A STUDY OF THE BLOOD CHOLESTEROL IN SOME DISEASES OF CHILDHOOD.

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PREFACE.

This investigation was carried out in the Biochemical laboratory and wards of the Royal Hospital for Sick Children during the tenure of a Muirhead Scholarship.

I should state that I am greatly indebted to Professors G. B. Fleming and Noah Morris for having suggested to me this subject of research.

I am obliged to Professor Fleming for the facilities afforded me in his wards, and to Mr. White for access to the surgical cases.

I have further to acknowledge the favour of Professor J. W. S. Blacklock and Dr. Montgomery for the use of autopsy reports; and I have to thank Dr. K. J. G. Guthrie for the translation of the Italian and Spanish references.

No part of this work has been published.

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Glasgow.

PART I.

HISTORY - CHEMISTRY - PHYSIOLOGY.

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PART IV (contd.):

HISTORY.

The substance now known as cholesterol was first isolated from gallstones about the middle of the eighteenth century[1]. Almost fifty years elapsed, however, before its chemical nature became known and before it received its present name, from χολή (bile) and στέαρ (stiff fat)[2]. Some years later, slightly over a hundred years ago, it was demonstrated in the blood for the first time[3]. Little was known, however, about the rôle of cholesterol in disease, and few investigations had been carried out, until the classical work of Dorée and Gardner and their collaborators[4] was published between 1908 and 1912. Since then a vast literature has accumulated concerning all aspects of cholesterol.

CHEMISTRY.

The first to review the "Chemical, Physical and Biological," aspects of cholesterol was Moore in 1907[5]. Since then much intensive research has been carried out, and many potent substances have been shown to be chemically related to cholesterol ($C_{27}H_{46}O$). Gainsborough (1935)[6] has given a brief account of this work, he quotes Windaus and Wieland, showing that cholesterol, bile-acids, ergosterol, vitamin D and the male and female hormones have a common skeleton. Parkes and Callow (1937)[7] quote the work of Ruzieka and his collaborators, who prepared androsterone, the equivalent of the male hormone from cholesterol. Vollmer (1927)[8], Waddell (1934)[9], and Hathaway and Koch (1935)[10], have demonstrated that irradiated cholesterol has definite antirachitic properties. It is obvious therefore that cholesterol belongs to a highly important group of substances, the precise chemical relationships of which are not yet clear.

PHYSIOLOGY.

Cholesterol metabolism.

Numerous investigations into the cholesterol cycle in man, and especially in animals, have been carried out. It is not proposed however to discuss this work, but merely to indicate very briefly a few outstanding findings.

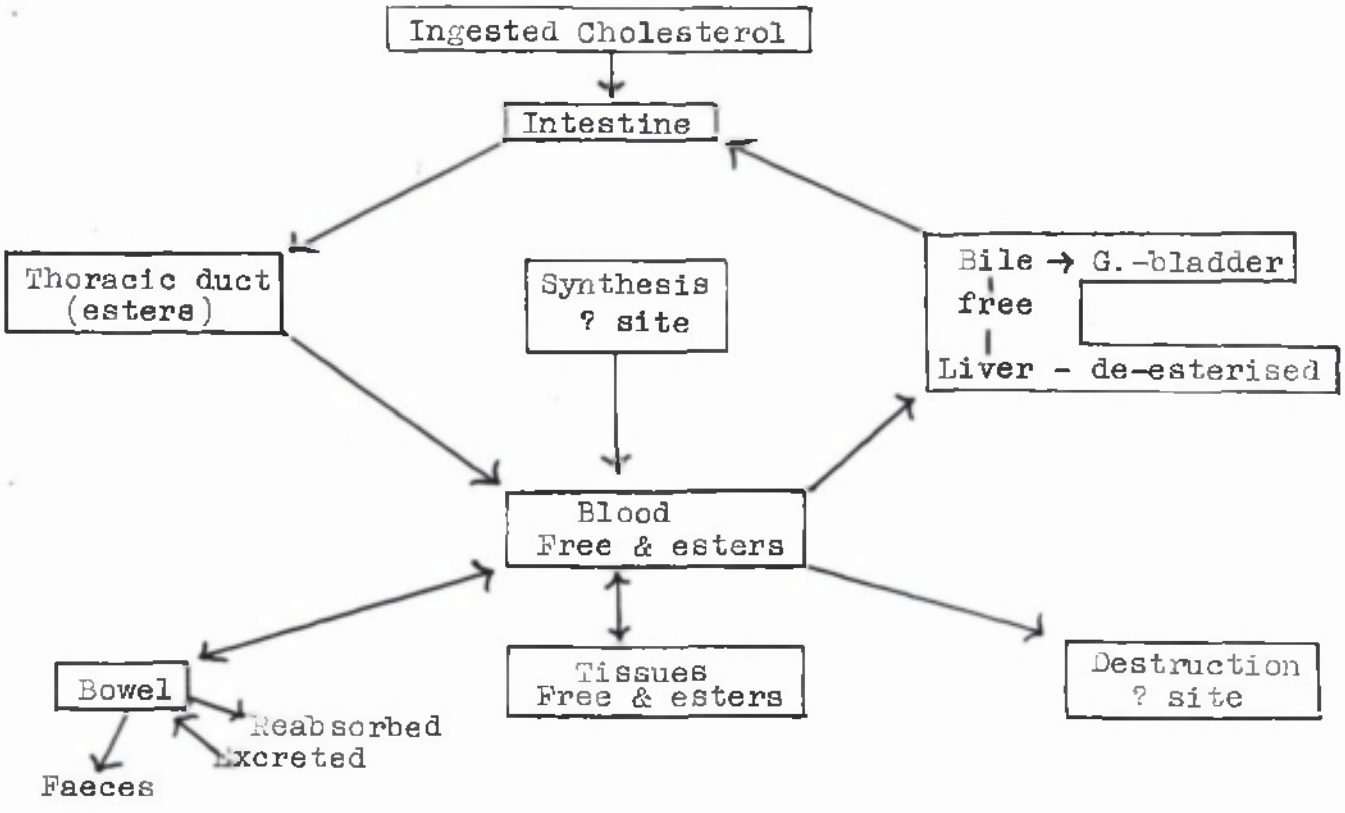
One of the first researches into this elusive process of cholesterol metabolism was carried out by Austin Flint, Jr. in 1862[11]. While some of his results have not been confirmed by modern workers with more reliable methods, his belief that cholesterol is formed in the nervous system, and excreted by the liver is still supported by some authors. Flint concluded from his experiments on animals that the quantity of cholesterol added to the blood during its passage through the brain, was equal to that removed by the liver. Almost fifty years later Dorée and Gardner (1909)[12] published the following well known hypothesis:

1. "That cholesterol is a constant constituent of all cells, and when these cells are broken down in the life process, the cholesterol is not excreted as a waste product, but is utilized in the formation of new cells.

2. A function of the liver is to break down dead cells - for example, blood corpuscles - and eliminate their cholesterol in the bile.

3. After the bile has been poured into the intestines in the process of digestion the cholesterol is reabsorbed, probably in the form of esters, along with the bile salts, and carried by the blood to the various centres and tissues for reincorporation into the constitution of new cells."

At this stage these authors, together with Ellis,[4] were unable to demonstrate synthesis of cholesterol within the organism. Most of their subsequent work is in conformity with the conclusions just quoted, and Gardner in 1932[13] was able to adhere to his original hypothesis, though he admitted that it was "by no means the whole story." Fox and Gardner,[14] at a later date, demonstrated the synthesis of cholesterol within the organism, and this work has been confirmed by Schönheimer and others[15]. Most workers agree that the cholesterol ingested with the food is utilized in the metabolic process. Hurxthal and Hunt (1935)[16] are of the opinion that cholesterol is derived in part from animal food, but that the greater part results from synthesis within the organism. The following is their diagrammatic conception of cholesterol metabolism.



The consensus of opinion seems to be that the body derives its cholesterol both from synthesis within the organism, and from cholesterol intake, though exactly how this occurs is still the subject of dispute. The ester fraction is said to play an important part in the absorption and transport of cholesterol from the intestine. While J. H. Mueller[17] was unable to demonstrate cholesterol esters in the intestine, he was of the opinion that this was due to their being absorbed as quickly as they were formed. The ingestion of food and also cholesterol in animals is followed by an increase of cholesterol in the chyle from the thoracic duct[17]. Yet in man, many recent workers[18,19,20,21,22,23,24,25,30,43] state that there is no such thing as alimentary hypercholesterolemia. Nevertheless the blood cholesterol does not remain uninfluenced by certain special diets, given over a period of time[23,26,27,28,29]. The absence of any diurnal variation[30, 31,34] of the blood cholesterol, in spite of intestinal absorption would appear to suggest the presence of some intermediate regulating mechanism. However, the absence of alimentary hypercholesterolemia is by no means undisputed. Bloor (1932)[29] reviewed the effect of diet on the blood cholesterol, and supported the assertion, as many others have done, that the ingestion of a single meal may produce a temporary increase of the blood cholesterol, though few of his own results showed increased values after food. All the workers just quoted have used reliable methods, and one cannot devise any good reason for refuting either of these divergent

results. It is therefore suggested that alimentary hypercholesterolemia may occur from time to time in the same individual, and possibly more frequently in some individuals than others, and that it is dependent on some temporary deviation of the cholesterol metabolism at present inexplicable.

The distribution of cholesterol and its esters in the body.

Salisbury[46] in the year 1863 was apparently the first to demonstrate the presence of cholesterol in every bodily secretion and excretion. The ubiquity of cholesterol in the animal organism has also been established by Dorée and Gardner[12] and many other investigators.

Cholesterol exists in the bile,[32] red blood corpuscles[42][33] and brain[42] almost entirely in the free state. Of the total cholesterol in the blood plasma, about forty two per cent is in the free form[33]. According to Gardner[42] other tissues, such as liver, kidneys and suprarenals contain both free and ester cholesterol. The pathological deposits of cholesterol in the tissues were shown by Panzer and Aschoff in 1907[37] to be composed almost wholly of the ester fraction. It is interesting to note here that Boyd[35] and others[36] have found a parallel between the state of activity of cells and their percentage of free cholesterol, and that their combined cholesterol increases as they proceed towards degeneration.

A low percentage of cholesterol has been recorded in

amniotic and oedema fluids[38] and traces only have been found in normal urine.[38,44] Weston[39] noted very low values in the cerebrospinal fluid, and the cholesterol content of the bile[32,40] is usually considerably less than that of the serum. A fact of some interest is the remarkable constancy of the low cholesterol values of oedema fluid,[38,45] even when the blood cholesterol is high, as in nephrosis[41].

PART II.

PATHOLOGY.

Some interpretations of the pathological oscillations of the blood cholesterol.

SOME INTERPRETATIONS OF THE PATHOLOGICAL OSCILLATIONS OF THE BLOOD CHOLESTEROL.

There have been numerous contributions to the literature on the pathology of cholesterol metabolism, during the last thirty years. Much of the work is so controversial, and many of the results so diverse, that an impartial perusal of it all would probably leave one with no little confusion of ideas regarding this subject.

The following are some outstanding reviews: Grigaut[1] in his thesis in 1913 gave a comprehensive account of cholesterol in various pathological conditions. In 1914 McNee[2] reviewed the English, French, German and Russian literature of the preceding seven years. Campbell[3] in 1925 published a "Critical Review of Cholesterol in Health and Disease," and the subject was again reviewed by Schally[4] in 1936.

THE CHOLESTEROL DIATHESIS. Some authors[2,5] consider that hypercholesterolemia, per se, may produce gallstones, or other cholesterol deposits, (xanthomata, atheroma, arcus senalis) and it has been suggested[2] that the high incidence of gallstones in pregnancy is associated with the hypercholesterolemia so often observed. Some of the authors[5] just quoted believe that certain individuals have an inherent weakness to retain cholesterol - thus postulating a cholesterol diathesis. These authors think that this may explain the predisposition of

certain individuals to gall stone formation. Many workers[6] refute this suggestion, and produce apparently convincing evidence to show that prolonged hypercholesterolemia does not produce gallstones, or cholesterol deposits.

VITAMIN B DEFICIENCY. According to Horvath[7], some investigators believe that beri-beri is consequent on cholesterol intoxication. This suggestion, however, has received little support, though Smith and Sure[8], working with rats, found definite hypercholesterolemia in vitamin B deficiency. They suggest that the blood cholesterol value might be used as an aid in the diagnosis of vitamin B deficiency.

HAEMOCONCENTRATION. This has been suggested by Man and Peters[9] as an important factor in the lipaemia of some diseases, especially diabetes. While this might explain the high cholesterol values found in acidosis, starvation, and following experimental anaemia, Hurxthal and Hunt[10] have shown that it does not explain the hypercholesterolemia observed in diabetes without acidosis. It will be shown in part IV , page 221, that the majority of recent investigators do not find any correlation between acidosis and the blood cholesterol. Smith and Sure[8] have shown that the hypercholesterolemia of vitamin B avitaminosis, was not due to haemoconcentration, and obviously, there are many conditions such as nephrosis, in which this cannot play any part.

OSMOSIS. Many investigators[11] find an inverse ratio between the blood cholesterol and the serum proteins in nephrosis. The lipoid increase is thought to be a compensatory phenomenon consequent on the lowered osmotic pressure, which is associated with low serum protein values. Fishberg attributes the lipaemia of experimental anaemia to the fall of the osmotic pressure following the depletion of serum proteins. This will be discussed in part IV, page 162, and it will be shown that there is no unanimity of opinion respecting the relationship of the blood cholesterol and the serum protein values.

THE DISSOLVING POWER OF THE SERUM. Several continental workers[20,48,49] have investigated the capacity of the serum to hold cholesterol in solution, by adding to it measured quantities of cholesterol, and leaving it for twenty four to seventy two hours. In children the serum tended to dissolve an excess of cholesterol, while in old age this power was considerably diminished, and often some of the serum cholesterol was precipitated out instead.[20]

The serum in various diseases was also studied, but the results do not appear to be sufficiently outstanding to throw much light on the cholesterol metabolism.

CHOLESTEROL RETENTION. Sperry[21][22] and others[23] have demonstrated the excretion of cholesterol by the intestinal mucosa, and it has been suggested that if this excretory mechanism were incapacitated cholesterol retention might ensue. It is interesting to note that Schönheimer[24] has reported a patient with

xanthomatosis, who could absorb cholesterol but was unable to excrete it. The blood cholesterol in this case fell from 852 mg.% to 300 mg.%, on a vegetarian diet. Low values are found in gastro-intestinal disorders[25,26,27].

Cholesterol retention associated with hepatic disorders will be considered, together with jaundice, on page 174.

DISORDERED FAT METABOLISM. That hypercholesterolemia is consequent on disturbed fat metabolism has received more support than many other suggestions. It is believed by some to be associated with the high cholesterol values found in diabetes,[28] experimental anaemia,[29] and nephrosis[30]. Petersilie[28] and others, believe that cholesterol esters play an important part in the transport of fat. On the other hand, many workers consider that there is little real evidence in support of these contentions[50]. In experimental hyperthyroidism, Simonds and Helpler[31] have shown that the blood cholesterol and neutral fat are not correlated.

THE NERVOUS SYSTEM. Flint[12] concluded that the nervous system was the source of cholesterol production, and Grigaut[1] quotes several investigators who consider the nervous system to be the centre of cholesterol formation. Inglessi[13] suggests that the hypercholesterolemia observed by him in poliomyelitis, is due to the degeneration and breaking down of nervous tissue, setting free cholesterol in the blood. Moukhine[14], as a result of his experimental work, concludes that cholesterol formation may be controlled by the greater hemispheres, and the work of Castex[15] apparently supports this view.

ENDOCRINE SYSTEM.

Supra-renal glands. There has been much controversy respecting the rôle of the endocrine system, and more especially the supra-renal glands, in cholesterol metabolism. Grigaut[1] and the French school hold the view that cholesterol belongs to the hormone group, and is secreted by the supra-renal glands, while Aschoff[52] and his school are of the opinion that cholesterol may be stored in these glands. These views have received little support from workers in this country and America. Joelson and Shorr[16] found that the blood cholesterol was increased in three dogs and diminished slightly in one, after bilateral supra-renalectomy. Baumann and Holly[17] did not find any significant change in rabbits after this operation, until the last week of life. The action of adrenalin on the blood cholesterol is equally inconclusive. According to Bruger and Mosenthal[18], few workers agree respecting the action of this substance on cholesterol, in children, adults or animals. On the other hand, Marañón[19] found that hypocholesterolemia coincides with supra-renal insufficiency, and hyperfunction is associated with hypercholesterolemia. He also found an increase in the blood cholesterol after injecting a preparation of the supra-renal cortex (corthormona).

Ovary. It has been suggested[2] that the increased cholesterol values found in pregnancy may be associated with ovarian disturbances, but Kaufmann and Mühlbock[32] were unable to demonstrate any change in the blood cholesterol after total hysterectomy, or at the menopause in normal women. Parhon and Marza[33] found no difference in the blood cholesterol of normal or castrated animals.

Pituitary gland. It will be shown in part IV, page 233. that little work has been done on the relation of the pituitary gland to cholesterol metabolism, and the results of this work are inconclusive. Moehlig[34] observed an increase of cholesterol in rabbits after giving posterior pituitary extract, and Long et alii[35] found that pitressin produced no significant change in the lipoid content of mice. Wartin[36] has reported two cases of pituitary dystrophy showing marked cholesterol retention at the autopsy.

Thyroid gland. Hypercholesterolemia is invariably observed in cretinism[37], hypothyroidism[38,42,45], and in post operative myxoedema[39,40], and the action of thyroid extract, in lowering the cholesterol in this condition, is practically undisputed. Many workers find that the blood cholesterol value is a useful and simple aid to the control of thyroid therapy,[37,41,45] and also of radio-therapy of the thyroid gland[43]. Hypocholesterolemia is usually found in hyperthyroidism[44] though some authors[46,47] have recorded normal values in this condition.

THE LIVER AND THE RETICULOENDOTHELIAL SYSTEM. Muller[51] has written a comprehensive review of the literature on this aspect of the subject, and has shown that many recent investigators hold the reticuloendothelial system responsible for cholesterol metabolism. The literature concerning the rôle of the liver in cholesterol metabolism, will be reviewed very briefly in the section on diseases of the liver and blood.

PART III.

THE BLOOD CHOLESTEROL IN NORMAL CHILDREN.

A brief review of the literature, with personal observations.

THE BLOOD CHOLESTEROL IN NORMAL CHILDREN.

Cholesterol metabolism.

Muller[26] found that cholesterol was excreted in the faeces without reduction to coprosterol or B cholesterol only after prolonged feeding on milk diet. Thus the possibility of estimating the quantity of cholesterol excreted became evident, and incited Gamble and Blackfan (1920)[1], and Fox and Gardner (1925)[25] to determine the cholesterol metabolism of infants. Gamble and Blackfan performed their estimations on children whose ages ranged from three to nineteen months. They found considerably more cholesterol in the stools than was contained in the food, and they accepted this as evidence of cholesterol synthesis within the organism. Sterols other than cholesterol were not observed in the stools.

Fox and Gardner found an excess of output over intake during the first three weeks of life. From the third to the seventh week the intake practically balanced the output, while from the seventh to the tenth week the intake exceeded the output. These authors concluded that the infant derives its cholesterol both from its diet and from synthesis.

Dietary regimen.

