194}{100}$ "	"	60.0	266.	++	+	Art. Sclerosis.
32.	F.	46.	$\frac{152}{105}$ "	V. Slight	46.0	187	++	+	Art. Sclerosis.
33.	F.	67.	$\frac{180}{120}$ "	Slight	69.6	266	++	+	Art. Sclerosis.
			$\frac{166}{120}$ "	Consid.	80.0	182. 234.	++	++	Uraemia, Asthma.

Consid. :- considerable oedema.
 R.R. :- Initial Reading.
 F.R. :- Final Reading.

GROUP 3.

Arterio Sclerotic Cases - Nos. 34 - 46.

It is convenient at this point to consider a group of cases in whom Arterio Sclerosis was the predominant clinical feature. Nine of these cases had evidence of renal disease.

The difficulty of differentiation between arterio-sclerotic cases with renal involvement and chronic nephritis with secondary vascular changes is generally acknowledged.

(7)
Evans states that there is no accepted clinical distinction between the two, and that a "pathogenic factor simultaneously causes both renal and vascular lesions, a varying incidence on renal or vascular tissue accounts for the unequal change in these tissues in different cases."

For the purposes of this investigation, distinction was made on two points:

- (1) the very marked cardio-vascular signs and symptoms found in arterio sclerosis, and
- (2) the absence of nitrogen retention in the blood, with a good response to the urea concentration test.

In general also, the arterio-sclerotic patient was stout and florid whereas the chronic nephritic tended rather to be pale and thin.

The maximum, minimum and mean readings for the whole group were 314, 166 and 245 mgms. respectively, while for those having nephritis, the figures ranged from 314 to 182, giving an average of 256 mgms. Three cases had readings of under 200 mgms; one of these had nephritis, case No. 44, while of the other two, one had asthma (case No. 39) and the other had haemoptysis for which he was sent to hospital as an urgent case. It will be seen therefore that the figures for the group are considerably higher than those for the previous group of interstitial nephritis cases.

Case/

Case No. 41 is of interest. The blood urea nitrogen was 18 mgms. while a urea concentration test gave excellent results. On post-mortem examination however, the right kidney was found to be almost entirely fibrous with only a narrow rind of renal tissue, while the vessels were markedly sclerotic. The left kidney was less contracted than the right but shewed marked interstitial change and arterio-sclerosis. In this case the urea concentration test was no measure of the degree of renal damage which had occurred in the course of generalised vascular disease. The plasma cholesterol in this case was 307 mgms. In the light of these findings, it is possible that in many cases of arterio-sclerosis the degree of renal damage is much greater than is indicated by routine tests of efficiency.

Two cases of the group, Nos. 40 and 42, were exceptional in that they shewed nitrogen retention. They are included in this group rather than group 2 because the clinical picture was that of advanced arterio-sclerosis. Both were stout florid men, whose chief complaint was dyspnoea and weakness. The peripheral vessels were hard and tortuous, and there was hypertrophy of the heart. Albuminuric retinitis was absent. Patient No. 40 gave a good response to the urea concentration test, but he was extremely ill, and died four days after admission. The cholesterol content was 244 mgms.

Case No. 42 had had a mild nephritis eight years before. At that time, albuminuria was moderate, there were no casts in the urine and the blood pressure was not raised. On readmission the patient presented the picture described above. He had some oedema which was most likely of cardiac origin, being slight and confined to the lower extremities. The cholesterol content was 245 mgms. It is probable that in this/

this case, there was a recrudescence of the original kidney affection at the time of readmission to hospital, but that in the interval since the first attack, the "pathogenic factor", whatever its nature, had affected the vascular tissues more severely than the renal, thus producing a clinical picture of arterio/sclerosis, rather than of chronic nephritis.

From consideration of this group, therefore, it is apparent that the presence of arterio/sclerosis is usually associated with a hypercholesterinaemia, particularly if a renal lesion is also present. In cases shewing no albuminuria, the cholesterol content would appear to vary, but the number of cases of this type investigated is much too small to allow of any deductions.

Difference of opinion exists regarding the association of hypercholesterinaemia and arterio/sclerosis, but a big majority of workers have found that arterio/sclerosis is accompanied by a high cholesterol content. Much experimental and other work has been done in an attempt to determine the nature of this relationship, and also the relationship of hypercholesterinaemia to hypertension. Experiments on rabbits by feeding with cholesterol have been made by various workers, (8) (9) and seemed to prove that arterio/sclerosis was the result of hypercholesterinaemia.