The blood cholesterol is said to be higher in breast fed than in artificially fed infants[2,4,11,19]. It is not easy to assign the cause of this difference, since cows' milk[18] is alleged to be richer in cholesterol than human milk. Nevertheless it is not easy to estimate the quantity of cholesterol received by the breast fed infant, for it has been shown, that the cholesterol content of milk varies widely in specimens taken from the same breast at different times[15,16]. Possibly the better general condition of the breast fed infant, and the lower incidence of gastro-intestinal disorders, may account for the higher values in these children. On the other hand, some investigators[12] have been unable to demonstrate higher figures in breast fed infants. Strathmann-Herweg[17] compared the cholesterol values of infants during a six-week period on breast milk, with the values during a similar period on artificial feeding, but the blood cholesterol did not show any significant variation.

Many investigators have observed hypercholesterolemia in pregnancy, but the majority of them have failed to demonstrate any definite parallel between the cholesterol content of the maternal and foetal blood[20,21,22,23].

Age.

Cholesterol differs from the other chemical constituents of the blood in being thought by many workers to be lowest in the neonatal period and to increase coincidently with the age of the child[2,3,4,5,6,7,24].

It is believed that this may be related to the process of growth, and Baylac and Sendrail[24] attribute these low values to the avidity of the young organism for the lipoids necessary for growth. Acuña and Winocur[2] give some support to this view, and Ward[3] has demonstrated a parallel between the variability of the growth curve, and the variability of the cholesterol curve.

The acquisition of immunity consequent on a series of infections is said to be an additional factor in raising the blood cholesterol[2,4,24].

Hinglais and Govaerts[8] found an excess of cholesterol in the foetal adrenals. They suggest that the rapid increase of the blood cholesterol during the first few days after birth is due to the activity of these glands.

Sperry[9] found a wide range of cholesterol values in the neonatal period and he has suggested that the regulating mechanism, which keeps the blood cholesterol within narrow limits is not fully developed at this period.

In view of the association of low blood cholesterol values with hepatic inefficiency, (vide page 174), it is interesting to note that Hirsch[10] found evidence of liver inefficiency in young and in premature infants, while Bingenheimer[6] observed that the blood cholesterol was lower and rose more slowly in premature infants.

On the other hand one may doubt the reality of this hypocholesterolemia in infancy, and accept the findings of Galdó[11] and Simonini[12] and others[13] who did not observe any difference in the cholesterol values of children of different ages. Increased values in young children have been noted by Goldbloom and Gottlieb[14] but these results have not been confirmed. The range of cholesterol values found by nineteen different authors in normal adults and children, are indicated in tables 1a and 1b respectively.

In children the widest range of values was observed by Acuña and Winocur[2]; their lowest figure being 50 mg.% and their highest 230 mg.%. The smallest range was noted by Offenkrantz and Karshan; their minimum and maximum values being 174 mg.% and 186 mg.% respectively.

Table 1a.

Values observed by different authors in healthy adults.

Author	Year	Cholesterol mg.% range of values.	* B. P. S.	Method.
Grigaut[21]	1913	140-190	S.	Grigaut.
Denis[37]	1917	167-255	B.	(Bloor's modification (of Autenrieth-Furk.
Campbell[38]	1924	110-190	P.	Myers & Wardell.
Gardner[39]	1932	80-230	P.	
Teilum[36]	1935	150-230	S.	Rappaport & Engelberg.
Sperry[41]	1936	146-392	P.	Schönheimer & Sperry.
Schube[40]	1937	100-200	B.	Myers & Wardell.

* B. = Blood.
P. = Plasma.
S. = Serum.

TABLE 1b.

Values observed by different authors in healthy children.

Author.	Year	Subjects' age. (years)	Cholesterol mg.% range of values.	B. P. S.	Method.
Baranski[13]	1926	8/365 - 12	125-170	S.	Grigaut.
Manicatide, Bratesco & Rusescu[19]	1927	2/52 - 14/12	100-180	S.	"
Baylac & Sendrail[24]	1928	1/12 - 15	95-169	S.	"
Sylvestre[4]	1928	1/12 - 14	80-160	S.	"
Gordon & Cohn[7]	1928	1/52 - 6	85-190	S.	Bloor.
Acuña & Winocur[2]	1931	3/365 - 15	50-230	B.	Sackett's modification of Bloor.
Kaiser & Gray[33]	1934	5 - 16	108-201	S.	Bloor.
Molitch & Poliakoff[34]	1936	8 - 18	81-204	S.	Reinhold's modification of Sackett.
Ward[3]	1931	6 - 13	125-158	B.	Leiboff.
Sperry[9]	1936	1/365 - 25/365	71-190	P.	Schönheimer & Sperry.
Offenkrantz & Karshan[32]	1936	3/12 - 12	174-186	S.	" " "
Gørtz[35]	1937	1/365 - 12	108-166	B.	Gørtz.
Present series	1938	6/12 - 12	96-134	B.	Leiboff.

Comparing the results in the two tables it is obvious that in the majority of cases the range of values is higher in adults than in children. The wide variation in both sets of figures is, however, somewhat remarkable.

Method employed in the present investigation for estimating the blood cholesterol.

Attention has already been drawn to the wide discrepancies in the results of different authors. This may be partly explained by the diversity of methods in use and the fact that some workers do not adhere strictly to the details of the original methods. Many of these methods have been reviewed by Gardner and Williams[27], Weidman and Sunderman[28], and Teilum[36].

In children it is often either undesirable or impossible to withdraw more than a small quantity of blood, and in the present investigation the micro-method of Leiboff[29] was used. This method has been shown to be accurate, simple and moderately rapid. Leiboff, himself, checked it against the method of Myers and Wardell on over a hundred samples of blood, and obtained slightly higher results in practically all cases, this being explained by the absence of loss during extraction. Dutton[30] has also vindicated the accuracy of this method, obtaining practically duplicate results with measured quantities of cholesterol. He also made the following comparative estimations, with the methods of Bloor, and Myers and Wardell.

Method	Experiment Number	1	2	3	
	Bloor	168	160	235	Mg.%
	Leiboff	164	152	210	
	Myers & Wardell	132	128	182	

Ward[3] has produced further confirmatory evidence - checking it against the method of Myers and Wardell, she did not find any significant difference between the two sets of results.

This method depends on the development of the well known Liebermann-Burchard colour reaction. It has been shown that the time taken for the maximum colour development in this reaction varies according to the temperature. Consequently it is essential that both the temperature and the incubation period should be carefully controlled. Bloor[31] tested the accuracy of this reaction at temperatures varying from 10°C. to 34°C., and obtained the most accurate results at 22°C., after incubation in the dark for fifteen minutes. The following is a brief description of the procedure followed in the present investigation.

0.2 c.c. blood is pipetted on to an ether extracted filter paper disc, which is then dried at 37°C. Slightly less than 5 c.c. chloroform is placed in the extractor tube and the disc dropped in. A constriction in the extractor tube holds it above the level of the chloroform.

The tube is connected to a reflux condenser and is placed in a bath of boiling water for 35 minutes. After cooling, the condenser is detached, the discs removed, and chloroform added to the 5 c.c. mark. 2 c.c. of acetic anhydride and 0.1 c.c. of concentrated sulphuric acid are added, and it is incubated for 15 minutes at 22°C., and the results read with the Pulfrich Photometer.

The estimations were made on oxalated whole blood.

Although the majority of workers agree that cholesterol does not undergo any diurnal variation, it was thought desirable to withdraw the blood at about the same time each day. This was done between 9 and 10 a.m., after a four or five hour fast, in practically all cases, a few of the diabetics attending as out-patients being excepted.

Personal observations.

In view of the controversy respecting the normal cholesterol value, it is essential to establish a standard of normality for oneself. Accordingly, in the present investigation, determinations were made on sixty two apparently healthy children who had not suffered from any recent acute illness (vide table 5). The majority were admitted for the purpose of some surgical procedure, in respect of congenital dislocation of hip, talipes, or for herniotomy, and a few of them were out-patients attending the dental clinic. Cases of alveolar abscess were of course excluded and the estimations were made prior to any surgical interference.

These children exhibited a comparatively small range of values, the lowest being 96.0 mg.% and the highest 134.0 mg.% The average figures for each year of life are indicated on table 2. Perusal of this table shows that there is no outstanding difference between the cholesterol values of the various age groups. Nevertheless, the lowest average result (103.7) occurs in children under one year, and from then onwards there is a gradual increase until at six years the average figure is 119.3 mg.%. Between six and twelve years, the cholesterol does not display any significant variation, remaining within a comparatively narrow range. One concludes therefore that in children under six years of age there is a slight parallel between the age of the child and the cholesterol value. In older children there does not appear to be any correlation between the cholesterol level and the age of the child.

TABLE 2.

Average cholesterol value for each age group in healthy children.*

No. of children.	Age Group	Cholesterol mg.% Av.
2	under 1 yr.	103.7
3	1 year	107.0
5	2 years	110.4
4	3 "	108.6
5	4 "	117.9
5	5 "	116.8
8	6 "	119.3
7	7 "	112.5
6	8 "	109.8
7	9 "	112.0
5	10 "	116.5
1	11 "	108.5
4	12 "	109.3

Total 62

TABLE 3.

No. of children.	Sex	Cholesterol mg.% Av.
39	Males	114.1
23	Females	110.9
62	Both sexes	112.9

* Vide Table 5, page 24, for individual values.

Sex. (Vide Table 3.)

The results of various workers are not in agreement respecting the influence of sex on the blood cholesterol. While a decided difference in the cholesterol values of male and female children has not been observed by any author, slight differences have been recorded[3][42]. Other workers have been unable to demonstrate any variation according to sex[32].

In the present series the average figure for females of all ages is 110.9 mg.%, and the corresponding figure for males is 114.1 mg.%. This slight difference is not considered to be of any significance. Ward[3] and Rothbart[42] found slightly higher results in females. Sex does not appear therefore to play any prominent part in cholesterol metabolism.

Season.

Currie[43] observed a seasonal variation of the blood cholesterol in adults, and Kaiser and Gray[33] found a very slight seasonal variation in children.

In the present group of healthy children the mean values for the winter and summer months are practically identical. The average figure for all estimations made between the beginning of April and the end of September is 114.8 mg.% and the corresponding figure for the winter months is 110.7 mg.%.

Table 4.

No. of children	Season	Cholesterol mg.% Av.
34	April-Sept.	114.8
28	Oct.-March	110.7

TABLE 5.

The blood cholesterol in sixty two healthy children

Case No.	Date	Name	Age in Years	Sex	Cholesterol mg.%.	Remarks
1	26. 5.36	A.T.	6/12	M.	108.5	Normal Child.
2	4.11.36	D.M.	11/12	M.	98.9	Hernia.
3	19. 8.37	E.D.	1	M.	109.7	Hernia.
4	11.11.36	J.L.	1 4/12	F.	105.7	Cleft palate.
5	2.12.36	D.B.	1 4/12	F.	105.7	Hernia.
6	2.12.36	J.H.	2	M.	117.2	Talipes
7	19.11.36	C.H.	2	F.	120.6	Congenital dislocation of hip.
8	12. 8.36	J.C.	2	F.	108.5	Cleft palate.
9	12. 8.36	T.D.	2 2/12	M.	96.0	Cleft palate.
10	19. 3.36	M.R.	2 2/12	F.	110.0	Normal child.
11	4.11.36	P.O'N.	3	M.	102.3	Hernia.
12	19.11.36	J.C.	3	M.	131.0	Torticollis.
13	4.11.36	H.F.	3 6/12	M.	98.9	Hernia.
14	20. 1.36	J.McM.	3 6/12	M.	102.3	Admitted to hospital for tonsillectomy.
15	21.11.35	J.D.	4	M.	108.6	Dental out-patient.
16	13. 2.36	W.M.	4	M.	98.9	" "
17	7. 5.36	W.McL.	4 6/12	M.	131.0	" "
18	7. 5.36	A.W.	4 6/12	M.	134.0	" "
19	7. 5.36	B.K.	4 6/12	F.	117.2	" "
20	27. 2.36	J.B.	5	F.	114.3	" "
21	27. 2.36	J.T.	5	M.	120.7	" "
22	13. 2.36	R.H.	5	M.	111.5	" "
23	21.11.35	W.McD.	5	F.	127.6	" "

Table 5 continued.

Case No.	Date	Name	Age in Years	Sex	Cholesterol mg.%.	Remarks.
24	28. 7.36	M.C.	$5\frac{3}{12}$	M.	110.0	Normal child.
25	28.12.35	G.McI.	6	M.	124.1	Dental out-patient.
26	13. 2.36	D.McE.	6	F.	116.6	" "
27	2.12.36	J.H.	6	M.	111.5	Congenital disolcation of hip.
28	27. 2.36	W.T.	6	M.	127.6	Dental out-patient
29	27. 6.36	D.H.	6	M.	124.1	Admitted to hospital for tonsillectomy.
30	6. 2.36	M.L.	$6\frac{5}{12}$	F.	131.0	Dental out-patient.
31	11. 8.37	G.T.	$6\frac{6}{12}$	M.	117.2	Birth injury.
32	30. 3.36	N.McI.	$6\frac{6}{12}$	M.	102.3	Normal child.
33	11.11.36	C.S.	7	F.	98.9	Admitted to hospital for tenotomy.
34	12. 8.36	E.B.	7	F.	98.9	Normal child.
35	11. 8.37	W.M.	7	M.	105.7	Appendicectomy two months previously.
36	3. 7.36	J.S.	7	M.	131.0	Neck cyst.
37	3. 7.36	A.C.	7	M.	117.2	Normal child.
38	3. 7.36	A.B.	7	M.	131.0	Hernia.
39	24.11.36	J.McK.	7	M.	105.0	Admitted to hospital for tenotomy.
40	16. 8.37	N.H.	8	F.	98.9	Poliomyelitis 4 years ago.
41	27. 8.36	C.M.	8	F.	114.3	Normal child.
42	23. 8.37	J.C.	8	F.	105.7	Talipes.
43	4. 6.37	C.McP.	8	F.	98.9	Normal child.
44	16. 8.37	E.B.	8	M.	124.1	Poliomyelitis 5 years ago.
45	11. 8.37	J.G.	$8\frac{6}{12}$	M.	117.2	Mastoid abscess 6 months ago.

Table 5 continued.

Case No.	Date	Name	Age in Years	Sex	Cholesterol mg.%.	Remarks.
46	23. 8.37	J.A.	9	M.	131.0	Laceration of leg 8 months ago.
47	30. 3.36	E.McI.	9	F.	111.5	Normal child.
48	13. 8.36	E.P.	9	F.	108.5	" "
49	9.11.35	T.L.	9	M.	98.9	" "
50	16. 8.36	J.W.	9	M.	105.7	Poliomyelitis 3 years ago.
51	16. 8.36	R.D.	9	M.	117.2	Poliomyelitis 6 years ago.
52	27. 8.36	J.A.	9	M.	111.5	Talipes.
53	18. 5.37	G.D.	10	F.	108.5	Poliomyelitis 6 years ago.
54	13. 2.36	E.L.	10	F.	102.3	Dental out-patient.
55	30. 8.37	N.McB.	10	F.	131.0	Normal child.
56	30. 8.37	G.C.	10	M.	126.5	" "
57	30. 8.37	S.B.	10	M.	114.2	" "
58	3. 7.36	J.C.	11	M.	108.5	" "
59	7. 7.36	L.K.	12	F.	105.7	" "
60	12. 8.36	N.H.	12	F.	111.5	Talipes.
61	11. 8.37	J.F.	12	M.	124.1	Poliomyelitis 1 year ago.
62	24.11.36	D.McI.	12	M.	96.0	Admitted to hospital for tenotomy.

PART IV.

THE BLOOD CHOLESTEROL IN SOME DISEASES OF CHILDHOOD.

PART IV.

THE BLOOD CHOLESTEROL IN SOME DISEASES OF CHILDHOOD.

In the following pages an account is given of the pathological variations of the blood cholesterol in children whose ages range from three days to twelve years.

Baranski and others have shown that the blood cholesterol in disease usually exhibits the same modifications in children as in adults. It is, for example, increased in nephrosis and hypothyroidism, and diminished in acute infections, and in parenchymatous diseases of the liver.

The possible causes of these pathological oscillations apply equally to adults and children.

SECTION 1.

The blood cholesterol in some acute infections with special reference to pneumonia.

A. PNEUMONIA.

That hypocholesterolemia occurs in acute infections is recognised by many authorities, and a number of workers have shown that the cholesterol values in pneumonia are no exception to this general statement. Kipp,[1] and Chauffard et alii[2], working with adults, have demonstrated hypocholesterolemia in pneumonia. The latter workers found low values in the febrile period - sometimes the cholesterol fell as low as 50 mg.% - while increased values were observed during convalescence.

In children, Goldbloom and Gottlieb[3] did not discover any significant variation from the normal in broncho-pneumonia or empyema, and Simonini[4] found low values in only one of his cases of pneumonia. Many other workers[5,6,7,8] however, have been able to produce substantial evidence in favour of hypocholesterolemia in broncho-pneumonia and lobar pneumonia in children. Lesné et alii[9] estimated the cholesterol in twenty infants with pneumonia and observed low values in thirteen, normal values in five, and increased values in two. These investigators found that the blood cholesterol returned to normal during convalescence, and that markedly low figures occurred in fatal cases. Raspi[10] obtained somewhat similar results. In two of his fatal cases he found values of 90 mg.%, while in another subject the cholesterol

was 110 mg.% in the acute stage and two days after the crisis it was 130 mg.%.

PERSONAL OBSERVATIONS.

Three hundred and thirteen determinations were made on sixty nine cases of pneumonia in children, between the ages of ten weeks and eleven years.

The children have been classified according to whether they were suffering from a first, or a recurrent attack of pneumonia, and according to whether they were over, or under, two years of age.

1. First attack
   (a) under two years (vide Table 6a)
   (b) over two years (vide Table 6b)

2. Recurrent pneumonia
   (a) under two years (vide Table 7a)
   (b) over two years (vide Table 7b)

In the various tables the day of illness has been calculated from the date of sickening obtained from the parent. In many children it was difficult to obtain the exact date of onset, but in most cases it is probably correct to within a few days. It is possible that this inexactitude may account, partly, for the irregularity of the composite curves.

First attack.

The results are summarised in the composite curves on chart 1, and it is apparent that the values tend to be higher during convalescence than during the acute stage of the illness.

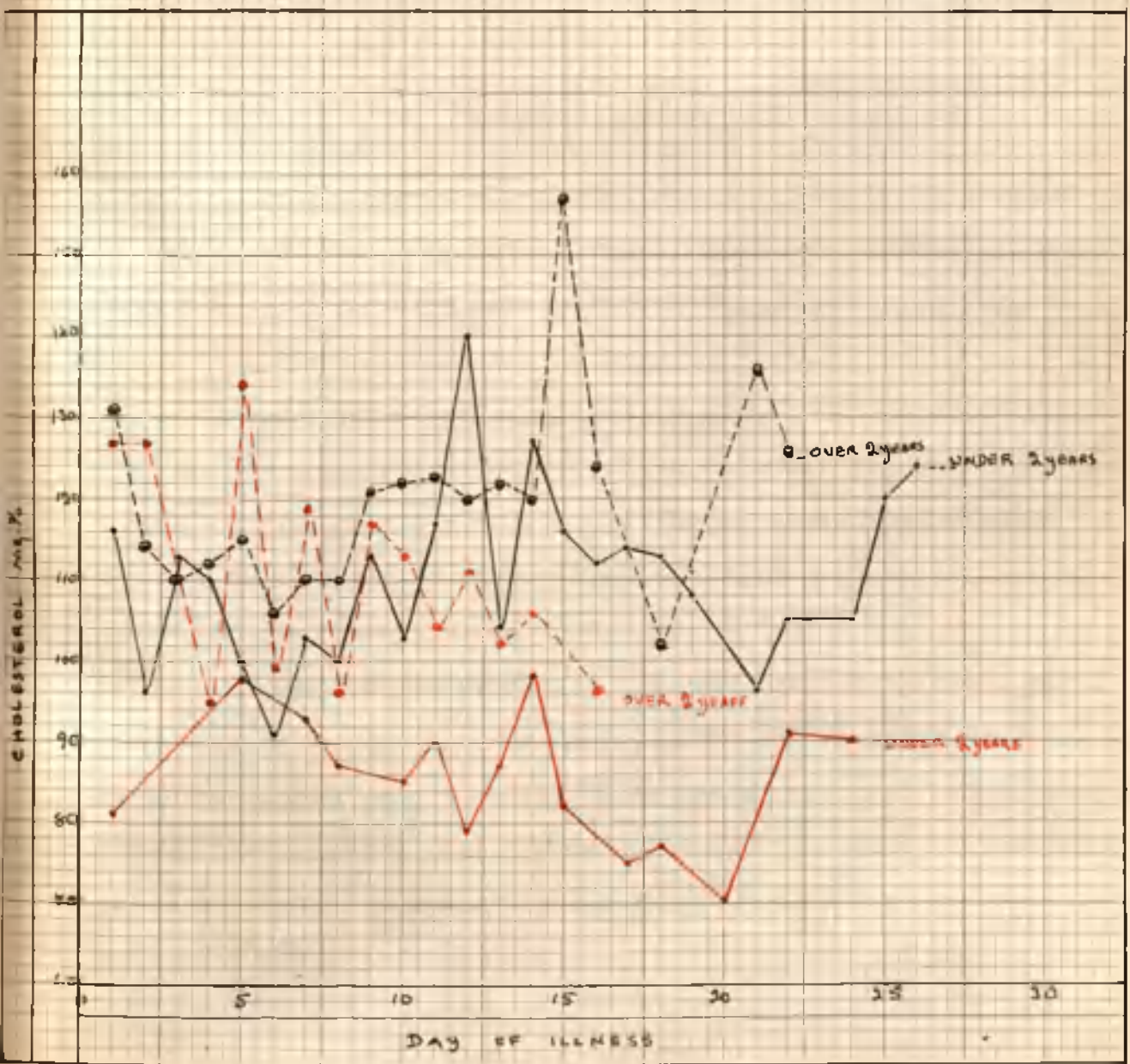
The average figures for children under two years of age are lower throughout the illness than for the older children, and the two curves are practically parallel during both the acute and the convalescent phase. The lowest figures of both groups occur between the second and the eighth day, and the highest figures after the fourteenth day in the older children, and between the twelfth and sixteenth day in children under two years. In individual cases values of less than 100 mg.% were observed in only three children over two years (20%), while in subjects under two years, thirteen (68%) displayed values of less than 100 mg.% at some period of the acute illness, this being a much higher percentage of low values than is found in normal children of this age group (vide page 24).

It is interesting to compare these results with the findings of Stroesser[6], who made estimations on a series of cases of pneumonia between three and thirteen months old, and he noted a fall to less than 100 mg.% in the majority of his subjects. In the present investigation values of less than 100 mg.% were observed in 82% of the children under one year. Nevertheless the lowest value was not found in the youngest child, nor was the highest figure observed in the oldest child. The lowest reading was 81.6 mg.% in a child of thirteen months (No. 7) and the highest was 157.4 mg.% in two children aged two and six years respectively (Nos. 19 and 20).

Chart 1.

COMPOSITE CURVES SHOWING DIMINISHED VALUES IN RECURRENT PNEUMONIA

BLACK LINES = FIRST ATTACK PNEUMONIA.
RED LINES = RECURRENT PNEUMONIA



In all except one patient from each group, the blood cholesterol rose to over 100 mg.% before dismissal from hospital. This increase in the majority of cases followed the crisis or lysis, and the maximum cholesterol values were observed within 10 days from the cessation of fever (vide chart 2). In cases terminating by crisis the average increase was 24.6 mg.% with a maximum of 49.6 mg.% and a minimum of 6 mg.%, while after lysis the average increase was 19.9 mg.% with a maximum of 50.9 mg.% and a minimum of 2.8 mg.%.

Recurrent Pneumonia.

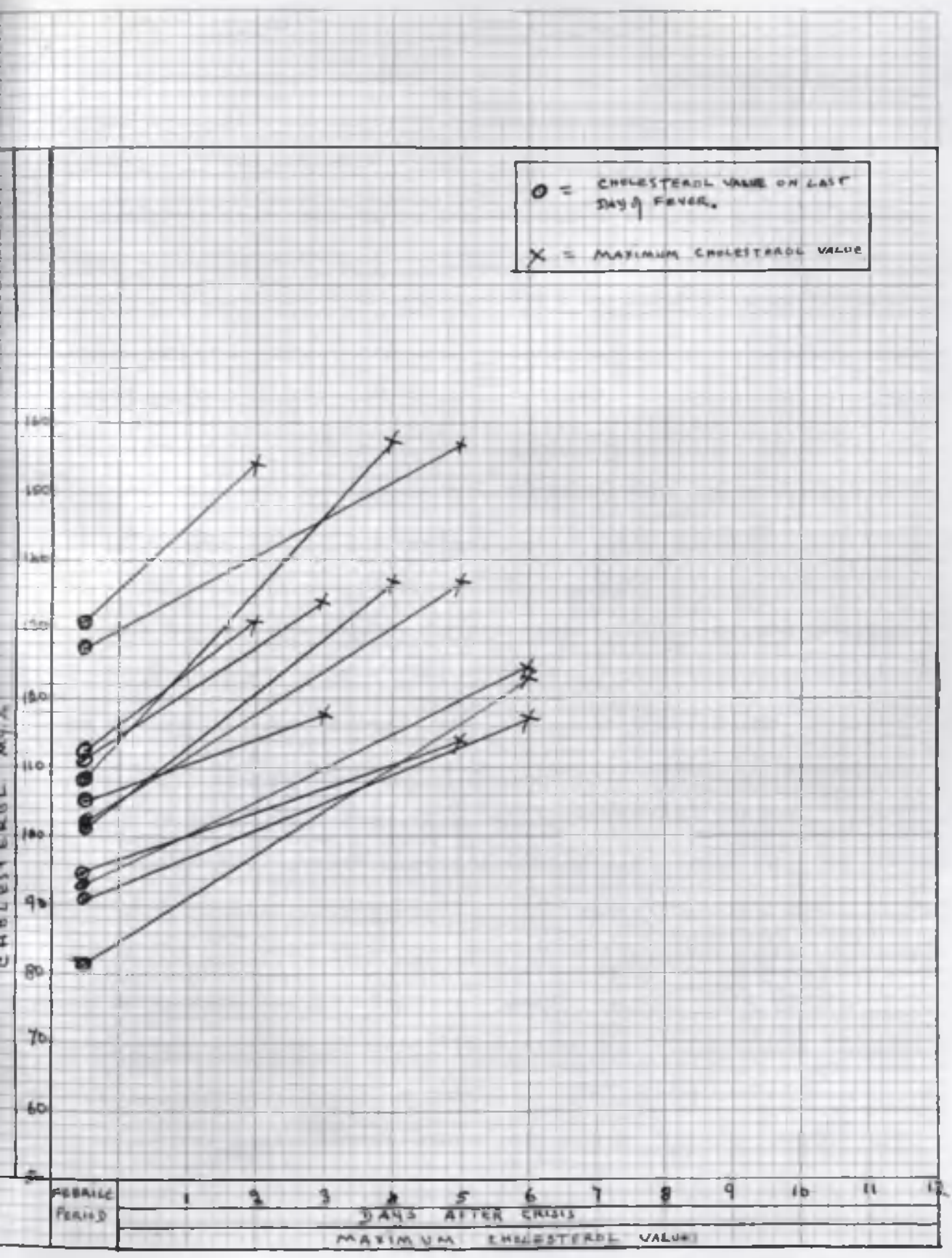
The results of the serial observations in this group are summarised in two composite curves, which are compared in chart 1 with the corresponding curves for children suffering from their first attack of pneumonia.

(a) Children under two years (5 cases).

The average values for children under two years are the lowest of the four curves, for, with one exception, all the figures are below 100 mg.%. The results for the acute and convalescent phase are on the whole equally low.

There are however only five patients in this group. Reviewing them individually they all displayed definite hypocholesterolemia and in two of them the cholesterol remained below 100 mg.% throughout convalescence, and in the other three there was a slow rise to a maximum of 102.3 mg.%, 111.5 mg.% and 124.1 mg.% respectively. None of these children had had more than two attacks of pneumonia.

Chart 2.


O = CHOLESTEROL VALUE ON LAST DAY OF FEVER.
X = MAXIMUM CHOLESTEROL VALUE
CHOLESTEROL MG%
160
100
120
140
130
120
110
100
90
80
70
60
50
FEBRILE PERIOD
1
2
3
4
5
6
7
8
9
10
11
12
DAYS AFTER CRISIS
MAXIMUM CHOLESTEROL VALUES

(b) Children over two years (8 cases).

The composite curves (vide chart 1) for subjects over and under two years of age with recurrent pneumonia are more or less parallel. The values for the older children being decidedly higher, and the absence of any definite rise in the two curves, during the convalescent period is somewhat remarkable. Reviewing the cases individually, however, one receives a slightly different impression, for a slight increase during convalescence was noted in practically every case, though of course the substantial increment seen in many of the subjects with their first attack was not observed in the recurrent cases. In one case (No. 39), for example, the cholesterol rose from 70.0 mg.% to 117.2 mg.%, while in case No. 40 it rose from 87.3 mg.% to 98.9 mg.%. The lowest figure, 53.0 mg.%, in recurrent pneumonia, was noted in a child of seven months (No. 36), while the highest was 134.0 mg.% in a child of eleven years (No. 46). In the patient (No. 46) four years had elapsed since the previous attack of pneumonia, while in the other child only twenty weeks had elapsed. Seven of these children were observed during the second and one during the third attack of pneumonia. The previous pneumoccocal infections had occurred from four months to four years earlier, and children with longer intervals between the attacks tended to have higher values. The patient with the third attack (No. 44) did not, however, display a proportionately lower figure.

The most interesting of the above results are the low values in recurrent pneumonia for which it is difficult to give any explanation.

It has been shown by Grigaut that prolonged acute infections produce considerable diminution of the blood cholesterol, and it would seem feasible that recurrent infections might act on the blood cholesterol in the same manner.

Convalescence.

Convalescence was prolonged in six subjects (Nos. 3,5,10, 12,17 and 31) and the blood cholesterol rose during convalescence in four of them, maximum values of 136.9 mg.% and 154.0 mg.% respectively were noted in two of these cases.

A steady diminution of the blood cholesterol to less than 100 mg.% during an uninterrupted convalescence was not observed in any patient. Nevertheless it is obvious that a marked cholesterol increase was not necessarily associated with a rapid recovery.

Convalescence was not unduly prolonged in any of the children with recurrent pneumonia.

Extent of lung involvement and toxaemia.

(Temperature, respiratory and pulse rates.)

Extent of lung involvement.

Kipp[1] has suggested from his findings in adults that the serum cholesterol varies inversely with the extent of disease in the lung.

In many young children, however, it was impossible to form an accurate estimate of the amount of lung involved, but the post-mortem findings of seven fatal cases give little support to Kipp's suggestion.

In case No. 48 (vide table 8) the blood cholesterol was estimated frequently during the course of the illness and two days before death it was 117.2 mg.%. Extensive broncho-pneumonia was found at the autopsy. In another subject (No. 47) the cholesterol was 111.5 mg.% twenty four hours before death, and an extensive suppurative broncho-pneumonia was seen post-mortem. The lowest value, 52.9 mg.%, was noted in No. 30, twenty four hours before death. The pneumonia was complicated by tetany in this case. In Nos. 49 and 50 the cholesterol was 114.3 and 108.6, seven and three days, respectively, before death. In the remaining two subjects (Nos. 52 and 53) the blood was obtained just after death. In case No. 52 the blood cholesterol was 108.5 mg.% and the post-mortem examination revealed extensive broncho-pneumonic consolidation, chiefly of both lower lobes. No. 53 had a cholesterol value of 93.1 mg.% and an extensive broncho-pneumonic consolidation of both sides was found at the autopsy.

It is obvious, therefore, that although there was extensive involvement in all the cases noted above, the final cholesterol determination was less than 100 mg.% in only two children. One cannot of course draw any general conclusions from such a small series of cases, but it is apparent that there was no definite correlation between the extent of lung involved and the blood cholesterol, in these cases.

Temperature, and respiratory and pulse rates.

Lavergne and Kissel[11] believe that fever produces hypocholesterolemia and they attribute this to (a) hydraemia, (b) shock, from microbes and foreign proteins, (c) general increase of the metabolism and stimulation of the thyroid gland.

Stroesser[12] on the other hand has shown that a high temperature per se is not productive of hypocholesterolemia. He raised temperature artificially in nine children, and estimated the blood cholesterol before, during, and after the fever. Stroesser has also demonstrated that the lowest lipoid values were not found in the patients with the highest temperature, or in those most acutely ill. Man, and Gildea[13] did not observe any correlation between the body temperature and the blood cholesterol. Grigaut[14] frequently found an inverse ratio, and one of his charts which demonstrates this is reproduced on chart 3.

In the present investigation, an inverse ratio (vide chart 3) was observed in the majority of the cases. No parallel was observed between the fall in blood cholesterol and in temperature, in any

Chart 3

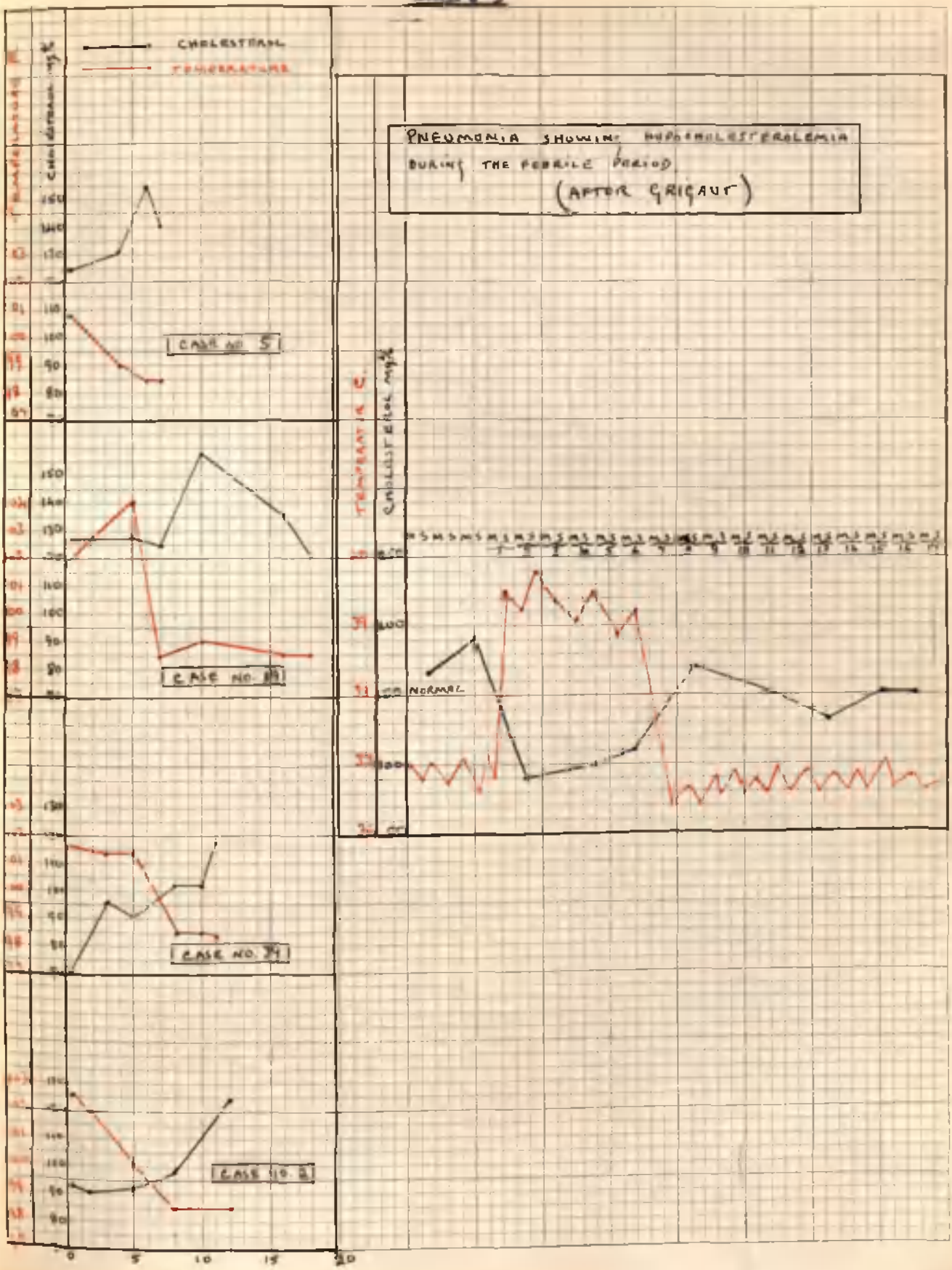
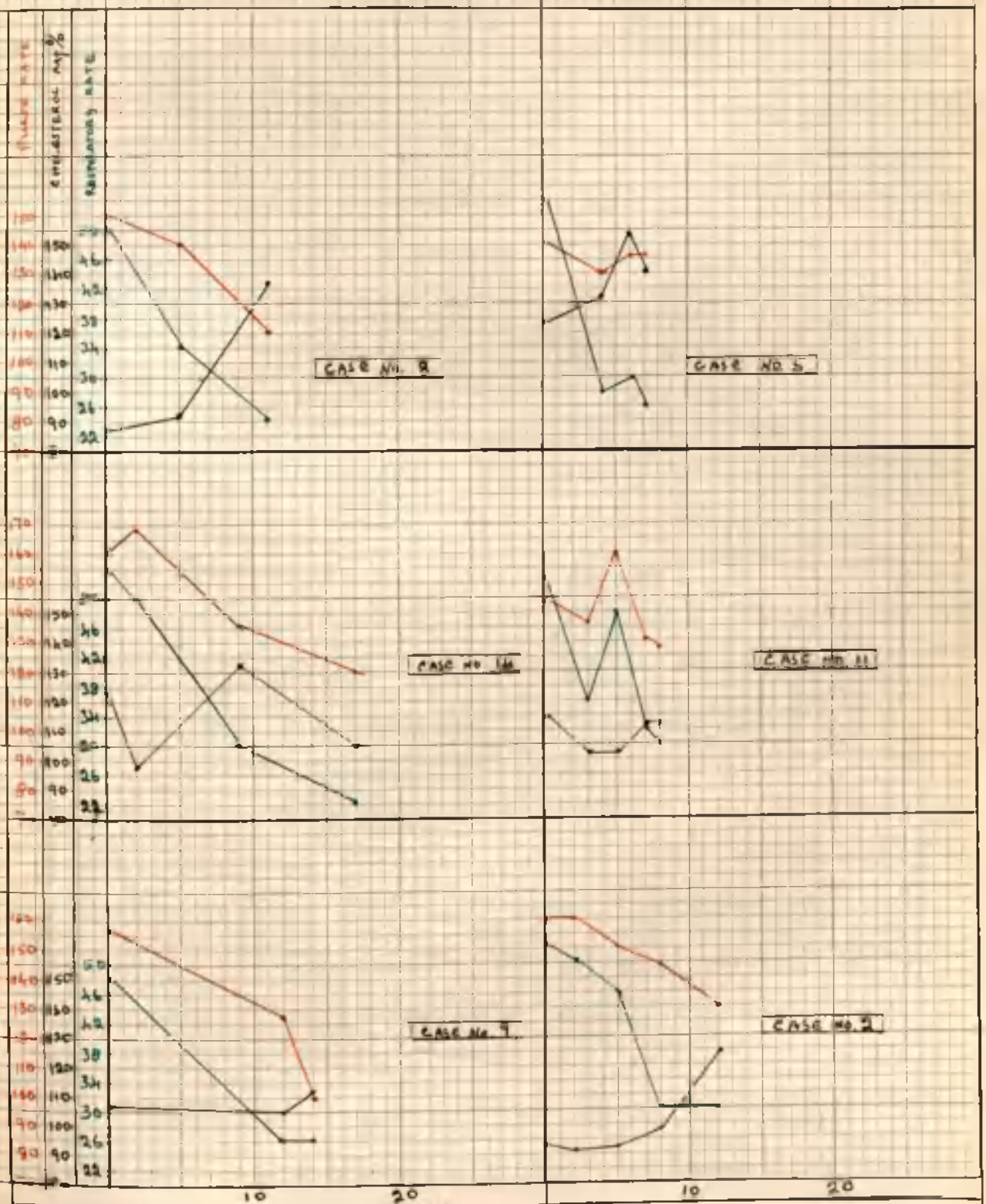

CHOLESTERAL
TEMPERATURE
CASE NO. 5
CASE NO. 89
CASE NO. 34
CASE NO. 2
PNEUMONIA SHOWING HYPERCHOLESTEREMIA
DURING THE FEBRILE PERIOD
(AFTER GRIGAUT)
TEMPERATURE C.
CHOLESTEROL mg%
NORMAL

Chart 4.