These results however were not confirmed in carnivorous animals. (10) Dewey found that feeding with cholesterol produced not only arterio/sclerosis but definite lesions in the tubules of the kidney. (11)

Newburgh in 1923 found that by feeding rabbits with a diet rich in protein but with a low cholesterol content, lesions resembling human arterio/sclerosis could be produced. Later/

(12)
Later in 1926 he confirmed this, but found also that where arterio/sclerosis was present, a hypercholesterinaemia also developed. This elevation of blood cholesterol, Newburgh believed to be due to a metabolic disturbance, directly referable to the excess of protein in the diet, and not to its cholesterol content. Other workers, Nuzum, Siegal, (13) Garland and Osborne produced hypertension and arterio/sclerosis by high protein feeding and found that these phenomena were most pronounced when the acid base balance resulting from prolonged feeding with protein was most disturbed.

(14)
Recent work by Moscovitz on experimental Arterio/Sclerosis is of interest. He found that the arterial lesions produced by cholesterol feeding were not permanent - i.e. the lesions were of the nature of a deposition of cholesterol in the intima and were not hyperplastic in character. Moreover, in investigations in the human subject he failed to find a constant hypercholesterinaemia in arterio sclerosis, unless a complication was present. He concludes therefore that cholesterol plays only a part in the production of experimental arterio sclerosis, and that the mechanical factor of pressure is important.

(15)
Waldorp also, from his own work and from a study of the results of various other workers, concludes that hypercholesterinaemia in itself is not sufficient to cause hypertension, and arterio/sclerosis, but that in its presence the hypertensive action of certain substances in the blood, such as adrenalin, is increased.

It is therefore evident from this brief summary of investigations on the subject, that the problem is complex and that much work is still necessary.

Conclusions.

The main findings in this group are:

1./

1. In Arterio Sclerosis, with renal lesions, the cholesterol content of the plasma is high.
2. The present series does not include a sufficient number of cases without renal involvement to justify any conclusions as to the level of cholesterol in such cases. From a review of the literature it is apparent that although divergent views are held regarding the cholesterol content, the majority of workers have found it to be above normal.

— o o o —

GROUP 13. ARTERIO SCLEROTIC CASES.

CASE No.	Sex.	Age.	Blood Pressure.	Oedema.	Blood Urea Nitrogen mgms. per 100 c.c.s.	Plasma Cholesterol mgms. per 100 c.c.s.	URINE.		COMMENTS.
							Albumin	Blood Casts.	
34.	M.	54	$\frac{250}{140}$ mm. Hg	Absent	28	250	++	absent	Nephritis.
35.	F.	52.	$\frac{220}{156}$ "	"	14	253	++	absent +	"
36.	M.	50.	$\frac{250}{155}$ "	"	22.4	260	++	absent -	"
37.	M.	62.	$\frac{196}{78}$ "	"	11.5	241	++	absent +	"
38.	M.	65.	$\frac{200}{100}$ "	"	21.5	283	++	absent +	(Nephritis (Myocarditis.
39.	M.	61.	$\frac{164}{120}$ "	"	--	166	trace	absent	Asthma.
40.	M.	46.	$\frac{220}{140}$ "	"	66	244	++	absent +	Myocarditis.
41.	M.	57.	$\frac{210}{140}$ "	"	18	307	++	absent + +	Nephritis Myocarditis.
42.	M.	53.	$\frac{128}{110}$ "	"	64	245.	++	absent +	Nephritis
43.	M.	59.	$\frac{180}{112}$ "	Slight	15.2	314	+	+	Nephritis Myocarditis.
44.	M.	54.	$\frac{190}{100}$ "	Absent	18.6	182	++	absent +	Nephritis
45.	M.	64.	$\frac{196}{115}$ "	"	18.5	190	absent	absent	Haemoptysis.
46.	M.	64.	$\frac{148}{90}$ "	"	22.9	260	absent	absent	Valvular disease of Heart.

GROUP 4.