PULSE RATE
CHOLESTEROL mg%
RESPIRATORY RATE
CASE No. 9
CASE No. 5
CASE No. 10
CASE No. 11
CASE No. 7
CASE No. 2
10
20
10
20

of the patients. There are however so many other changes coincident with the decline of the fever that one cannot, on the above evidence, assign the elevation of the blood cholesterol to the fall of the temperature alone. Inverse ratios were also observed between the cholesterol and the respiratory and pulse rates (vide chart 4).

It is difficult therefore to come to any conclusion respecting the relationship between the blood cholesterol and the fever, the respiratory and pulse rates.

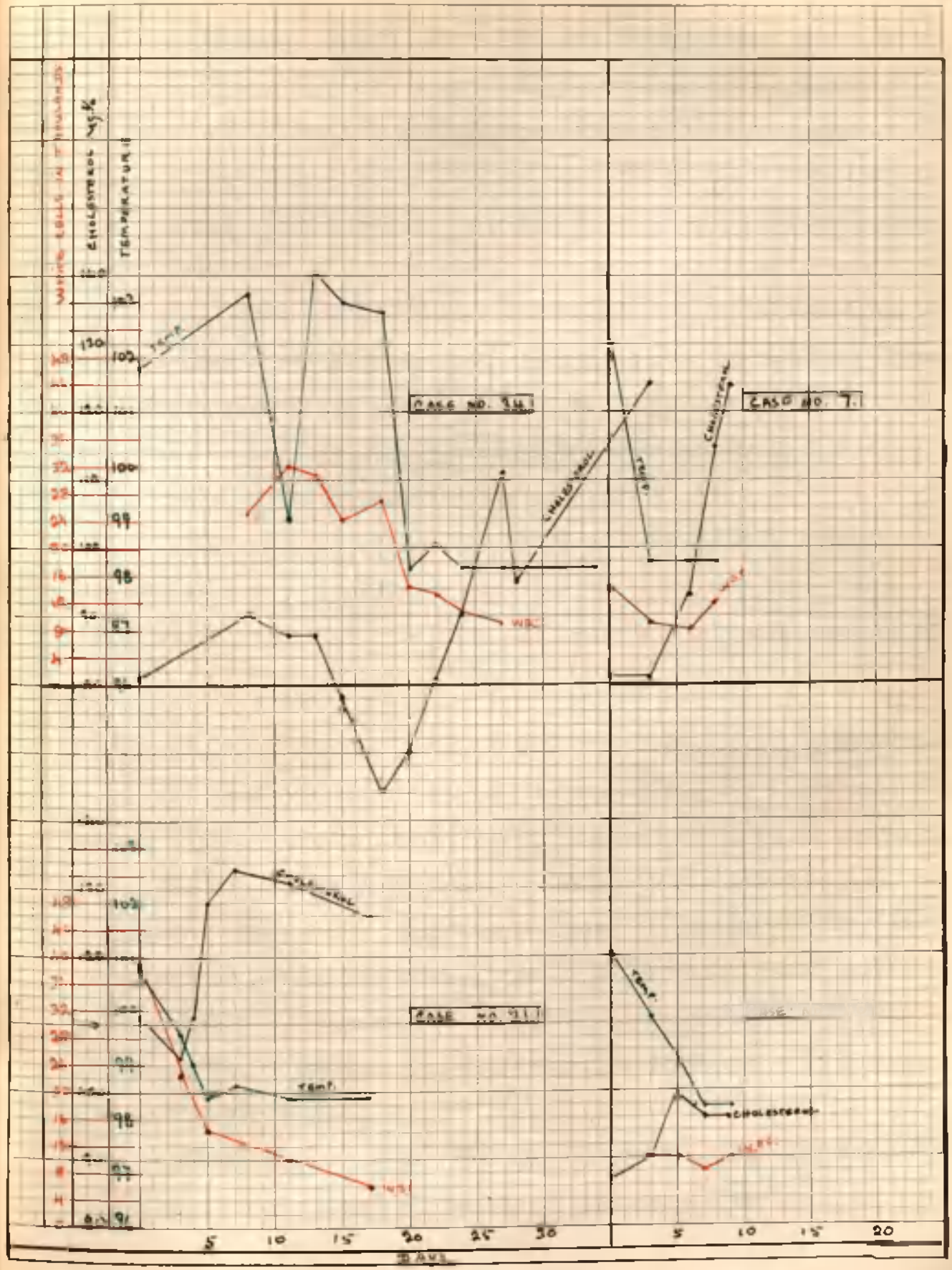
Leucocytosis.

Kipp[1] in his study of pneumonia in adults found an initial leucocytosis of short duration, followed by a diminution of white cells parallel to the fall of the serum cholesterol. The subsequent cholesterol increase concurred with the return of the white blood cells to the circulation. With the exception of six observations, however, the cholesterol and the leucocytes appear to have been estimated on different dates.

Stroesser and McQuarrie[12] working with children, found that the white blood cells usually varied inversely with the lipoid values, where the same specimen of blood was used for both observations. They also noted that a high leucocytosis was not always found in the patients with the lowest cholesterol values. The results of the present investigation are in complete agreement with these findings.

Serial observations were made in fourteen subjects and the cholesterol and leucocytic estimations were made from the same

Chart 5 (vide Table 10).



specimen of blood (Table 10). An inverse ratio was found in practically all the children, a parallel being noted only in the one fatal case. It was also seen that the lowest cholesterol value did not occur in the patient with the highest leucocytosis.

Stroesser[6] has demonstrated that the hypocholesterolemia of acute infections is due almost entirely to a reduction of the ester cholesterol, while Boyd[15] has shown that the white cells contain four times as much free cholesterol as the plasma. These findings therefore do not appear to support the suggestion that the blood cholesterol is dependent on the activity of the white blood cells in mobilizing the cholesterol.

From the findings of the authors quoted above, and the results of the present investigation one concludes that the cholesterol variations are not due to the migration of the leucocytes.

Nutrition.

Man and Gildea[13] state that in adults the blood cholesterol varies with the state of nutrition. They found that it was below normal in emaciated patients and within normal limits in the non-emaciated. They quote experimental work on animals to show that malnutrition lowers the cholesterol. On the other hand Offenkrantz and Karshan[16], working with children, were unable to demonstrate any correlation between the cholesterol and the percentage, over, or under weight.

In the present investigation it was thought that malnutrition might be associated with the diminished cholesterol values

in some of the acutely ill children. Accordingly in table 11 the cholesterol values of a group of children with pneumonia, are compared with the percentages of their expected weights. The complete lack of correlation is obvious from this table. No obvious dehydration was noted in any of these babies, and they were all under one year.

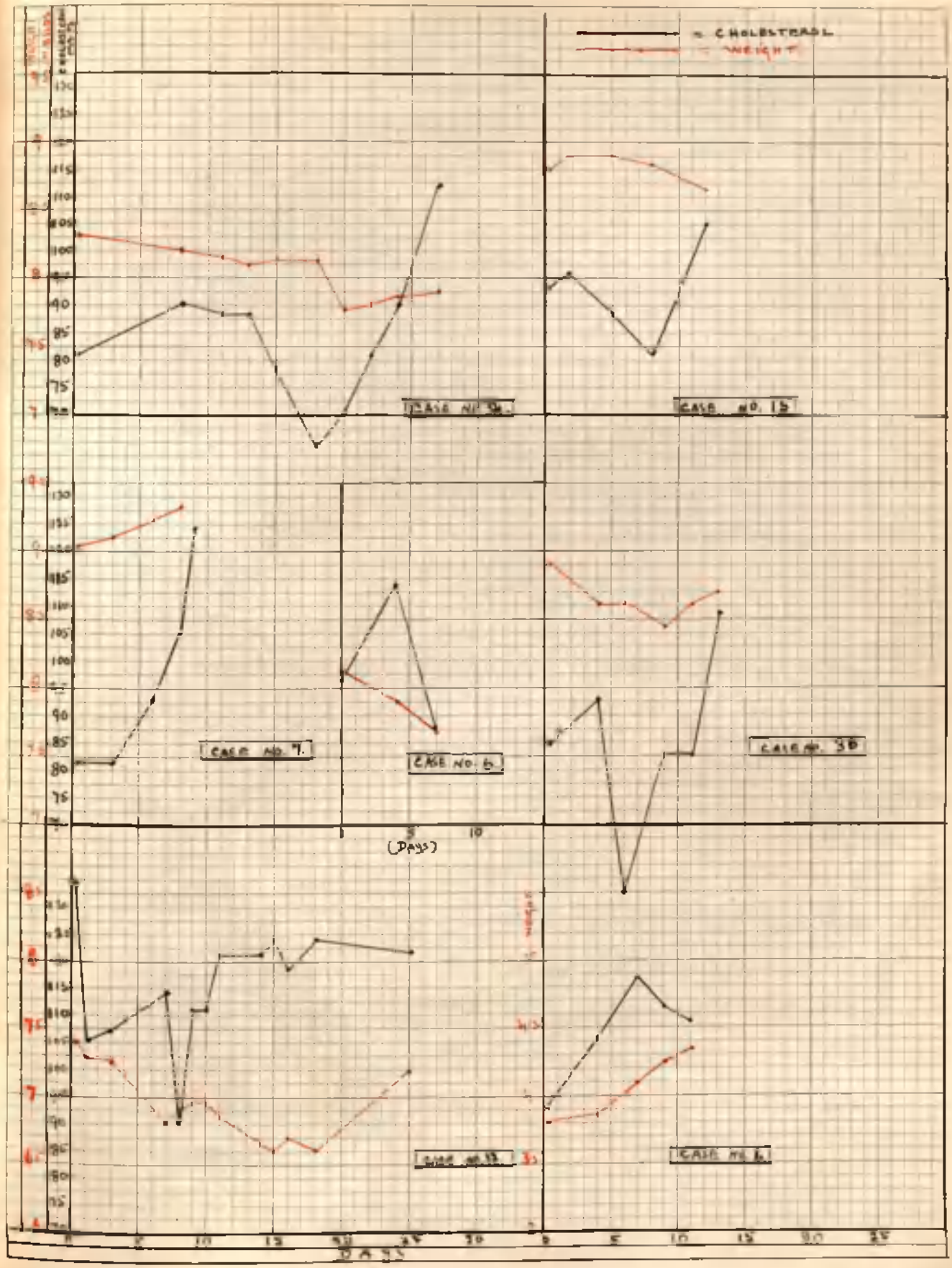
One may conclude therefore that, at least in subjects under one year, there is no correlation between the state of nutrition and the total blood cholesterol.

Cannata[17] found an increase of the cholesterol with age, proportionate with the increase in weight. This suggested the possibility of the cholesterol rise during convalescence being coincident with an increase in weight. In this group, children under one year were studied, as it was more convenient to follow out their variations in weight. Accordingly, the corresponding changes in the weight and the cholesterol values during the course of pneumonia in seven subjects under one year, are shown on chart 6. It is apparent from a study of this chart that the cholesterol increase is not consequent on the gain in weight.

Diet.

It has been suggested[18] that the hypocholesterolemia observed in acute infections is the result of the diminished cholesterol intake, due to the poor general condition of the patient.

Chart 6.


= CHOLESTROL
= WEIGHT
CASE NO 14.
CASE NO. 15
CASE NO. 7.
CASE NO. 6.
CASE NO. 30
(DAYS)
CASE NO. 33
CASE NO. 6.
DAYS

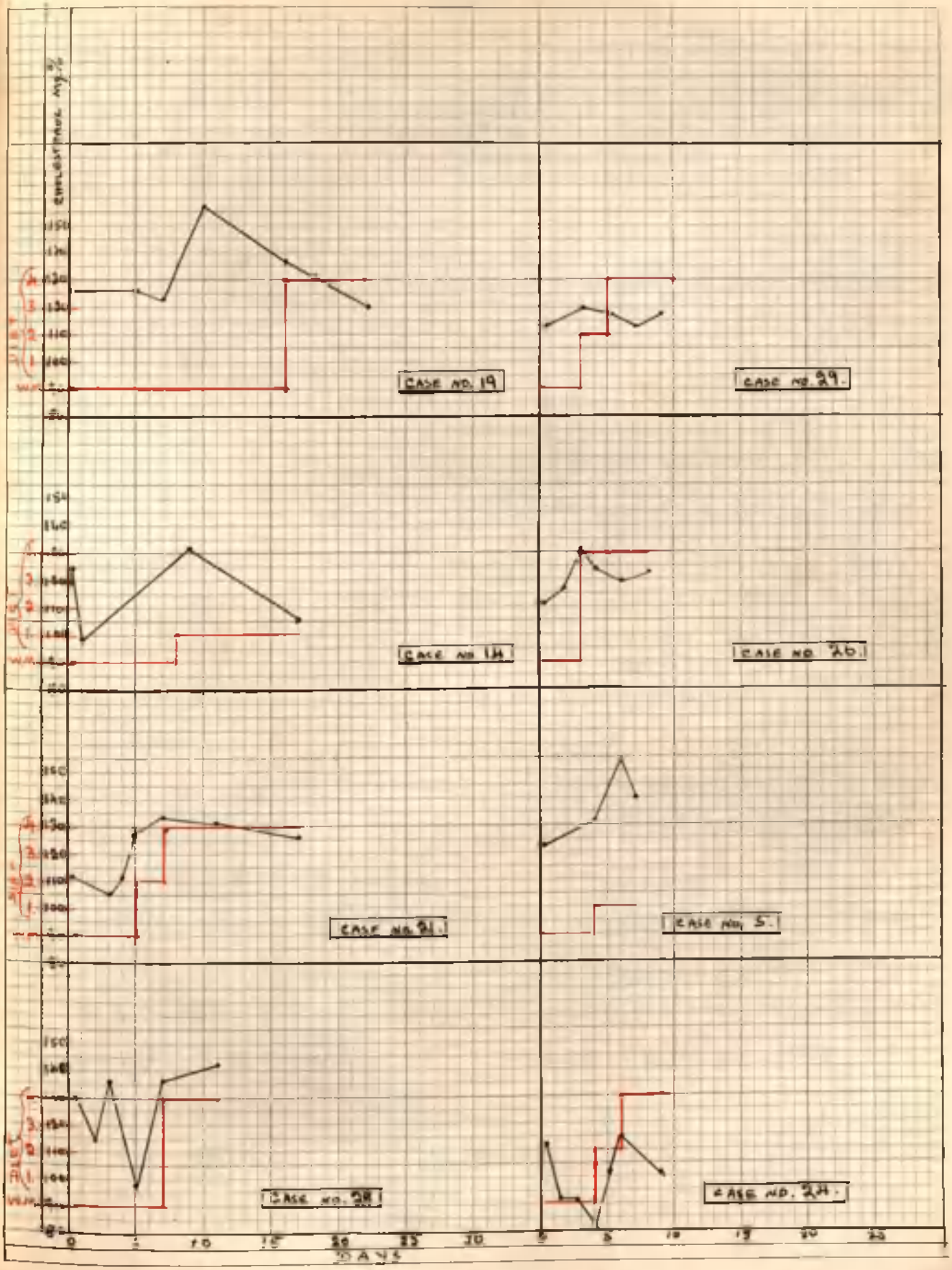
Stroesser and McQuarrie[12] have come to the conclusion that diet has no demonstrable influence on the blood cholesterol. They made their observations on sixteen children with pneumonia, and eleven with upper respiratory infections. They divided them into two groups - one received a special maintenance diet, while the other received only the hospital diet. No difference was found in the cholesterol values of the two groups.

In the present investigation the cholesterol variations and the dietary increase have been charted (vide chart 7) in eight subjects. All the children received whole milk and sugar while the fever lasted. Thereafter they received the ordinary diets for their respective ages.

In four subjects the cholesterol rose on the day the diet was increased. The cholesterol, however, was estimated in the morning, while the dietary increase did not take place until mid-day. In one child the cholesterol rose from 98 mg.% to 131 mg.% the day after the diet was augmented from whole milk to diet I. This involved the addition of oat flour, potatoes and gravy to the diet. In the six cases raised to Diet IV there was no cholesterol increase which could be attributed to the diet.

One may conclude, therefore, that in pneumonia, at least, there is no correlation between the blood cholesterol and the diet.

Chart 7.


CASE NO. 19
CASE NO. 29.
CASE NO. 14
CASE NO. 20.
CASE NO. 21.
CASE NO. 5.
CASE NO. 28
CASE NO. 24.
DAYS

Empyema.

The association of prolonged infection and hypocholesterolemia has been observed by Grigaut[14] and others[4], and the results of the present investigation are in agreement with these findings.

Serial determinations have been made on nine cases of pneumococcal empyema and the results are indicated on table 12.

The figures are equally low in subjects over and under two years of age.

In this small series no difference was found between the cholesterol values of children suffering from their first or second pneumococcal infection.

The cholesterol values of the four fatal cases do not differ markedly from the three that recovered. The blood cholesterol would appear therefore to be of little prognostic value in empyema.

Low values throughout the illness were observed in five subjects. Cases Nos. 59, 60 and 62 had a protracted convalescence and the blood cholesterol was low throughout. The cholesterol remained above 100 mg.% in only one subject (No. 61). In this patient it was 108.5 mg.% on the fifth day and it rose to 124.1 mg.% on the tenth day. The child made a particularly rapid recovery and the illness did not last any longer than many cases of uncomplicated pneumonia.