Parenchymatous Nephritis - Cases Nos. 47-59

Estimations were made in thirteen cases of this type, which was characterised by (1) the presence of albuminuria, haematuria and oedema, and (2) the absence of cardio-vascular changes and nitrogen retention. In most cases also, anaemia was a marked feature.

The maximum, minimum and mean values for the group were 408, 166 and 259 mgms. respectively, i.e. there is a definite hypercholesterinaemia in these cases.

A second point of considerable importance is the general tendency to a rise in the cholesterol content during convalescence. This is shewn by the following results which were obtained in nine cases in whom subsequent estimations were made. The average initial reading was 252 mgms., while the average of the subsequent reading was 283 mgms. In these nine cases, all oedema had disappeared at the time of the final estimation.

This feature has a special diagnostic value, which is illustrated by the following cases, Nos. 47, 49, 54, 55 and 59. These cases were admitted as acute nephritis, but subsequent progress proved the diagnosis to be wrong. The oedema in Nos. 47, 54 and 55 was of moderate degree and disappeared in a few days but the albuminuria and haematuria persisted. Case No. 49 had considerable oedema which persisted and even increased for several weeks after admission. For no apparent reason, the oedema suddenly and completely subsided and the patient appeared to be making a good recovery. The plasma cholesterol was found however to have risen to 400 mgms. and the urine still contained abundant albumin and blood. The findings suggested progressive tubular damage, and seemed to indicate a poor prognosis. Subsequent examination, six months/

months later confirmed this view. The patient then had a moderate degree of anaemia and was still passing a considerable quantity of albumin and blood in the urine. Of the four other cases, Nos. 47, 54 and 55 all shewed a rise in their cholesterol values during convalescence while No. 59 shewed very little change. Thus in an apparently acute attack, an increase in the cholesterol content when accompanied by persistent albuminuria is indicative of a chronic lesion.

In the above cases, the chemical findings served to differentiate acute and chronic varieties of the same type of nephritis. The following cases illustrate the application of the cholesterol reading to the differentiation of types of renal lesion. In cases Nos. 48 and 52, nephritis had been present for several months before admission to hospital, but the type of lesion was in doubt. Clinically, they were regarded as cases of acute nephritis which were slowly resolving. A study of the plasma cholesterol however shewed it to be unduly raised and suggested that the lesion was of a more chronic nature. Later observations proved this surmise to be correct. Case No. 52 was a girl of 12 years of age whose renal condition dated from an attack of scarlet fever four months before. There was no oedema or nitrogen retention on admission and the blood pressure was not raised. There was however a considerable degree of anaemia. The urine contained abundant albumin and blood with numerous granular casts. The cholesterol content was found to be 240 mgms. and the case appeared to be of a parenchymatous type. Two months later however the blood pressure had risen by 10 mm of Hg., and the urea concentration test shewed a less efficient excretion, while the cholesterol content had fallen to 215 mgms. The latter finding in itself was confirmatory of the first diagnosis, but when considered in the light of the rising blood/

blood pressure and decreasing excretory power, it seemed rather to indicate an interstitial change in the kidneys. In other words the patient was developing into the "mixed type" of nephritis.

Reference has already been made to the opinion of (6) Henes that in chronic nephritis which is progressing favourably there is a hypercholesterinaemia, whereas in uraemic cases and fatal cases low values are found. It is of interest therefore to note that case No. 57 who had a cholesterol content of 166 mgms. one of the lowest values in the group, died within six months after leaving hospital. No uraemic symptoms developed, the oedema remained more or less the same in extent and distribution as when the patient was in hospital and death appeared to have resulted from progressive weakness and anaemia.

In contrast to this, are three cases, Nos. 48, 49 and 50, who all had high values, and in two of whom final readings were over 400 mgms. On examination, one and a half, and two years later, these patients were found in good health, and able for work, although still excreting considerable quantities of albumin in the urine. In each case the cholesterol content had fallen to normal. The conclusion reached by Henes would therefore appear to be justified.