Prolonged infection would appear therefore to lower the cholesterol more than a short acute illness, and it has already been indicated (vide table 8) that a fatal termination is not necessarily preceded by hypocholesterolemia.

Pneumonia complicated by nephritis.

This group comprises five subjects and serial determinations were made on three of them (vide table 13).

In Nos. 63 and 64 the cholesterol variations differed little from what had been observed in uncomplicated pneumonia. In No. 63 the blood cholesterol was 93.1 mg.% on the day following the crisis; six days later it was 140.3 mg.%, while two weeks after the crisis it was111.5 mg.%. In No. 64 the cholesterol rose from 114.3 mg.% on the seventeenth day of the illness to 134.0 mg.% on the twenty sixth day. Both these cases had slight oedema. Nos. 65 and 66 on whom single determinations were made, did not have any oedema, and the cholesterol values were 124.1 mg.% and 96.0 mg.%, respectively.

The highest value (189.0 mg.%) was noted in No.67. Convalescence was somewhat prolonged in this case and the blood cholesterol oscillated between 150 mg.% and about 130 mg.% for fifteen weeks. In the twenty second week of the illness the cholesterol fell to 98.9 mg.%. This case differed from the others in having had generalised anasarca for three weeks before the initial determination was made, and the urine contained abundant albumen but no blood.

The cholesterol values in pneumonia would appear, there-

fore, to be little affected by the complication of acute nephritis.

Pneumonia complicated by jaundice (2 cases).

Case No. 68 (vide table 14) had moderate jaundice. The blood cholesterol was 171.2% on the fifth day of the illness, and it fell to 154.0 mg.% on the seventh day. On the ninth day the jaundice had practically faded, the general condition was much better and the cholesterol rose slightly to 157.4 mg.%. Case No. 69 was fatal and the blood cholesterol was low (81.6 mg.%).

In the following tables the presence or absence of fever is indicated thus:

-	=	afebrile.
±	=	Temp. not higher than 99°
+	=	Temp. 99° to 101·8°
++	=	Temp. 102° or higher.

TABLE 6.

First attack of pneumonia.

(a) Under two years.

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History.
1	J.B.	10	7	93.1	++	History - Diarrhoea for eight weeks and vomiting for two weeks. Physical signs were indefinite on the 7th day but on the 11th day of the illness there was some fine râle at the left base.
			10	105.7	+	
			13	117.2	-	
			15	111.5	-	
			17	108.5	-	
2	M.W.	32	5	93.1	++	History - Cough, vomiting and dyspnoea for 5 days. On the 5th day there was much râle scattered over both sides of the chest and radiographic examination revealed consolidation of both bases. The child was acutely ill. On the 11th day the general condition was much better and on the 15th day the child was very well.
			6	90.2	++	
			8	93.1	+	
			11	98.9	-	
			15	124.1	-	
3	A.G.	23	1	98.9	+	History - Cough for two weeks; dyspnoea for one day. Child acutely ill from the 1st to the 5th day, tubularity and râle on right side. On the 8th day the child's general condition had improved a little, but convalescence was protracted and the child was readmitted to hospital frequently during the succeeding 6 months.
			3	98.9	+	
			5	105.7	++	
			7	102.3	-	
			8	111.5	+	
4	M.M.	60	8	117.2	+	History - Vomiting, cough and dyspnoea for 7 days. On the 8th day the child was moderately ill and
			11	131.0	-	

TABLE 6 (Contd.)

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History.
						there was much wheezing over all areas. On the 11th day the child's condition was much improved.
5	I.R.	78	5	124.1	+	History - Dyspnoea for 5 days. On the 5th day
			9	131.0	+	there was dulness and tubularity on the left side.
			11	154.0	-	There was also some albuminuria. On the 11th day
			12	140.0	-	the child's condition was much better and the urine was clear. Convalescence was however somewhat slow.
6	G.M.	78	16	96.0	++	History - Fever for 16 days. On the 16th day the
			19	114.2	+	child was acutely ill and radiographic examination
			21	87.3	-	revealed consolidation of the left lung. On the 21st day the child's general condition was much better but on the 22nd he was transferred to fever hospital with whooping cough.
7	D.H.	78	6	81.6	++	History - Cough for 6 days. on 6th day child was moder-
			8	81.6	+	ately ill, and there was tubularity and dulness on
			11	93.1	=	the left side. On the 8th day patient's condition
			13	105.7	-	was better. On the 14th day the child was very
			14	124.1	-	well, though the note was still impaired on the left side, but there were no adventitiae.

TABLE 6 (Contd.)

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History
8	E.S.	78	2	87.3	+	History - Cough for 6 months. dyspnoea for 2 days. On the 2nd day, acutely ill and dyspnoeic, and tubularity and fine râles left side. Radiographic examination revealed consolidation of both lungs. Crisis occurred on the 5th day and on the 14th day child was very well and the chest was clear.
			8	93.1	-	
			14	136.9	-	
9	C.B.	91	4	108.6	++	History - Fever for 4 days. On 4th day child moderately ill and impaired note and râles left side. On the 18th day child's condition was much improved.
			16	105.7	-	
			18	111.5	-	
10	M.McA.	15	13	90.2	-	History - Fever and dyspnoea began 13 days ago. Radiographic examination revealed consolidation of both lungs. On the 13th day the child's condition was improving, the temperature having fallen by lysis between the 8th and the 10th day. Convalescence was however prolonged.
			19	102.3	-	
			21	96.0	-	
			22	105.7	-	
11	J.G.	40	4	114.3	++	History - Fever for 4 days. Crisis on the 4th day. Tubularity and râles audible on 3rd day. There was a return of fever for one day only on the 8th day, though the general condition seemed good. On the 11th day the child was very well and the chest was practically clear.
			6	102.3	-	
			8	102.3	++	
			10	111.5	-	
			11	111.5	-	

TABLE 6 (Contd.)

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History
12	M.McD.	45	4	124.1	++	History - Cough and fever for 4 days. On the 4th day child dyspnoeic and ill, and there were râles on both sides, radiographic examination revealed consolidation of both lungs. On the 18th day general condition was much improved but there was still considerable wheezing. A somewhat protracted convalescence followed.
			5	98.9	++	
			7	117.2	+	
			18	105.7	-	
13	J.G.	44	1	134.0	++	History - Cough and rapid breathing for one day. On examination there was slight nuchal rigidity and coarse râle over left side of chest. The urine contained albumin, and both ears were discharging. On the 10th day he was still acutely ill and somewhat cyanosed. On the 21st day radiographic examination revealed consolidation of right lung, but the general condition was much improved. On the 26th day the child was very well.
			2	105.7	++	
			3	108.7	+	
			7	114.3	+	
			8	90.1	+	
			9	111.5	++	
			10	111.5	++	
			11	120.7	++	
			14	120.7	+	
			15	124.1	+	
			16	117.2	+	
			17	120.1	-	
			18	124.1	-	
			25	120.7	-	
			16	124.1	-	

TABLE 6 (Contd.)

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History
14	E.M.	65	8	124.1	++	History - Cough, fever and dyspnoea for 8 days. On the 8th day was acutely ill and there was dulness and fine râle right side. Radiographic examination showed consolidation of both lungs. On the 18th day the general condition was greatly improved, on the 24th day it was very good and the chest was clear
			9	98.9	++	
			16	131.0	-	
			24	105.7	-	
15	T.O'R.	47	4	93.1	+	History - Dyspnoea and cough for 4 days. Rhonchi over all chest areas on the 4th day. On the 11th day child was still ill and there was some dulness, râles and rhonchi in chest. On the 15th day the child's condition was considerably improved.
			5	96.0	++	
			8	87.3	+	
			11	81.6	+	
			15	105.7	-	
16	A.F.	43	3	134.1	±	History: Dyspnoea for 3 days. Acidosis ++, unconscious. 2 days later acutely ill with high fever and had crisis on the 7th day. On the 10th day she was very well.
			10	108.6	-	
17	A.S.	52	11	114.3	+	History: Cough for 11 days. Râles over all areas on the 9th day and consolidation of both lungs shown by X-ray examination, but the general condition was beginning to improve and the chest was clearing on the 11th day.
18	W.C.	26	5	81.6	+	History: Slight cyanosis for 5 days, much wheezing and cough and child moderately ill, but condition complicated by tetany.

SUMMARY of TABLE 6a (vide Chart 1.)

Day of Illness.

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1							93.1			105.7			117.2		111.5		108.5								
2					93.1	90.2		93.1			98.9				124.1										
3	98.9		98.9		105.7		102.3	111.5																	
4								117.2			131.0														
5					124.1				131.0		154.0	140													
6																96.0			114.2						
7						81.6		81.6			93.1		105.7	124.1											
8		87.3						93.1						136.9											
9				108.6												105.7		111.5							
10													90.2						102.3		96.0	105.7			
11				114.3		102.3		102.3		111.5	111.5														
12				124.1	98.9													105.7							
13	134.0	105.7	108.5				114.3	90.1	111.5	111.5	120.7			120.7	124.1	117.2	120.1	124.1							120.7
14								124.1	98.9							131.0								105.7	
15				93.1	98.0			87.3		81.6					105.7										
16			134.0							108.6															
17											114.3														
18					81.6																				
	116.4	96.5	113.8	110.0	100.0	91.3	103.2	100.0	113.8	103.8	117.6	140	104.4	127.2	116.8	112.5	114.3	113.7	108.8		96.0	105.7		105.7	120.

Average Cholesterol mg.%.

TABLE 6.

First attack of pneumonia.

(b) Over two years.

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
19	M.L.	2	5	127.6	+	Listlessness for two weeks. On the 5th day tonsils enlarged and red, and left side of chest dull. Radiographic examination showed consolidation left lung. Crisis occurred on the 10th day. There was a recurrence of fever on the 14th day, but she remained afebrile and improved steadily after the 16th day.
			10	127.6	++	
			12	124.1	-	
			15	157.4	±	
			21	136.9	-	
			23	131.0	-	
			28	120.7	-	
			34	111.5	-	
20	P.G.	6	3	108.5	++	Three days ago, headache, rigors and delirium. On the 3rd day child was acutely ill, R.M. diminished at left base and rhonchi audible over all areas. On the 8th day the general condition had improved considerably and the chest was clear and on the 10th day he seemed very well.
			4	111.5	+	
			5	126.5	+	
			6	108.5	+	
			8	114.3	-	
			9	131.0	-	
			10	157.4	-	
21	R.McC.	7	6	111.5	+	Drowsy and dyspnoeic 6 days ago. On the 6th day child was moderately ill, and there was some râle and tubularity and friction on the left side of the chest. Temperature fell by lysis between the 8th and the 9th day. On the 26th day the child was well and the chest was clear.
			8	105.7	+	
			9	111.5	±	
			10	128.0	-	
			12	133.9	-	
			16	131.0	-	
			22	126.5	-	

TABLE 6 (Contd.)

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
22	S.M.	5	7	102.3	++	Cough for 7 days. On the 7th day child cyanosed and acutely ill. Scattered rhonchi in chest, dulness and tubularity at left base. Crisis on the 8th day. On the 12th day general condition much better, still some dulness and râles left base. On the 14th day general condition good and no adventitiae in chest.
			10	117.2	-	
			12	136.9	-	
			14	143.0	-	
23	D.McS.	4	8	111.5	++	Eight days ago drowsy and headache. On the 8th day child acutely ill. Physical signs in chest indefinite but radiographic examination revealed consolidation right chest.' On the 16th day general condition very good, no definite signs in chest.
			11	127.5	+	
			16	124.1	-	
24	A.G.	11	5	111.5	+	Listless for 17 days, pain in back 5 days ago. On the 5th day child moderately ill, and R.M. tubular right side of chest and at left base. On the 11th day general condition was improving steadily, and on the 14th day he seemed very well and there were no definite physical signs in chest.
			6	93.1	+	
			7	93.1	-	
			8	81.6	-	
			10	102.3	-	
			11	114.3	-	
			12	108.5	-	
			14	102.3	-	

TABLE 6 (Contd.)

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
25	D.McD.	6	9	127.6	±	Fever for 9 days. Radiographic examination showed consolidation right lower lobe. Crisis occurred on the 9th day. On the 16th day the general condition was good and the chest was clear.
			11	131.0	-	
			13	131.0	-	
			16	134.0	-	
26	J.H.	4	7	111.5	±	Cough for 7 days. On the 5th day there was dulness and almost absent R.M. Radiographic examination revealed consolidation right base. On the 14th day the child was very well and there were no physical signs in the chest.
			8	117.2	-	
			9	131.0	-	
			10	124.1	-	
			12	120.6	-	
			13	126.5	-	
			14	124.1	-	
27	M.C.	3	3	96.0	+	Recurrent bronchitis. Dyspnoea for 3 days. Some tubularity and slight dulness of left side of chest. Radiographic examination shows bronchiectasis L.base and consolidation right middle lobe. Radiographic examination on the 16th day showed the right lung to be clearing, and on this date the general condition was improving. Fever recurred from time to time in the ensuing 2 months, convalescence being considerably prolonged.
			6	111.5	+	
			8	111.5	+	
			10	111.5	-	
			13	136.9	-	
			16	108.5	-	
			18	102.3	+	

TABLE 6 (Contd.)

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
28	R.McC.	7	1	131.0	++	Fever and praecordial pain for 10 hours. Child acutely ill, dulness and rhonchi left apex. Radiographic examination confirmed the clinical findings. Temperature fell by lysis and on the 11th day the general condition was good, though resolution was somewhat slow in this case.
			2	114.3	+	
			3	136.9	+	
			5	98.9	-	
			7	136.9	-	
			11	143.9	-	
29	A.D.	6	5	114.3	++	Pain in chest 5 days ago. On 5th day child moderately ill. Impaired note and rale over right side of chest. Radiographic examination revealed consolidation right chest. On the 14th day the child's general condition was good and there were no physical signs in the chest.
			7	120.6	-	
			9	117.2	-	
			11	114.3	-	
			13	117.2	-	
			14	111.5	-	
30	B.B.	8	3	98.9	+	Cough and dyspnoea for 2 days. Child acutely ill and impaired note right apex. Radiographic examination revealed consolidation of right lung. On the 7th day the general condition had improved considerably and on the 12th day child was well and there were no physical signs in the chest.
			4	111.5	+	
			7	96.0	-	
			9	111.5	-	
			10	98.9	-	
			11	98.9	-	
			12	98.9	-	
31	J.McB.	2	8	131.0	++	Ill for 8 days. Left side of chest dull and tubular R.M. present. Child acutely ill. Temperature settled by lysis between 25th and 28th day. Child had a prolonged convalescence.
			13	102.3	++	

TABLE 6 (Contd.)

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
32	W.K.	3	8	111.5	+	Cough for 8 days. Child acutely ill and dyspnoeic. Much râle over both sides of chest and dull over left upper lobe. On the 10th day general condition much better though still a few râles audible.
			10	131.0	±	
33	G.McF.	9	10	131.0	-	Had impaired note and tubularity at left base. Temperature fell by crisis on the 7th day and on the 11th day child appeared to be making a good recovery.
			11	134.0	-	

SUMMARY of TABLE 6b (Vide Chart 1).

Day of Illness.

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
19					127.6					127.6		124.1			157.4						136.9	
20			108.5	111.5	126.5	108.5		114.3	131.0	157.4												
21						111.5		105.7	111.5	128.0		133.9				131.0						126.5
22							102.3			117.2		136.9		143.0								
23								111.5			127.5					124.1						
24					111.5	93.1	93.1	81.6		102.3	114.3	108.5		102.3								
25									127.6		131.0		131.0			134.0						
26							111.5	117.2	131.0	124.1		120.6	126.5	124.1								
27			96.0			111.5		111.5		111.5			136.9			108.5		102.3				
28	131.0	114.3	136.9		98.9		136.9				143.9											
29					114.3		120.6		117.2		114.3		117.2	111.5								
30			98.9	111.5			96.0		111.5	98.9	98.9	98.9										
31								131.0					102.3									
32								111.5		131.0												
33										131.0	134.0											
	131.0	114.3	110.0	111.5	115.7	106.1	110.0	110.5	121.6	122.9	123.4	120.5	122.8	120.2	157.4	124.4		102.3			136.9	126.5

Average Cholesterol mg.%

TABLE 7.

Recurrent pneumonia.

(a) Children under two years.

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%.	Fever	History
34	B.B.	10	1	81.6	++	Pneumonia 4 months ago. Remained fairly well until had two convulsions some hours before admission. Moderately ill child, with some râles at the base of both lungs, but no definite dulness. Radiographic examination revealed fluid and consolidation right side. On the 13th day child was acutely ill and chest signs were still present. On the 18th day child was still acutely ill and X-ray examination showed fluid and consolidation right lung. Crisis occurred on the 19th day. Thereafter she improved steadily and was in good general condition on the 28th and 38th days.
			8	90.1	++	
			11	87.3	+	
			13	87.3	++	
			15	78.7	++	
			18	64.3	++	
			20	70.0	-	
			22	81.6	-	
			24	90.1	-	
			27	111.5	-	
			28	93.1	-	
			38	124.1	-	
35	S.T.	28	11	93.1	-	Pneumonia 8 weeks ago. Cough for 11 days. On the 11th day child moderately ill, and some râles over both sides of chest. Fever ceased on the 5th day. Radiographic examination showed consolidation of both lungs. On the 22nd day her general condition was good and the chest was clear.
			15	93.1	-	
			18	90.2	-	
			22	102.3	-	

TABLE 7 (Contd.)

Case No.	Name	Age in weeks	Day of illness	Cholesterol mg.%	Fever	History
36	J.M.	30	8	85.0	++	Pneumonia 20 weeks ago, cough for 8 days. On the
			10	93.1	+	8th day impaired note R.side and radiographic examina-
			12	53.0	+	tion showed consolidation right side. On the 15th
			15	75.9	++	day child was still acutely ill, dulness on the right
			17	75.9	-	side persisted. On the 19th day child was very well.
			19	111.5	-	
37	A.K.	78	8	81.6	++	Pneumonia 35 weeks ago. Cough for 8 days. Moderate-
			10	78.7	+	ly ill, R.M. harsh and some râles right side. On the
			12	87.3	-	11th day child seemed much better but fever returned
			14	98.9	-	on the 26th day and lasted 10 days. Child was dis- charged 4 weeks later.
38	T.M.	36	5	98.9	++	Pneumonia 6 weeks ago. Made good recovery after
			7	93.0	+	2 weeks and remained well until 5 days ago. X-ray
			8	93.1	+	examination on the 5th day showed consolidation
			12	89.9	-	right lung. Convalescence was somewhat slow, but child was very well 2 months later.

SUMMARY of TABLE 7a (Vide Chart 1).

Day of Illness.

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
34	81.6							90.1			87.3		87.3		78.7			64.3		70.0		81.6		90.1
35											93.1				93.1			90.2				102.3		
36								85.0		93.1		53.0			75.9		75.9		111.5					
37								81.6		78.7		87.3		98.9										
38					98.9		93.1	93.1				98.9												
	81.6				98.9		93.1	87.4		85.9	90.2	79.7	87.3	98.9	82.5		75.9	77.2	111.5	70.0		91.9		90.1

Average Cholesterol mg.%.

TABLE 7.

Recurrent pneumonia.

(b) Children over two years.