(3)
In this connection the views of Maxwell are directly opposed to those of Henes. Maxwell found that cases where the plasma cholesterol remains high long after the subsidence of oedema are the cases in which uraemia supervenes, and in whom most marked vascular changes occur. The results of the present investigation indicate that this divergence of opinion is probably due to a lack of observations on all cases over a sufficiently long period. It is possible that in cases with high values on dismissal from hospital the/

the cholesterol content would have been found to fall gradually as in cases Nos. 48, 49 and 50. This prolonged observation modifies the significance to be attached to hypercholesterinaemia in that the condition is not always permanent. Moreover, this fall, as shown in cases Nos. 48, 49 and 50, may be regarded as comparable to the ~~more~~ rapid decline which occurs in acute nephritis. The cases reported by Maxwell in whom hypercholesterinaemia proved to be an unfavourable sign, were all between 30 and 50 years of age, whereas the patients in this series were only half that age, so that in the former, the renal lesions were probably of a much more chronic nature.

The association of cholesterol and oedema in parenchymatous nephritis will now be considered.

The greatest oedema occurred in a boy of fourteen years, case No. 50, who had been decapsulated two years before. The diagnosis of parenchymatous nephritis had been confirmed by histological examination of tissue excised at the time of operation. The cholesterol content in this case was 400 mgms.

Three of the six cases shewing the greatest oedema, Nos. 49, 50, 51, 54, 55 and 58, gave values of over 300 mgms. Three cases, Nos. 47, 54, and 57, had normal readings, with slight and moderate degrees of oedema, while case No. 48 with no greater a degree of oedema, had a cholesterol content of 400 mgms. Thus although the majority of oedematous cases shewed a hypercholesterinaemia, there were a few noticeable exceptions. While comparison of cardiac cases with oedema makes it certain that oedema of renal origin and increase in the cholesterol content of the blood are closely related, it seems evident that other factors most influence the condition and determine the

the incidence of oedema and hypercholesterinaemia in various cases.

Case No.56 developed pneumonia and empyema shortly after dismissal, while case No.55 died of appendicitis and septicaemia, three months after leaving the medical wards. Post mortem examination of the latter case shewed enlarged kidneys with a subacute nephritis. Case No.56 is of interest in view of the possibility of the pneumococcus being a causative agent in the production of the antecedent renal condition. (16) Elwyn suggests the possibility of a pneumococcal infection in the acute nephritis preceeding the development of lipoid nephrosis.

The correlation of the plasma cholesterol with plasma Proteins.

It has been found in parenchymatous nephritis that the albumin globulin ratio of the blood is disturbed, the albumin being much reduced, while the globulin is relatively, or it may be absolutely, increased. (17) Bang suggested that the cholesterol of the serum may be in combination with the proteins and most probably with the globulin fraction.

(18) Gardiner and Gainsborough working on the cholesterol content of normal human plasma, found that it was difficult to dissociate Sterol from the globulin fraction of protein and that a very large proportion of both esters and free cholesterol was associated with globulin, while a very much smaller fraction was associated with albumin. They suggested that possibly changes in the albumin-globulin ratio of the plasma might be associated with variations in the Sterol content of the plasma both in health and disease. Such an explanation is in accordance with the association of hypercholesterinaemia with chronic parenchymatous lesions.

(19) It has also been found by Handovsky, Lohman and Bosse working

working with ox serum, that the stability of the cholesterol-protein combination depends on the water and salt content of the serum. The latter are known to vary in nephritis, and, if the findings of these workers hold for human as well as for ox sera it is obvious that the cholesterol content will be influenced by several factors. In this connection more recent work by Peters, Wakeman, Eisenman and Lee ⁽²⁰⁾ is of interest. They found that the only abnormality which was characteristically and constantly present in nephritic cases with oedema was the reduction in concentration of protein, especially the albumin fraction, in the plasma, and that this was the only change that could be related with any consistency to the occurrence of, or tendency to oedema. Another finding of importance was that these patients had difficulty in the excretion of both chloride and water.

Conclusions.

From consideration of this group it will be seen that:-

1. High cholesterol values are the rule in chronic parenchymatous nephritis.
2. That oedema is usually associated with hypercholesterinaemia, although occasional exceptions may occur.
3. During convalescence, the cholesterol level tends to rise rather than to fall.
4. Further observations suggest that this rise may be temporary, to be followed by a gradual decrease to normal.

GROUP 4. CHRONIC PARENCHYMATOUS NEPHRITIS.