Case No.	Name	Age in years	Day of illness	Cholesterol mg.%	Fever	History
39	D.L.	2	4	70.0	+	Pneumonia 2 years ago. Eyes swollen for 4 days.
			6	96.0	+	Child not acutely ill, no definite oedema. Urine
			8	90.1	+	clear. Dulness and high pitched R.M. on left side.
			11	102.3	-	Radiographic examination shows consolidation left
			13	102.3	-	lung and early consolidation right lung. Crisis
			14	117.2	-	occurred on the 10th day. On the 14th day child was very well.
40	S.R.	2	8	87.3	+	Pneumonia 10 months ago. Cough and vomiting for a
			10	90.1	+	week. Child not acutely ill. Dulness and R.M.
			12	98.9	±	tubular on left side of chest. On the 14th day
			14	96.0	-	the general condition was good but dulness and tubu-
			16	96.0	-	lar in left side of chest persisted.
41	M.R.	3	4	93.1	±	Pneumonia 6 months ago. Cough and rapid breathing
			7	105.7	-	for 4 days. Child moderately ill and moist râles
			33	131.0	-	all over both sides of chest. Condition better on the 7th day, râles still audible. On the 33rd day was very well, chest clear, readmitted to hospital for tonsillectomy.
42	M.K.	4	8	98.9	-	Pneumonia 3 years ago. Cough for 8 days. Dulness
			9	114.8	-	and râles right base. On the 14th day child was very well and chest almost clear

TABLE 7 (Contd.)

Case No.	Name	Age in Years	Day of Illness	Cholesterol mg.%	Fever	History
43	M.B.	5	6	102.3	+	Pneumonia 4½ years ago. Fever and dyspnoea for 6 days. Râles at bases. On the 10th day the child was well and the chest practically clear.
			10	136.9	-	
44	C.T.	6	9	124.1	-	Pneumonia 4 years ago and again 3 years ago. Heavy breathing and fever noticed 9 days ago. X-ray examination showed consolidation right upper lobe, chronic consolidation left base. On the 12th day child was very well and there were no physical signs in the chest.
			10	114.3	-	
			12	124.1	-	
45	P.M.	7	8	111.5	+	Pneumonia 3 years ago. Ill for 8 days. On the 8th day was acutely ill, had tubular R.M., and much râle. On the 11th day child much better and on the 12th was dismissed to the country.
			9	114.3	+	
			11	105.7	-	
46	M.E.	11	1	127.6	++	Pneumonia 4 years ago. Acutely ill and delirious. Dulness all over right side of chest and much fine râle. Radiographic examination showed consolidation right lung. Crisis on the 6th day. On the 7th day was much better, much rhonchus and frequent loose cough.
			2	127.6	++	
			4	124.1	++	
			5	134.0	++	
			7	134.0	-	

SUMMARY OF TABLE 7b. (Vide Chart 1.)

Day of Illness.

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
39				70.0		96.0		90.1			102.3		102.3	117.2		
40								87.3		90.1		98.9		96.0		96.0
41				93.1			105.7									
42								98.9	114.8							
43						102.3				136.9						
44									124.1	114.3		124.1				
45								111.5	114.3		105.7					
46	127.6	127.6		124.1	134.0		134.0									
	127.6	127.6		95.7	134.0	99.1	119.8	96.9	117.7	113.7	104.0	111.5	102.3	108.6		96.0

Average Cholesterol mg.%

TABLE 8.

Fatal cases uncomplicated by empyema.

Case No.	Name	Age in weeks	Date	Cholesterol mg.%	Temperature.	
47	P.C.	21	15.1.36	93.1	102.4	History - Cough for one week.
			16.1.36	93.1	102.0	Exam.- Typical mongol. Dyspnoea and abundant
			17.1.36	111.5	103.0	rhonchi and râles all over chest.
			18.1.36	Died	-	Post-mortem report - "Extensive suppurative broncho-pneumonia."
48	A.T.	19	2.1.36	98.9	101.6	History - Vomiting for 4 weeks, cough for 5
			3.1.36	105.7	99.6	days.
			4.1.36	108.5	99.8	Exam. - Acutely ill, dulness and moist râles on left side.
			7.1.36	98.9	102.0	Post-mortem report - "Fine type of broncho-
			8.1.36	111.5	103.4	pneumonia. Pneumococci and streptococci ob-
			10.1.36	124.1	102.0	tained from bronchial exudate."
			11.1.36	120.7	100.8	
			14.1.36	117.2	100.8	
			16.1.36	Died	-	
49	H.C.	21	12.4.37	114.3	102.4	History - Vomiting, cough and fever began
			19.4.37	Died	-	12 days ago. Marked oedema of legs on 12.4.37.
						Post-mortem report - "Broncho-pneumonia, acute otitis media, toxaemia, extensive consolidation both lobes."

TABLE 8 (Contd.)

Case No.	Name	Age in weeks	Date	Cholesterol mg.%	Temperature.	
50	M.M.	26	19.12.35 22.12.35	108.6 Died	104.4 -	History - Fever and dyspnoea for 1 week. Exam.- Acutely ill, and abundant râles all over right side. Diagnosed - "broncho-pneumonia". No P.M.
51	C.C.	30	19.3.36 20.3.36	52.9 Died	105.0 -	History - Cough for 2 months. Convulsions began 4 days ago. Fine râles at right base. Post-mortem report - "Diffuse broncho-pneumonia in both lungs."

TABLE 9.

Estimations obtained on blood obtained immediately after death.

Case No.	Name	Age in weeks	Date	Cholesterol mg.%	Post-mortem reports
52	P.G.	2	6.4.36	108.5	Broncho-pneumonic consolidation, chiefly both lower lobes.
53	M.B.	9	29.12.35	93.1	Extensive broncho-pneumonia consolidation both sides.

TABLE 10.
(Vide chart 5)

Case No.	Day of illness	Cholesterol mg.%	W.B.C.	Case No.	Day of illness	Cholesterol mg.%	W.B.C.
36	8	85.0	14,000	30	4	111.5	15,000
	10	93.1	10,000		7	96.0	20,000
	12	53.0	17,000		9	111.5	25,000
	15	75.9	14,000		11	98.9	21,200
	17	75.9	10,000				
	19	111.5	-	59	4	-	26,000
					6	81.6	-
1	7	93.1	10,700		8	93.1	24,200
	10	105.7	28,800		10	96.0	18,600
	13	117.2	28,000		12	87.3	21,600
	15	111.5	15,000		15	87.3	19,000
	17	108.5	8,600		17	93.1	19,800
					20	81.6	12,000
40	8	87.3	-		22	75.9	33,000
	10	90.1	10,000		24	93.1	20,000
	12	98.9	10,300				
	14	96.0	8,400	37	8	81.6	13,800
	16	96.0	10,800		10	78.7	-
					12	87.3	13,200
7	6	81.6	14,000		14	98.9	11,400
	8	81.6	9,200				
	11	93.1	8,800				
	13	105.7	12,800				

TABLE 10 (Contd.)

Case No.	Day of illness	Cholesterol mg.%	W.B.C.	Case No.	Day of illness	Cholesterol mg.%	W.B.C.
62	4	98.9	18,200	21	6	111.5	39,600
	7	105.7	40,000		8	105.7	22,600
	9	111.5	34,200		9	111.5	-
	11	70.0	40,000		10	128.0	14,500
	12	64.3	33,000		12	133.9	-
	14	87.3	28,000		16	131.0	10,200
	16	75.9	32,000		22	126.5	6,500
	18	87.3	17,000				
	20	85.0	12,000	39	4	70.0	18,000
	23	87.3	21,800		6	96.0	21,600
	26	-	20,600		8	90.1	19,000
	28	98.9	26,000		11	102.3	10,000
	30	75.9	32,000		13	102.3	7,000
	32	70.0	-		14	117.2	9,000
34	1	81.6	-	29	5	114.3	20,000
	8	90.1	25,000		7	120.6	13,000
	11	87.3	32,000		9	117.2	8,400
	13	87.3	31,000		11	114.3	7,000
	15	78.7	24,000		13	117.2	7,400
	18	64.3	27,000		14	111.5	-
	20	70.0	14,600				
	22	81.6	13,200	56	6	75.9	31,000
	24	90.1	10,000		7	70.0	23,000
	27	111.5	-		10	87.3	33,600
	28	93.1	-				
	38	124.1	-				

TABLE 10 (Contd.)

Case No.	Day of illness	Cholesterol mg.%	W.B.C.
19	5	127.6	43,700
	10	127.6	23,000
	12	124.1	16,800
	15	157.4	-
	17	-	30,000
	28	120.7	15,000

TABLE 11.

Showing the absence of any correlation between the blood cholesterol and the percentage of expected body weight in twelve infants.

Case No.	Cholesterol mg.%	Percentage of expected weight.
13	134.0	71
12	124.1	68
11	114.3	86
54	102.3	98
3	98.9	61
55	96.0	89
35	93.1	66
47	93.1	57
1	93.1	80
2	93.1	84
10	90.2	90
34	81.6	94.

TABLE 12a.

Empyema (following first attack of pneumonia).

Case No.	Name	Age	Day of illness	Cholesterol mg.%	Fever	
54	R.D.	25 wks.	12	102.3	104.0	History - Cough, fever and dyspnoea for 12 days.
			15	85.0	102.8	Post-mortem report - "Right empyema and right diffuse
			21	Died	-	broncho-pneumonia. Patchy broncho-pneumonia left lower lobe."
55	C.R.	40 wks.	7	96.0	105.0	History - Cough began 7 days ago. Child acutely
			8	93.1	104.0	ill on the 7th day. Chest explored on the 8th day
			10	93.1	104.0	but no pus obtained. General condition became
			11	96.0	103.8	gradually worse. Post-mortem report -
			17	105.7	103.8	"Diffuse broncho-pneumonia, purulent pleural exudate
			19	Died	-	on left side."
56	V.L.	2 yrs.	6	75.9	102.0	History - Cough, vomiting and diarrhoea 6 days ago.
			7	70.0	102.0	Child acutely ill on ad-
			10	87.3	103.4	mission. Post-mortem report -
			12	Died	-	"Double suppurative broncho-pneumonia, left pleura contains pus."
57	H.McN	2 yrs.	4	111.5	100.0	History - 4 weeks ago tonsillitis and otitis
			5	114.3	99.8	media. 2 weeks ago tonsils inflamed, but
			7	120.7	99.8	child not acutely ill. Radiographic examination
			8	114.3	99.8	of chest showed only some pleural thickening at
			9	114.3	101.0	left base. 4 days ago child became acutely ill
			11	98.9	99.6	with swinging temperature and left side of chest
			12	111.5	99.8	dull. On the 8th day

TABLE 12a (Contd.)

Case No.	Name	Age	Day of illness	Cholesterol mg.%	Fever	
57 (Ctd.)			14	105.7	99.2	of this acute illness 240 c.c. of pus removed from left side. On the 15th day child was transferred to the surgical side for rib resection.
58	E.McA.	32 wks.	9	143.7	103.0	History - Good health until 9 days ago. Child acutely ill on admission. Chest was explored twice and pus obtained. Post-mortem report - "Right pneumo-thorax, right lung is the seat of diffuse broncho-pneumonia. Left lung normal apart from basal congestion."
			13	Died	-	
59	I.A.	4 yrs.	4	-		History - A "cold" for 11 days, cough for 4 days. Child acutely ill and radiographic examination of chest shows fluid and consolidation of right lung. Chest explored on 10th day and pus obtained. Chest explored on 14th, 16th and 21st days. Transferred to surgical side on the 24th day, for rib resection. On the 46th and 49th days the child's condition was improving considerably and there was practically no discharge from the wound.
			6	81.6	103.0	
			8	93.1	102.4	
			9	98.9	101.2	
			10	96.0	101.8	
			12	87.3	100.4	
			14	96.0	99.8	
			15	87.3	99.0	
			16	85.0	100.0	
			17	93.1	-	
			19	81.6	100.0	
			21	75.9	99.8	
			23	93.1	99.2	
			31	93.1	-	
			44	105.7	-	
			49	105.7	-	

TABLE 12a (Contd.)

Case No.	Name	Age	Day of illness	Cholesterol mg.%	Fever	
60	J.R.	11 yrs.	24 30 37	96.0 87.3 93.1	99.8 99.0 99.8	History - Pneumonia 3 weeks ago, followed by empyema and rib resection. On the 24th day discharge from the wound was diminishing and on the 37th day the wound was healing and child's condition was improving.

TABLE 12b.

Empyema (following second attack of pneumonia.)

Case No.	Name	Age	Day of illness	Cholesterol mg.%	Fever	
61	J.S.	1 yr.	5	108.5	+	History - pneumonia 14 months ago. Acutely ill and dyspnoeic for 5 days. Chest explored on 5th day and 30 c.c. pus removed. Child made a rapid recovery after this and no further exploration was necessary.
			8	108.5	-	
			10	124.1	-	
			11	114.3	-	
62	J.H.	7 yrs.	4	98.9	++	History - Pneumonia 5 yrs. ago. 4 days ago pain in chest and cough. Examination on the 5th day - child acutely ill, left side of chest dull and much râle audible over all areas. On the 18th day general condition much better, dull lower half of left side of chest, R.M. tubular. On 28th day improving slowly. On 30th day temp. and pulse persistently high. Child very ill. Rib resection performed on the 33rd day. Child eventually made good recovery.
			7	105.7	+	
			9	111.5	+	
			11	70.0	+	
			12	64.3	-	
			14	87.3	+	
			16	75.9	++	
			18	87.3	+	
			20	85.0	+	
			23	87.3	+	
			26	-	+	
			28	98.9	+	
			30	75.9	+	
			32	70.0	+	

TABLE 13.

Pneumonia complicated by nephritis.

Case No.	Name	Age (yrs)	Day of illness	Cholesterol mg.%	Fever	Oedema	Urine	
63	J.C.	3	8	93.1	99.0	±	Blood & casts.	History - Oedema for 8 days. Exam. - Dulness over lower half of right side of chest where R.M. tubular. High fever until 7th day of illness.
			14	140.3	-	±	Blood & Casts.	
			20	105.7	-	-	Tr. alb. No blood.	
			21	111.5	-	-	Tr. alb. No blood.	
64	M.C.	9	15	120.7	100.0	±	Casts & R.B.C.	History - Ill for 15 days. Exam. - Child acutely ill cyanosed and dyspnoeic, evidence of cardiac failure. Impaired note right side of chest where R.M. tubular. On the 20th day, condition was improving slowly. On the 25th day X-ray exam. showed chronic consolidation behind heart. On the 29th day, the general condition was moderately good and on the 46th day she was discharged "well."
			17	114.3	-	±	Casts & R.B.C.	
			18	120.7	-	-	Casts & R.B.C.	
			19	120.7	-	-	R.B.C.	
			20	127.6	-	-	R.B.C.	
			21	124.1	-	-	R.B.C.	
			26	134.0	-	-	R.B.C.	
			28	124.1	-	-	R.B.C.	
			32	127.6	-	-	R.B.C.	
			34	117.2	-	-	R.B.C.	
			42	117.2	-	-	Clear.	
65	D.T.	5	4	124.1	102.0	-	Alb. & casts	History - Illness began 4 days ago with sore throat and praecordial pain. On the 4th day, acutely ill, face puffy though no definite oedema. Signs of pneumonia became evident on the 7th day. The child made a good recovery.

TABLE 13 (Contd.)

Case No.	Name	Age (yrs)	Day of illness	Cholesterol mg.%	Fever	Oedema	Urine	
66	M.L.	8	8	96.0	100.4	-	blood ++	History - Pneumonia 4 weeks ago; appeared to recover after 2 weeks. 8 days ago general condition became much worse. 2 days ago 500 c.c. of pus removed from chest.
67	R.B.	2	21	189.0	100.0	++	No blood Alb. ++	History - Oedema for 3 weeks. Has frequent cough, R.M. tubular over scapular region; râles and rhonchi over all areas. N.P.N. = 28.7 mg.%. In 10th week placed on salt-free diet. In 17th week, general condition good. Chest clear.
			56	136.9	-	++	"	
			63	150.6	-	+	Alb. +	
			70	127.6	-	±	Alb. ± No R.B.C. or casts.	
			119	150.6	-	±	Alb. ± No R.B.C.	
			154	98.9	-	±	Haze alb. only.	

TABLE 14.

Pneumonia with jaundice.

Case No.	Name	Age (yrs.)	Day of illness	Cholesterol mg.%	Fever	
68	J.S.	3	5	171.2	+	History - Third attack of pneumonia. Radiographic examination shows consolidation right side. Urine contains bile++ and the V.d.Bergh is direct - biphasic; indirect 8.0 units. On the 8th day the jaundice was fading and on the 9th day child was dismissed to country branch.
			7	154.0	-	
			8	154.0	-	
			9	157.4	-	
69	D.C.	12/52	3	81.6	++	History - Increasing jaundice since 1/12 of age. Blood normal. Urine contains bile ++. Stools pale. Van den Bergh - direct biphasic; indirect 20 units. Post-mortem report - "Bronchopneumonia both lungs, extensive consolidation both lower lobes. Liver enlarged but no cirrhosis."
			4	Died		

Discussion.

Rich[19] has pointed out that jaundice is sometimes observed in acute infections, and that it occurs more often in pneumonia than in other acute febrile diseases. He found definite evidence of hepatic damage in pneumonia, and he believes that anoxemia is an important factor in its causation.

The association of hypocholesterolemia and liver damage is recognised by many workers, but it is impossible to decide to what extent the anoxemia, and the alleged liver damage, are related to the cholesterol variations in pneumonia. It will be seen later that the cholesterol values in other infective processes do not differ markedly from those in pneumonia.

Temperature, toxaemia, leucocytosis, together with other factors already indicated, do not appear to have any direct influence on the blood cholesterol. It is obvious from the results in this series that a short acute illness like pneumonia, even when accompanied by severe toxaemia, produces only a feeble and often evanescent hypocholesterolemia. On the other hand prolongation of fever and toxaemia by an empyema, is frequently accompanied by a definite lowering of the cholesterol, and a slow rise during the period of recovery, without any tendency to hypercholesterolemia. Kipp[1] has indicated that the cholesterol is utilized in proportion to the severity of the disease. The results of the present investigation suggest, rather, that it is utilized in proportion to the duration of the illness. The low cholesterol values found in successive pneumonias and the fact

that they are proportionate, in many cases, to the interval between the attacks, suggest that repeated infection may act in the same way as a prolonged infection.

It might be suggested that young children are unable to produce sufficient cholesterol to deal with a prolonged or recurrent infection and that the store becomes exhausted after a few weeks of fever. This suggestion is in accordance with the findings of Simonini,(4) who concluded that long standing malnutrition, emaciation and infection exhaust the cholesterol producing organs, and the reticulo-endothelial system.

The rôle of cholesterol in immunity has been stressed by some workers, but if one accepts the suggestion that immunity increases proportionately with the increased cholesterol values it is difficult to explain why children displaying the nephrotic syndrome should be so susceptible to pneumococcal infection. It has clearly been shown (vide page33) that there is no correlation between the increased cholesterol values and the progress of convalescence.

Summary.

1. Children of both age groups suffering from a first attack of pneumonia, showed a slight diminution during the acute stage, and an increase of the blood cholesterol during the convalescent period.

2. Children of both age groups with recurrent pneumonia displayed low values throughout the illness, and did not exhibit the marked rise of the blood cholesterol seen in many cases with their first attack.