CASE NO.	Sex.	Age.	Blood Pressure	Oedema.	Blood Urea Nitrogen mgms. per 100 c.c.s.	Plasma Cholesterol mgms. per 100 c.c.s. I.R. F.R.	Albumin	URINE. Blood Casts.
47.	F.	23.	$\frac{150}{110}$ mm Hg	Slight	12.4	$\frac{184}{220}, \frac{235}{235}$	+++	++
48.	F.	23.	" $\frac{110}{90}$	Slight	12.5	400, 400, 500	+++	trace
49.	M.	16.	" $\frac{140}{100}$	Consid.	24.3	200 401	+++	+
50.	M.	14.	" $\frac{90}{40}$	Extensive	18.	408 --	+++	+
51.	F.	62.	" $\frac{148}{98}$	"	18.1	333 --	+++	absent
52.	F.	12.	" $\frac{118}{88}$	Very Slight	15.7	240 215	+++	+
53.	M.	27.	" $\frac{144}{85}$	absent	27.0	206 --	+++	+
54.	M.	29.	" $\frac{134}{94}$	Consid.	39.4	160 190	+++	Scanty.
55.	M.	44.	" $\frac{170}{110}$	Consid.	13.	230 250	+++	++
56.	M.	37.	" $\frac{140}{90}$	Absent	26	207 285	+++	+
57.	M.	34.	" $\frac{124}{90}$	Slight	18.6	166 --	+++	trace
	F.	31.	" $\frac{147}{100}$	Consid.	12.7	400 238	+++	absent
	F.	54.	" $\frac{168}{100}$	Absent	21.5	243 232	+++	Scanty.
							++	"
							+	+

I.R.:— Initial Reading.

F.R.:— Final Reading.

GROUP 5.

Mixed Type of Nephritis - Cases Nos. 60-64.

Five cases have been classed in this group, the characteristic features of which were the association of oedema and massive albuminuria with cardio-vascular changes.

Oedema was present in every case at some time, but was greatest in case No. 63, who had a cholesterol content varying from 333 mgms. to 208 mgms.

Three of the patients shewed very definite deficiency of urea excretion, while the fourth had only slight impairment of this function. All the patients had severe headache, and varying degrees of gastro-intestinal disturbance.

The maximum, minimum and mean values for this group were 333, 195 and 245 mgms. per 100 ccs - i.e. the cholesterol level tends to be raised.

The behaviour of the cholesterol during the course of the disease in each case will now be discussed.

Cases Nos. 60 and 63 are of special interest because the subsequent history is available. Case No. 60 shewed little improvement clinically while in hospital. Although the oedema disappeared, the severe headache and dyspnoea persisted. The cholesterol content which was 200 mgms. on admission fell in six weeks time to 166 mgms. This fall was co-incident with the disappearance of the oedema, so that the cholesterol value seemed in this case to run parallel with the oedema, rather than with the patient's true condition. The patient died from cardiac failure four months after dismissal from hospital.

Case No. 63 was extremely oedematous on admission, the cholesterol reading then being 333 mgms. Two months later this figure had fallen to 303 mgms; the oedema had disappeared and the patient looked and felt much better. There was no decrease

decrease in the albuminuria however, and the urea concentration test shewed a less satisfactory excretion than on admission. Headache was persistent. Seven months later, the patient was readmitted to hospital with generalised oedema, severe headache, visual disturbance, dyspnoea, and gastro-intestinal upset. The cholesterol content was now found to be 208 mgms. This case, therefore, like case No.23, of the interstitial nephritis group, shewed a decrease in the cholesterol content with the onset of uraemic manifestations. Moreover, this decrease in the cholesterol content, occurred co-incidentally with the reappearance of oedema which was no less extensive than on his previous admission when the cholesterol content was at its highest level.

The results in this case shew that the presence of extreme oedema is not invariably associated with a high cholesterol content and that the same degree of oedema in the same patient may be found when the cholesterol content shews such divergent readings as 333 and 208 mgms. The interpretation of this phenomenon cannot however be fully discussed at this stage and the question will be referred to later when a series of oedematous cardiac cases have been considered.

In case No.61 oedema on admission was very slight and had disappeared before the first estimation was made. The reading at this time was 285 mgms. The urea concentration test gave a satisfactory result. Six months later, the patient was readmitted on account of persistent and severe headache, but otherwise his condition seemed no worse than before. The blood pressure indeed had fallen slightly, but a urea concentration test shewed definite impairment, which had not been present on the previous admission. The cholesterol content was 196 mgms. It is presumed, in the light of the findings in cases of chronic interstitial nephritis/

nephritis, that changes of an interstitial nature were progressing in this case. Unfortunately, no subsequent details of the man's condition are available.

Case No.62 was admitted on account of great weakness and pallor. Oedema was slight but headache and gastro-intestinal symptoms were very severe. The initial reading in this patient was 250 mgms. Two weeks later when all oedema had subsided, a second estimation gave a reading of 172 mgms. while a third estimation made three weeks after the second, shewed that the cholesterol had risen to 192 mgms. At that time, beyond a slight amelioration in the gastro-intestinal symptoms, there was little change in the patient's condition. The significance of these variations is doubtful. The fall which occurred during the first two weeks may have been associated with the disappearance of oedema, but if this were so, it is difficult to account for the subsequent rise in the absence of any definite change in the clinical condition. On the other hand comparison with case No.28 of the interstitial group suggests that the low figure followed by a rise may have been associated with subsidence of the uraemic symptoms. It is to be noted however that these were already diminishing when the second estimation was made and the lowest reading obtained. Another possible explanation suggests itself in this case. By reason of long continued gastro-intestinal disturbance before admission to hospital this patient had reached a very low state of nutrition. As starvation has been found to be associated with hypercholesterinaemia, it is possible that the initial high reading may have resulted in some measure from inanition.

Case No.64 had considerable oedema, and slight ascites on admission. The onset three weeks before had been acute, and there was no history of renal disease. Examination revealed/

revealed an unusually high blood pressure which did not fall to any great extent. The arteries were palpable but not markedly thickened. The cholesterol content which was over 300 mgms. on admission remained high, and shewed no tendency towards a decrease. Clinically, the patient improved considerably although there was no corresponding improvement in the state of urine or blood.

Conclusions.

As might be expected in the "mixed" type of case, the significance of variations in the cholesterol content is more difficult to interpret, and indeed so many factors are involved, that the readings per se, are of little diagnostic value.

The fact of greatest interest which emerges from a study of this small group is the association of a fall in the cholesterol content of the plasma with the onset of uraemia, irrespective of the presence or absence of oedema.

GROUP 5. MIXED TYPE OF NEPHRITIS.

CASE No.	Sex.	Age.	Blood Pressure	Oedema	Blood Urea Nitrogen. mgms. per 100 ccs.	Plasma Cholesterol mgms. per 100 c.c.s.	URINE.		Casts.	COMMENTS.
							Albumin	Blood		
60.	M.	47.	$\frac{160}{100}$ mm Hg	Slight	28.	200	++	++	+	
61.	M.	37.	$\frac{170}{130}$ "	Absent	28.	285	++	++	+	
Readmitted			$\frac{140}{90}$ "	Absent	24.5	195	+	absent	+	
62.	F.	30.	$\frac{142}{90}$ "	Consid.	15.6	250	++	trace	++	
63.	M.	26.	$\frac{190}{140}$ "	Extensive.	36.	333	++	absent	+	
Readmitted			$\frac{170}{112}$ "	"	146.	208	+	+	+	
64.	F.	46.	$\frac{230}{186}$ "	Consid.	18.6	303, 307, 333	++	trace	absent	

Consid. :- Considerable Oedema.

Extensive. :- generalised and of considerable degree.

Renal Cases other than Nephritis.

Cases Nos. 65-71.

Estimations were made in seven cases of this type,
as follows:-

Pyelitis	3 cases
Pyelonephritis	1 case
Cystic and Tubular Kidney	1 "
Polycystic Kidney	1 "
Functional Albuminuria	1 "

One case of angioneurotic oedema was investigated
and is included in this group.

The cholesterol content ranged from a minimum of
130 to a maximum of 208 mgms., with a mean value of 171 mgms
that is to say the readings were within normal limits. It
is of interest that the case of pyelonephritis shewed no
hypercholesterinaemia - 182 mgms. Presumably, the
infective nature of the lesion, tending rather to a hypo-
cholesterinaemia would counterbalance any increase in
cholesterol which might have been associated with the
nephritis.

Cardiac Cases with Oedema.

Cases Nos. 72-78.

This group comprises nine cardiac cases all of whom had extensive oedema, and of whom several had also hydrothorax and ascites. In every case there was a slight albuminuria, the result of venous congestion associated with a failing heart.