3. The lowest values in pneumonia were found in children under one year.

4. A marked cholesterol increase was not necessarily associated with a rapid convalescence, and a fatal issue was not always preceded by hypocholesterolemia.

5. Prolonged infection produced a much more marked diminution of the blood cholesterol, than a short acute illness.

6. There was no correlation between the blood cholesterol and the state of nutrition, the diet, the temperature or the degree of leucocytosis.

B. TUBERCULOSIS.

Eichelberger and McClusky[1], also Spoujitch and Boritch[2] found that the blood cholesterol values were an index of the degree of resistance of the patient. King and Bruger[3] found that hypercholesterolemia is unusual in tuberculosis without amyloid disease and that hypocholesterolemia predicts any early fatal termination. Varone[4] found a definite correlation between the blood cholesterol and the powers of resistance of children to tuberculosis. He observed hypocholesterolemia in the cachetic forms, in meningitis and miliary tuberculosis. Gottlieb and Goldbloom[5] found increased values in tuberculous meningitis. Baylac and Sendrail[6] found that the blood cholesterol was increased in children who were sensitive to the intradermal tuberculin test, and their figures, for the younger children at least, are convincing. In the older children, however, the difference in the cholesterol values of the reactors and the non-reactors is much less apparent. The results of these authors show a diminishing disparity between the values of these two groups of children, coincidently with their increasing ages (vide Table 15).

Personal observations.

This group comprises twenty five children with active tuberculosis. The controls consist of the group of normal children referred to on page 21. Their tuberculin reactions were not tested, and they appeared to be in good health.

The blood cholesterol in all but two patients, with tuberculosis, was within normal limits. On examining the figures

TABLE 15 (after Baylac and Sendrail[6])

Age			Cholesterol mg.%
$\frac{1}{12}$ to $\frac{3}{12}$	Mantoux	+	-
	"	-	95
$\frac{3}{12}$ to $\frac{6}{12}$	"	+	-
	"	-	100
$\frac{6}{12}$ to 1 yr.	"	+	176
	"	-	110
1 to 2 yrs.	"	+	245
	"	-	133
2 to 5 yrs.	"	+	179
	"	-	134
5 to 10 yrs.	"	+	171
	"	-	150
10 to 15 yrs.	"	+	173
	"	-	164

more closely one noted a resemblance to the results of Baylac and Sendrail (vide Table 15), who found higher values in children with tubercle. This difference, however, between the values of the healthy and tuberculous children in the present series is slight (vide chart 8).

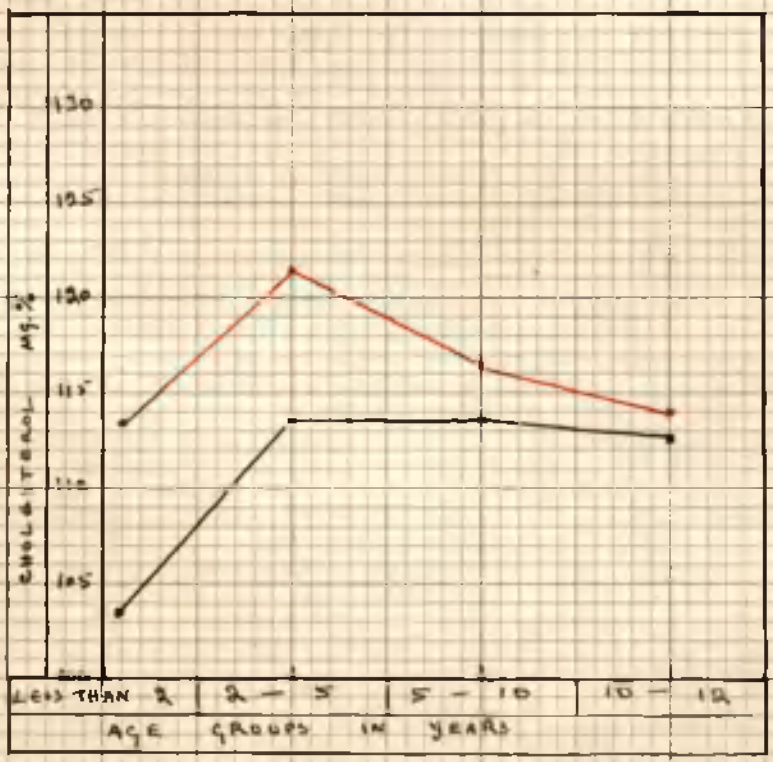
In children with tuberculosis the highest values were found between two and five years of age, apart from this the figures for the other age groups differ little from one another, and are practically the same as for healthy children between the ages of ten and twelve years (vide Tables 16 and 2). It is interesting to note similar results in Baylac and Sendrail's series for the gradual rise of the cholesterol values coincidently with the increasing ages of the children shown in the non-reactors, is not seen in the children reacting to the Mantoux test.

TABLE 16.*

Age Group	Cholesterol mg.%(Av.)	Number of cases
Under 2 yrs.	113.3	5
2-5 yrs.	121.4	6
6-9 yrs.	116.5	5
10-12 yrs.	114.0	9
Total:		25

* For values of individual cases vide Table 17.

Chart 8.



= HEALTHY CHILDREN.

= TUBERCULOUS CHILDREN.

TABLE 17.

The blood cholesterol in 25 children with tuberculosis.

Case No.	Name	Cholesterol mg.%	Diagnosis	Remarks
	(a) Under two years.			
70	P.M.	111.5	Miliary Tb.	Blood obtained a few hours before death.
71	J.C.	111.5	Miliary Tb.	Blood obtained just after death.
72	M.C.	117.2	Multiple Tb.abscesses.	Acutely ill. Eventually made a good recovery.
73	J.F.	120.7	Pulm. Tb.	Moderately advanced case. Dismissed irregularly.
74	E.McG.	105.7	Pulm. Tb.	Acutely ill. X-ray = "gross infiltration of both lungs."
	Av.	113.3		
	(b) Two to five years.			
75	E.M.	111.5	Pulm. Tb.	Acutely ill. Died.
76	N.S.	180.5	Tb. meningitis.	Acutely ill. Died.
77	H.H.	124.1	Miliary Tb.	Acutely ill. Died.
78	R.S.	98.9	Tuberculides.	General condition moderately good. Afebrile.
79	M.McG.	102.3	Pleur. effusion.	General condition fair. X-ray = "Consol. left apex" Made good recovery.
80	W.B.	111.5	Pulm. Tb.	General condition moderately good. Afebrile. X-ray = "Fibrosis right lung."
	Av.	121.4		
	(c) Six to nine years.			
81	J.C.	117.2	Pulm. Tb.	General condition moderately good. Afebrile. X-ray shows scattered mottling of lungs. Dismissed "improved."
82	R.Y.	131.0	Miliary Tb.	Acutely ill. Died.

Table 17 (Contd.)

Case No.	Name	Cholesterol mg.%	Diagnosis	Remarks
83	L.D.	105.7	Abd. Tb.	Intermittent fever. Moderately ill. Abdomen distended.
84	J.R.	114.3	Pulm. Tb.	Not acutely ill. Afebrile. Dismissed "improved."
85	C.M.	114.3	Pulm. Tb.	Afebrile. Not acutely ill.
	Av.	116.5		
	(d)	Ten to twelve years.		
86	W.B.	124.1	Pleur. effusion.	General condition fair. Afebrile. Good recovery.
87	F.D.	81.5	Tb. meningitis.	Acutely ill. Died.
88	H.B.	120.6	Pulm. Tb.	Moderately advanced adult type. Transferred to sanatorium.
89	J.M.	111.5	Pulm. Tb.	General condition fair. Afebrile. Dismissed well.
90	W.A.	134.0	Pleur. effusion.	General condition fair. Afebrile. Good recovery.
91	J.B.	108.5	Abdomin. Tb.	Advanced case. General condition poor.
92	M.G.	120.7	Abdomin. Tb.	General condition good. Calc. mesenteric glands.
93	M.H.	111.5	Pulm. Tb.	General condition fair. Afebrile. Ghon's focus.
94	I.B.	114.3	Pleur. effusion	Not acutely ill. Afebrile. Good recovery.
	Av.	114.0		

The results of these authors, together with those of the present series, suggest that tuberculosis raises the blood cholesterol in younger children, but produces little change in the cholesterol values of older children.

It was thought that the type of tuberculosis affecting the younger subjects might explain these slightly higher values. The children were therefore classified according to the type of tuberculosis (vide Table 18), but there was no significant difference in the mean values for pulmonary, abdominal, or miliary tuberculosis. There were only two cases of tuberculous meningitis and the blood cholesterol was high in one and low in the other. With the exception of these two cases, however, the blood cholesterol was unaffected by the type of tuberculosis.

There did not appear to be any correlation between the degree of toxaemia and the cholesterol values in this series, twenty three out of twenty five results being within normal limits. The figures for the four cases of miliary tubercle for example were almost identical with the figures for the four cases of pleurisy that made good recoveries. The absence of any marked disturbance of the cholesterol values is probably associated with the fact that neither gross emaciation, nor protracted fever, was found in any of these cases.

Briefly one may state that tuberculosis tended to cause a slight increase of the blood cholesterol in the younger children. With the exception of tuberculous meningitis, the cholesterol was unaffected by the location of the disease.

TABLE 18.

PULMONARY TUBERCULOSIS

Case No.	Age in years	Cholesterol mg.%
73	1	120.7
74	1	105.7
75	2	111.5
80	4	111.5
81	6	117.2
84	7	114.3
85	8	114.3
88	10	120.6
89	10	111.5
93	11	111.5
Av.		113.8

ABDOMINAL TUBERCULOSIS

83	6	105.7
91	10	108.5
92	11	120.7
Av.		111.6

MULTIPLE Tb. ABSCESSES

72	$\frac{11}{12}$	117.2

MILIARY TUBERCULOSIS

Case No.	Age in years	Cholesterol mg.%
70	$\frac{5}{12}$	111.5
71	$\frac{7}{12}$	111.5
77	3	124.1
82	5	131.0
Av.		119.5

PLEURAL EFFUSION

79	4	102.3
80	10	124.1
90	10	134.0
94	12	114.3
Av.		118.6

TUBERCULOUS MENINGITIS

76	3	180.5
87	10	81.6
Av.		131.0

TUBERCULIDES.

78	3	98.9

Summary of Mean values
in Table 18.

No. of cases	Cholesterol mg.%	Type of Tuberculosis
10	113.8	Pulmonary tuberculosis.
4	118.6	Pulmonary tuberculosis (pleural effusion).
2	131.0	Tuberculous meningitis.
3	111.6	Abdominal tuberculosis.
1	117.2	Multiple tuberculous abscesses.
4	119.5	Miliary tuberculosis.
1	98.9	Tuberculides.
Total 25	-	

C. GASTRO-ENTERITIS.

Schally[7] found the blood cholesterol unchanged in enteritis of the small intestine, but he noted marked hypocholesterolemia in ulcerative colitis. Galdó[8] observed diminished values in gastro-enteritis in children.

In the present investigation somewhat low values were noted in seven out of ten cases, and hypercholesterolemia was not observed in any subject. The lowest values were found in Case No. 95 (vide Table 19). Determinations were made on this baby over a period of seventeen days; the initial value was 78.9 mg.% and the cholesterol gradually increased to 111.5 mg.%, but soon

fell again to 93.1 mg.%, and finally to 81.6 mg.%. This child did not respond well to treatment, and had intermittent vomiting during practically the whole period of observation, convalescence was very slow, but the child eventually made a good recovery. Unfortunately the cholesterol was not estimated after the child had recovered completely, but the diminished values throughout this somewhat protracted illness are interesting in view of the low results found in other cases of prolonged infection (vide page 40).

In Case No. 96 the initial value was within normal limits, but convalescence had already begun when this estimation was made. Soon afterwards, however, an upper respiratory infection became evident, and the blood cholesterol fell from 120.6 mg.% to 102.3 mg.%, and during the period of recovery from this infection it gradually increased to 124.1 mg.%.

In Nos. 97, 98, 99 and 100 the initial values were between 96.0 mg.% and 98.9 mg.%, and in every case the cholesterol rose to over 100 mg.% after cessation of the diarrhoea. No. 101 has a cholesterol value of 131.0 mg.% twenty four hours before death. The remaining cases had values of 117.2 mg.%, 98.9 mg.% and 102.3 mg.%, respectively, and they all made good recoveries.

One concludes therefore that gastro-enteritis is frequently associated with a diminution of the blood cholesterol.

TABLE 19.

Gastro-enteritis and Dysentery.

Case No.	Name	Age (Yrs.)	Date	Cholesterol mg.%	History
95	J.S.	11/52	7.5.37	78.9	Diarrhoea and vomiting for 3 weeks. On 7.5.37 temp. 102.4. Afebrile after 8.5.37. Convalescence extremely slow. Intermittent vomiting until 21.5.37. Did not gain any weight during the period of observation. Examination of heart, lungs, abdomen and nervous system persistently negative. Eventually made a good recovery.
			10.5.37	98.9	
			13.5.37	111.5	
			15.5.37	105.7	
			17.5.37	93.1	
			19.5.37	98.9	
			21.5.37	81.6	
			24.5.37	81.6	
96	B.McC	22/52	29.9.36	120.6	Diarrhoea and vomiting 12 days ago. Cough for 4 wks. General condition much improved today (29.9.36). Chest nil. Gaining weight. Irreg. fever from 30.9.36 to 15.10.36, rhonchi and râles audible in chest during this period. On 20.10.36 - afebrile, chest clear.
			7.10.36	117.2	
			14.10.36	102.3	
			17.10.36	111.5	
			20.10.36	124.1	
97	A.L.	11/52	14.10.36	96.0	Diarrhoea and vomiting for 7 days. Condition gradually improved and he was dismissed on 17.10.36. Re-admitted 2 days later with diarrhoea, his condition gradually became worse.
			17.10.36	127.5	
			3.11.36	Died	
98	R.G.	2	25.7.36	98.9	Vomiting and severe diarrhoea 3 days ago. B. dysenteriae (flexner) isolated from stools. On 31.7.36 child was much better and stools were normal.
			31.7.36	102.3	

TABLE 19 (Contd.)

Case No.	Name	Age (Yrs)	Date	Cholesterol mg.%	History
99	I.R.	6/52	24.7.36	98.9	Vomiting for 6 days, slight diarrhoea.on 31.7.36 general condition very good taking feeds well.
			31.7.36	111.5	
100	T.D.	22/52	24.7.36	96.0	Vomiting and diarrhoea for 6 days. Temp. 101.0 on 23.7.36, thereafter afebrile. On 31.7.36 child very well.
			31.7.36	108.5	
101	A.D.	27/52	29.9.36	131.0	Recurrent diarrhoea and vomiting. Acutely ill. No fever. Emaciated and dehydrated.
			30.9.36	Died	
102	D.W.	14/52	12.5.36	117.2	Recurrent vomiting. Diarrhoea for a month. Marantic child. Made good recovery.
103	L.C.	13/52	11.8.37	98.9	Vomiting and diarrhoea 5 days ago for 3 days. Afebrile, general condition improving, still on very small feed, but made good recovery.
104	J.M.	18/52	1.10.36	102.3	Recurrent diarrhoea. Child is ill, undernourished. Made good recovery.

D. BRONCHITIS.

There are four cases in the group and the results are indicated in Table 20. No. 105 gave a history of vomiting and cough for 8 weeks; he was acutely ill and the blood cholesterol remained below 100 mg.% until two days after the cessation of fever. During the convalescent period it rose to 131.0 mg.% and finally fell to 102.3 mg.%. He made a good recovery. No. 106 had ~~had~~ bronchitis 2 months previously. The blood cholesterol was 75.9 mg.% in the acute stage, and it gradually increased during the period of recovery to 117.2 mg.%. In the remaining two subjects single estimations were made and the values were 105.7 mg.% and 102.3 mg.% respectively.

The low values in the first two cases (Nos. 105 and 106) may have been associated with the somewhat prolonged respiratory infection which occurred prior to the child's admission to hospital.

E. TONSILLITIS.

Determinations have been made on four subjects with tonsillitis (vide Table 21). The cholesterol remained below 100 mg.% during the whole period of observation in No. 110. This child gave a long history of listlessness and anorexia. Fever followed tonsillectomy and lasted about ten days. It is possible that the long period of ill health in this case may have been related to the low cholesterol values.

In No. 109 the cholesterol fell below 100 mg.% on only one occasion. This child was acutely ill, but only for a short period.

Single estimations were made in the remaining two cases and their cholesterol values were 102.3 mg.% and 108.5% respectively. Both patients were moderately ill.

F. SEPTICAEMIA.

There are only three cases in this group. The determinations were made twenty four hours before death in two subjects and a few hours before death in the third. The cholesterol figures were, 120.6 mg.%, 105.7 mg.% and 90,7 mg.% respectively. These results would appear to demonstrate that the blood cholesterol is of little prognostic value in septicaemia. One cannot, however, draw any conclusions from this small series of cases.

Summary and Conclusions.

The results in tuberculosis, gastro-enteritis, bronchitis and tonsillitis are in agreement with the findings in pneumonia that prolonged infection produces hypocholesterolemia, and that a short acute illness causes only a slight and often evanescent diminution of the blood cholesterol.

The findings indicate that the blood cholesterol is of little prognostic value in acute infections.

TABLE 20.

Bronchitis.

Case No.	Name	Age	Date	Cholesterol mg.%	History
105	M.R.	16/52	2.1.36	98.9	Vomiting and cough for 8 weeks. Rhonchi in chest. Irregular fever from 23.1.35 to 6.1.36. Intermittent vomiting until 13.1.36 thereafter gained weight steadily. Dismissed 19.1.36 "well".
			3.1.36	93.1	
			4.1.36	93.1	
			6.1.36	98.9	
			7.1.36	98.9	
			8.1.36	111.5	
			9.1.36	98.9	
			10.1.36	131.0	
			11.1.36	124.1	
			14.1.36	108.1	
			15.1.36	102.3	
106	J.S.	11 yrs.	5.5.37	75.9	Nephritis 4 years ago. Bronchitis 2 months ago. Vomiting and headache for past 3 days. Temp. 102.6. Severe widespread bronchitis. Temp. 99.0 on 7.5.37 thereafter afebrile. On 13.5.37 general condition much improved, chest clear. Dismissed home on 13.5.37.
			7.5.37	93.1	
			10.5.37	98.9	
			13.5.37	117.2	
107	J.H.	2 yrs	28.7.36	105.7	Persistent cough and fever for 12 weeks. Now afebrile. Made good recovery.
108	T.McH.	6 yrs	28.1.37	102.3	Illness began 8 days ago with sore throat. Now afebrile, still some râles in chest. Made good recovery.

TABLE 21.

Tonsillitis.

Case No.	Name	Age	Date	Cholesterol mg.%	History
109	R.S.	4	7.1.36	117.2	Convulsion 2 days ago, thereafter drowsy. Tonsils ++ red. Acutely ill. Temp.101.6 on 7.1.36 and gradually fell to normal. Afebrile after 10.1.36. General condition gradually improved and he was dismissed to country branch on 17.1.36.
			8.1.36	120.7	
			9.1.36	111.5	
			10.1.36	102.3	
			11.1.36	98.9	
			14.1.36	105.7	
			15.1.36	105.7	
			16.1.36	111.5	
110	A.McC	6	18.2.36	96.0	Listlessness and anorexia for 6 months. Tonsillectomy 5 days ago. Pus in tonsillar beds. Urine - acetone ++. Irregular fever until 24.2.36, thereafter afebrile. Dismissed "well" on 2.3.36.
			19.2.36	93.1	
			21.2.36	93.1	
			24.2.36	81.6	
			27.2.36	98.9	
111	E.C.	11	12.11.35	102.3	Attacks of fever and headache every 6 weeks. Child not acutely ill, though temp. 101.6 on 11.11.35, thereafter afebrile. Good recovery.
112	A.McP	4	27.6.36	108.5	Loss of weight and anorexia for several months. Tonsils ++ septic. Throat swab negative for K.L.B. but 5 days later it was positive.