The maximum, minimum and mean values were 196, 135 and 146 mgms. respectively. It is noteworthy that in no patient, however great the oedema, was the cholesterol content above 200 mgms.

This group forms an interesting contrast to the cases of parenchymatous nephritis, and raises the much debated question as to the nature of oedema of renal origin.

The fact that in nephritis oedema is frequently found in association with a hypercholesterinaemia while in the oedema of cardiac origin, this does not occur, shews that a close relationship exists between renal oedema and hypercholesterinaemia. As has been pointed out, in consideration of the foregoing cases, oedema is not always associated with an excess of cholesterol, and conversely a few cases of nephritis with hypercholesterinaemia shew no oedema. Further, when the two are co-existent, there is no constant proportion between them. It is to be remembered also that in other conditions such as diabetes and arterio/sclerosis hypercholesterinaemia is frequently found without any oedema. It is apparent, therefore, that the relationship between hypercholesterinaemia and oedema is not simply one of cause and effect.

Various theories as to the nature of oedema in parenchymatous nephritis have been advanced. Epstein⁽²⁾ considered/

considered that the oedema was due to changes in the plasma proteins and that parenchymatous nephritis was a metabolic disorder associated with hypothyroidism. In support of this theory is his own work⁽²²⁾ on the relationship of cholesterol to basal metabolism. He found in hypothyroidism, where the metabolic rate is low, that the cholesterol content was high.⁽²³⁾ Aub and Du Bois also found that the basal metabolism was decreased in the parenchymatous type of nephritis, thus lending further support to Epstein's conception of the disease.

⁽²⁴⁾ Bloor considered that there was retarded assimilation of fats associated with an acidosis, while Kinder, Lundsgaard and Van Slyke⁽²⁵⁾ believed that it was the mechanism of transfer of fat to the tissues which was upset.

⁽²⁶⁾ Fahr concluded that oedema resulted from changes in the capillary walls; that some extra-renal factor was responsible for lesions both in the capillaries and in the kidneys and for the cholesterol infiltration of the kidneys which occurs in these cases.

Until the validity of one or more of these arguments is confirmed, and until the metabolism of cholesterol is more fully understood, the exact relationship of cholesterinaemia to oedema must remain in doubt.

Summary and Conclusions.

1. While the majority of workers consider the normal range of the cholesterol content of the plasma to lie between 130 and 200 mgms. per 100 ccs., the results of this investigation suggest that the upper normal limit frequently exceeds the accepted figure.
2. In acute nephritis the main findings are:
 - (a) While the level of cholesterol may or may not be unduly high, recovery is accompanied by a decrease.
 - (b) A tardy fall is associated with a slow or incomplete recovery.
 - (c) The degree of oedema is not proportional to the amount of cholesterol in the plasma.
 - (d) The onset of convulsions is not closely related to an abnormal cholesterol content; where nitrogen retention is present (one case) the cholesterol content is normal.
3. Chronic Interstitial Nephritis.
 - (a) In this type of nephritis, the plasma cholesterol is within normal limits, unless very pronounced arterial degeneration is present.
 - (b) The onset of uraemia is accompanied by a fall in the cholesterol level.
 - (c) Recovery from uraemia is attended by a rise in the cholesterol content.
4. Arterio Sclerosis.
 - (a) In this condition, where a renal lesion is present, the cholesterol value is constantly high.
5. Chronic Parenchymatous Nephritis.
 - (a) The plasma cholesterol is raised to a greater degree in this type of nephritis than in any other.
 - (b) Oedema is usually associated with hypercholesterinaemia, but occasional exceptions may occur.

6. The Mixed Type of Nephritis.

No constant values are found in this group, but the average figure is above normal.

7. In Renal Conditions other than nephritis, no hypercholesterinaemia is found.
8. Cardiac cases with oedema shew no increase in plasma cholesterol.

The main diagnostic value of cholesterol estimations is in the differentiation between renal and cardiac oedema. In this connection, it should be noted that the differentiation is most certain in chronic cases, where a high value will almost certainly be obtained in the presence of a renal lesion. In acute cases, the test is not so trustworthy, but a high value favours the diagnosis of nephritis. In almost all cases, the necessary differentiation can be made from a single estimation.

In the second place, a single estimation is of value in establishing a diagnosis of uraemia but it is obviously necessary to consider this finding in conjunction with the other clinical features of the case.

The test is of value, in the third place, in that it supplies an aid to prognosis in renal cases. For this purpose, a single estimation is insufficient and a series of observations must be made.

In interpreting the behaviour of the cholesterol, the type of nephritis must be borne in mind. Thus in an acute nephritis a fall in the cholesterol level is a favourable sign, whereas in chronic nephritis, a fall is generally unfavourable, and associated with the onset of uraemia.

Conversely, a rise in cholesterol in acute nephritis suggests the development of a more permanent lesion, while in chronic nephritis especially of the interstitial type,

a rise frequently coincides with clinical improvement.

Additional information can be obtained by noting the rate of fall in cases of acute nephritis, a slow fall indicating a tardy recovery.

The above conclusions relate to the practical application of the test, but it is of interest to note the relationship of the cholesterol content of the plasma to nitrogen retention, and to oedema.

The cholesterol value, in general, varies inversely with the nitrogen retention.

As regards the relationship to oedema, this has been dealt with in detail in the different groups, but on the whole no direct proportion exists between the two.

The results of this investigation shew that cholesterol estimations have a definite diagnostic and prognostic value in the study of nephritis.

My thanks are due to the Muirhead Trustees for their grant of a Scholarship, and to Professor W.K.Hunter whose patients were investigated.

REFERENCES

-oOo-

1. Campbell, J.M.H. - Quart.Journ.Med. Oxford. 1925, XVIII 393.
2. McAdam, W and Shiskin C. - Quart Jour.Med. Oxford 1923
XVI 193.
3. Maxwell, J. - Quart.Jour.Med. Oxford, 1928, XXI 297.
4. Bloor, W.R. - J.Biol.Chem. Balt. 1916, XXV, 577.
5. Kipp, H. - J.Biol.Chem. Balt. 1920, XLIII 413.
6. Henes, E. - Arch.Int.Med. Chicago, 1920, XXV, 411.
7. Evans, G. - Quart.Jour.Med. Oxford, 1921 XIV 215.
8. Ignatowski, Starakadowski, Lubaroch, Stuckey, Anitschkow
& Chakatow - quoted by McNee, J.W. - Quart.Jour.Med.1914
VII, 221.
9. Klotz, O. - Jour.Med.Research, 1915-16 XXXIV 41.
10. Dewey, K. - Arch.Int.Med. 1916 XVII 575.
11. Newburgh, S.H. - Arch.Int.Med. 1923 XXXI 653.
12. Newburgh, S.H. and Clarkson, S. - Jour.Exper.Med. 1926
XLIII 595.
13. Nuzum, F.R., Siegal, B., Garland, R., Osborne, M. -
Arch.Int.Med. 1926 XXXVII 733.
14. Moscovitz, E. - Amer.J.Med.Sciences 1929 CLXXVIII 244.
15. Waldorp, C.P. - Semana Médica 1928 II 609.
16. Elwyn, H. - Arch.Int.Med. 1926 XXXVIII 346.
17. Bang, - Biochem.Zeit. LXXXX 383.
18. Gardner, J.A., & Gainsborough, H. - Biochem.Jour.1927 XXI 141.
19. Handovsky, Lohman & Bosse, Archiv.f.die Gesamte Physiologie
210, 63.
20. Peters, J.P., Wakeman, A.M., Eisenman, A.J. & Lee, C. -
Jour.Clin.Investig. 1929 VI 577.
21. Epstein, A.A. Amer.Jour.Med.Sc. 1917, CLIV 638.
" " Amer.Jour.Med.Ass. 1917 LXIX 444.
22. Epstein, A.A. and Lande, H. - Archiv.Int.Med. 1922 XXX 563.
23. Aub, J.C., and Du Bois, E. - Archiv.Int.Med. 1917 XIX 865
24. Bloor, W.R. - Amer.J.Physiol. Balt. 1917 XLII 586.
25. Linder, G.C., Lundsgaard, C., & Van Slyke, D.D. - J.Exper.
Med. 1924, 887.
~~XXXX~~
26. Fahr, Th. - Virchow's Archiv.f.Path.Anat. Berlin, 1922
CCXXXIX 32.