TABLE 22.

Septicaemia.

Case No.	Name	Age	Date	Cholesterol mg.%	History
113	H.F.	3	13.9.37 14.9.37	120.6 Died	Otorrhoea for several months. Pneumonia four times. Acutely ill. Post-mortem report - "Congenital cardiac disease, pyaemic abscesses in kidneys. Pyelitis."
114	R.C.	10	24.1.36 25.1.36	105.7 Died	Drowsy for 2 days, comatose for 6 hours. Post-mortem report - "Pyaemia, ulcerative endocarditis, metastatic abscesses."
115	C.L.	$\frac{4}{12}$	1.12.36	90.7	Fever, vomiting and diarrhoea for a month. Abscess in lower jaw discharging. Died several hours after cholesterol was estimated. The cause of death was osteomyelitis and pyaemia.

SECTION 2.

THE BLOOD CHOLESTEROL IN THE RHEUMATIC INFECTION OF CHILDHOOD.

Most workers agree that the blood cholesterol is diminished in acute infections, and one would therefore expect to find some degree of hypocholesterolemia in rheumatic fever. References to juvenile rheumatism in the literature on cholesterol are comparatively scanty, and the few observations published on the subject are somewhat conflicting.

Goldbloom and Gottlieb[1] made their determinations on whole blood and found hypercholesterolemia in rheumatic fever. Their work does not appear, however, to have been substantiated by more recent investigators. Respi[2] observed hypocholesterolemia in rheumatic endocarditis. Ward[3], and Kaiser and Gray[4] using whole blood and plasma respectively, and employing different methods of estimation, obtained results which differed little from their own normal figures. Offenkrantz and Karshan[5] found the serum cholesterol within normal limits in acute rheumatism. Lesné et alii[6] observed normal or slightly elevated values in Sydenham's chorea.

Personal observations.

Determinations have been made on sixty three cases of juvenile rheumatism.* In some patients it has been possible to observe the blood cholesterol values over a period of a year or longer, and the majority of the children are alive at the time of writing.

* These cases are referred to in various tables under the same case numbers.

The acute phase.

For the purpose of comparing the cholesterol values at corresponding stages of the illness, it was necessary to fix the date of onset of the rheumatism in each child, and in this series, evidence of arthritis was taken as the most reliable sign from which to make this calculation.

Nine patients had arthritis, either at the time of making the initial observation, or only a few days previously. Five of them displayed cholesterol values of less than 100 mg.%. In the remaining four, the cholesterol oscillated between 105.7 mg.% and 108.5 mg.% (vide Table 23). The average figure for the first week is 100.3 mg.% and for the second, third and fourth weeks after arthritis the figures are 111.8 mg.%, 111.8 mg.% and 118.2 mg.% respectively.

It is obvious, therefore, that the cholesterol values tend to be low during the articular phase, and to rise in the subsequent weeks of convalescence. One might conclude from these results that there is a definite correlation between rheumatic arthritis and the blood cholesterol, subsidence of the arthritis being followed by increased cholesterol values in practically every case. On the other hand, the hypocholesterolemia may be associated primarily with the acute general infection. It is difficult to assess the relationship between these low values and the arthritis, and the results of other investigators are of little assistance, for this aspect of the subject does not appear to have been discussed by any author. Most workers,

TABLE 23.

Acute rheumatism.

Showing the increase of cholesterol after subsidence of arthritis.

Case No.	Age in years	Number of days after arthritis			
		Less than 7	14	21	28
		Cholesterol mg.%			
2	7	96.0	117.2	102.3	-
3	8	98.9	105.7	111.5	-
4	9	105.7	105.7	117.2	-
*5	10	108.5	114.3	134.0	131.0
*6	9	-	-	105.7	111.5
7	11	90.1	96.0	102.3	111.5
8	12	96.0	117.2	111.5	111.5
9	6	93.1	114.3	102.3	117.2
10	12	105.5	102.3	114.3	-
*11	8	105.7	-	117.2	114.3
15	8	-	-	-	120.7
16	10	-	134.0	-	127.6
Av.		100.3	111.8	111.8	118.2

* Second attack of rheumatism.

however, agree that arthritis associated with infection is accompanied by a diminution of the blood cholesterol. Hartung and Bruger[7] working with adults, found that the plasma cholesterol tended to be low in rheumatoid arthritis, and elevated in osteoarthritis. Pemberton[8] observed normal cholesterol values in four hundred soldiers with chronic arthritis. It is interesting to note that Pemberton discovered a focus of infection in seventy two per cent of his cases.

The results of these workers are conflicting and it is impossible to decide to what extent the low cholesterol values of the present series are related to arthritis. Nevertheless, it is apparent that hypocholesterolemia and arthritis are often found together.

Convalescent phase.

An increase of the blood cholesterol during the convalescent period was observed by Kaiser and Gray[4] and also by Raspi[2]. Some of the figures of these authors are quoted below.

Author	Case No.	Date	Age in years	Cholesterol mg.%	
Kaiser & Gray	13	11-6	9	72	
		18-6		129	Acute rheumatism.
		5-7		165	Recovered.
Raspi	2	5-2	5	110	Rheumatic endocarditis.
		15-2		130	Afebrile.
	3	2-1	9	130	Articular rheumatism.
		10-1		150	Afebrile.

In the present investigation there was an elevation of the blood cholesterol during convalescence in fifteen out of sixteen subjects. These cases have been subdivided according to whether they show a steady increase, or an increase preceded or followed by oscillating values.

(a) A steady increase (vide Table 24a).

Eight cases belong to this subgroup, and although there was sometimes a slight diminution of the blood cholesterol in the later stage of convalescence, it never fell below 100 mg.%, and there was no definite oscillation of the values. In every patient the general condition improved steadily during the period of observation, and in seven of them convalescence was comparatively uneventful. In the eighth case (No. 1) a cardiac lesion became evident in the course of a more or less steady rise of the cholesterol.

(b) Oscillating values (vide Table 24b).

There are seven patients in this subgroup, and although marked variations of the intermediate values were observed, the final reading of the series was higher than the initial one in all but one case. In three of the children, the development of a cardiac lesion occurred at a time when the cholesterol values seemed somewhat unstable. One subject (No. 9) had an initial cholesterol value of 93.1 mg.%, two days later it was 124.1 and there was no evidence of a cardiac lesion. During the succeeding seven weeks this patient displayed, from time to time, the

following figures - 98.9 mg.%, 117.2 mg.%, 87.3 mg.% and 131.0 mg.% and the figure before dismissal was 111.5 mg.%. Convalescence in this child was slow, and during the course of the cholesterol oscillations an apical v.s. murmur became evident. In the second case (No. 10) the first cholesterol estimation was 108.5, and at this time there was no cardiac lesion. One week later a v.s. murmur became audible, and two days afterwards the cholesterol fell to 98.9 mg.%. In the third case (No. 11) the appearance of a diastolic murmur was accompanied by a slight fall (114.3 mg.% to 108.5 mg.%). In case No. 12 the appearance of chorea, about three weeks after the onset of acute rheumatism, was associated with a diminution of the blood cholesterol from 124.1 mg.% to 102.3 mg.%. This case is also referred to on page 117. In the fifth case (No. 13) the cholesterol rose gradually from 96.0 mg.% to 120.7 mg.% in early convalescence. Tonsillectomy and dental extraction took place in the succeeding two weeks, and the cholesterol varied between 96.0 and 98.9 during this period. The sixth child (No. 14) had a tuberculous arthritis of the knee joint, in addition to a definite rheumatic infection, and it is possible that the cholesterol oscillations may have been associated with this complication. In the seventh patient (No. 15) convalescence was uneventful, but as the lowest value was 114.3 mg.% and the highest 131.0 mg.%, it is thought that this slight fall to 114.3 mg.% during convalescence is of little significance.

It is noteworthy, therefore, that, with one exception, all the children who displayed a steady increase of the blood cholesterol had an uneventful convalescence, and seven out of the

eight children showing oscillating values exhibited some complication which might be associated with the variability of the cholesterol values.

A steady fall of the blood cholesterol together with a fair recovery was found only in case No. 16 (vide Table 25). In this child of ten years the cholesterol fell from 134.0 mg.% to 120.0 mg.% between the second and the fourteenth week. No explanation can be offered for this reduction. A further decrease was observed, however, between the sixteenth and the twentieth week, and this may have been associated with tonsillectomy followed a week later by a severe haemorrhage after dental extraction. The association of a low blood cholesterol with anaemia is recognised, but unfortunately the blood was not examined after the haemorrhage. The occurrence of lipæmia after haemorrhage will be discussed later (page 199).

RECURRENT RHEUMATISM.

Ward[3] found low values when acute rheumatism was superimposed on a chronic cardiac lesion. In the present series three cases (Nos. 5, 6 and 11) gave a definite history of a rheumatic infection three to five years previously. The cholesterol was not markedly diminished in any of them, and it rose during convalescence in every case. There was no significant difference between the cholesterol values of these three children and those suffering from their first attack of rheumatism.

TABLE 24a.

Cases showing a steady increase of cholesterol values during convalescence.

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
1	M.S.	7 9/12	16.1.36	105.7	Tonsillitis one month ago. Arthritis first complained of on 11.1.36. Poorly nourished child. No arthritic or cardiac lesion.
			17.1.36	114.3	General condition better, no cardiac lesion.
			20.1.36	120.7	I.S.Q.
			14.2.36	117.2	I.S.Q.
			26.2.36	124.1	General condition improving. No cardiac lesion.
			3.3.36	134.1	General condition improving. No cardiac lesion.
			18.3.36	124.1	Dental extraction on 5/3/36. Tonsillectomy today.
			24.3.36	127.1	General condition improving.
			26.3.36	-	V.S. murmur audible at apex for first time.
			31.3.36	136.1	General condition good. V.S. murmur at apex not conducted.
			6.4.36	131.0	I.S.Q.
			17.4.36	124.1	I.S.Q.
2	P.B.	7 5/12	23.7.36	96.0	Well until onset of rheumatism on 12.7.36. Arthritis observed on 19.7.36 and low fever. No cardiac lesion.
			28.7.36	117.2	Afebrile. No cardiac lesion.
			6.8.36	102.3	General condition improving. No cardiac lesion.

TABLE 24a (Contd.)

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
3	J.M.	$8\frac{6}{12}$	21.7.36	98.9	Vague rheumatic pains for 4 months, worse 3 weeks ago. Some arthritis and fever from 15.7.36 to 19.7.36. Now afebrile. No cardiac lesion.
			28.7.36	105.7	Condition improving.
			6.8.36	111.5	General condition fair. No cardiac lesion.
4	M.W.	9	6.8.36	105.7	Recurrent tonsillitis. Illness began on 25.7.36. Some arthritis on 30.7.36 now gone. Low fever until 2.8.36. V.S. murmur conducted to axilla.
			12.8.36	105.7	Slight fever today but general condition fairly good. V.S. murmur conducted to axilla.
			20.8.36	117.2	Afebrile.
			1.9.36	120.6	General condition good. V.S. murmur conducted to axilla.
*5	E.P.	$10\frac{9}{12}$	10.3.36	108.5	Acute rheumatism 5 years ago. Arthritis for 10 days. V.D. and V.B. murmur at apex, the latter conducted to axilla.
			12.3.36	120.7	No arthritis.
			15.3.36	114.3	I.S.Q.
			24.3.36	134.0	General condition better. Heart unchanged.
			31.3.36	131.0	I.S.Q.
			6.4.36	131.0	I.S.Q.
			17.4.36	134.0	I.S.Q.

TABLE 24a (Contd.)

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
*6	J.R.	9	4.2.37	105.7	Chorea 5 years ago. Thereafter in convalescent home for 18 months. Acute rheumatism started 3 weeks ago. No arthritis now. Aortic and mitral lesions. Low fever.
			10.2.37	111.5	Afebrile. No nodules.
			17.2.37	117.2	General condition slightly better.
			23.2.37	108.5	I.S.Q.
			2.3.37	111.5	I.S.Q.
			10.3.37	111.5	General condition better. Capillary pulsation & V.S. & V.D. murmurs as before.
			19.3.37	117.2	I.S.Q.
7	A.B.	11	27.1.37	90.1	Fever for 2 weeks before onset of arthritis on 22.1.37. No arthritis now. Poorly nourished child. Tonsils unhealthy V.S. murmur conducted to axilla.
			2.2.37	96.0	1 nodule on elbow. Afebrile.
			10.2.37	102.3	Low fever today.
			16.2.37	111.5	Still has occasional fever to 99°F.
			23.2.37	117.2	General condition improving. Afebrile.
			25.2.37	-	Tonsillectomy.
			2.3.37	108.5	General condition fairly good. V.S. murmur conducted to axilla.
8	C.McG	12	23.7.36	96.0	Rheumatic pains for 2 years. Tonsillitis and arthritis on 17.7.36. Fever of 101°F until 22.7.36. No arthritis now. Presystolic murmur at apex and V.S. conducted to axilla.

Table 24a (Contd.)

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
8 (Contd.)	C.McG.	12	28.7.36	117.2	Improving.
			6.8.36	111.5	I.S.Q.
			11.8.36	111.5	I.S.Q.
			18.8.36	111.5	General condition improved. V.S. murmur conducted to axilla. Presystolic murmur not heard.

* Cases marked thus are suffering from their second attack of acute rheumatism.

TABLE 24b.

Cases showing oscillating values during convalescence.

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
9	W.B.	8 10/12	9.1.36	93.1	Illness began on 5.1.36. Arthritis both knee joints. low fever. No cardiac lesion.
			10.1.36	96.0	Condition unchanged.
			11.1.36	124.1	Arthritis still present. No cardiac murmur.
			14.1.36	114.3	No arthritis, cardiac lesion or fever.
			16.1.36	114.3	I.S.Q.
			17.1.36	98.9	I.S.Q.
			20.1.36	105.7	General condition fair, no cardiac lesion.
			22.1.36	102.3	I.S.Q.
			31.1.36	117.2	Soft apical V.S. not conducted to axilla, audible on 28.1.36 for first time. Child does not look so well.
			6.2.36	114.2	Condition unchanged.
			14.2.36	87.3	I.S.Q.
			18.2.36	111.5	I.S.Q.
			28.2.36	131.0	Child still does not look well. V.S. murmur at apex.
			12.3.36	111.5	General condition better. V.S.at apex conducted to axilla.

Table 24b (Contd.)

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
10	J.O'N.	$12\frac{9}{12}$	3.1.36	108.5	Recurrent tonsillitis. Rheumatism began on 30.12.35, still some arthritis. Tonsils ++. No cardiac lesion.
			4.1.36	105.7	I.S.Q.
			6.1.36	102.3	V.S. audible over all areas. No arthritis. Low fever.
			8.1.36	98.9	I.S.Q.
			9.1.36	98.9	"
			10.1.36	102.3	"
			11.1.36	111.5	"
			13.1.36	111.5	V.S. murmur, conducted to axilla. Low fever.
			15.1.36	111.5	I.S.Q.
			16.1.36	114.3	Low fever persists, heart as on 13.1.36.
11	J.D.	8	16.6.36	105.7	Acute rheumatism with pericarditis 3 years ago. Second attack with arthritis began 10 days ago. Slight swelling of joint still. V.S. murmur conducted to axilla. Low fever.
			4.7.36	117.2	Afebrile for 2 days. No nodules.
			9.7.36	114.3	Slight fever today.
			21.7.36	108.5	Double murmur at apex. Nodule left elbow.
			28.7.36	108.5	I.S.Q.
			6.8.36	114.3	I.S.Q. Transferred to country branch.
			26.9.36	131.0	Returned from country. General condition much better.

Table 24b (Contd.)

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
12	R.W.	10	3.4.36	124.1	Health good until onset of rheumatism on 28.3.36. Fever and arthritis present. V.S. murmur at apex conducted to axilla.
			6.4.36	117.2	No fever. Arthritis almost gone.
			17.4.36	102.3	No arthritis. Slight chorea.
			29.4.36	-	Follicular tonsillitis.
			6.5.36	124.1	Arthritis of wrist. Chorea not very definite.
			7.5.36	-	Arthritis practically gone.
			15.5.36	124.1	Chorea active. No arthritis.
			28.5.36	127.6	Chorea practically gone. 4.6.36 Tonsillectomy.
			16.6.36	124.1	Slight chorea. One nodule on elbow. V.S. murmur at apex conducted to axilla.
13	H.R.	12 9/12	26.5.36	96.0	Acute rheumatism 3 months ago. No arthritis now. 1 nodule on elbow. Tonsils very large and septic. Double murmur at apex.
			28.5.36	111.5	I.S.Q.
			25.6.36	120.7	Tonsillectomy on 25.6.36. *
			4.7.36	98.9	One tooth extracted on 1.7.36.
			9.7.36	96.0	General condition good. V.S. murmur at apex conducted to axilla.
			4.9.37	114.2	Outpatient. General condition good. Heart I.S.Q. (Vide Table 33.)

* Cholesterol estimated before operation.

Table 24b (Contd.)

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Remarks.
14	C.H.	10	27.1.37	105.7	Tonsillitis 2 months ago. Arthritis of knee joint began on 24.1.37 and is still evident. ? Tb knee. Well nourished child. V.S. and V.D. murmurs, latter not conducted down the sternum, but V.S. conducted to axilla. Low fever. Mantoux +ve.
			30.1.37	93.1	Low fever. Arthritis unchanged.
			2.2.37	81.6	I.S.Q.
			10.2.37	102.3	Afebrile. Arthritis unchanged. V.S. at apex conducted to axilla and V.D. conducted down the sternum.
			18.2.37	111.5	I.S.Q.
			23.2.37	87.3	General condition better.
			4.3.37	108.5	Some fluid in knee joint.
			10.3.37	108.5	Arthritis and Heart I.S.Q.
			19.3.37	111.5	Knee much less swollen. Heart I.S.Q
			3.4.37	111.5	I.S.Q.
15	E.L.	8	27.6.36	120.7	Recurrent tonsillitis for 3 years. Articular rheumatism began on 1.6.36. Arthritis now gone, still has irregular fever. V.S. murmur not well conducted. Tonsils septic.
			4.7.36	131.0	Temperature not so high.
			21.7.36	114.3	Afebrile. Condition improving.
			28.7.36	117.2	Tonsillectomy on 23.7.36.
			6.8.36	127.6	General condition much better. V.S. murmur at apex, not well conducted.

TABLE 25.

Case showing a gradual diminution of the cholesterol during convalescence.

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Remarks
16	S.C.	10	12.12.35	134.0	Tonsillitis on 1.12.35, followed by arthritis which has now cleared up. Moderately ill. Aortic and mitral lesions present.
			15.3.36	120.7	General condition better, but heart as on 12.12.35.
			20.3.36	-	Tonsillectomy.
			24.3.36	127.6	General condition fairly good.
			26.3.36	-	Dental extraction followed by considerable haemorrhage.
			31.3.36	117.2	General condition fair. Heart I.S.Q.
			6.4.36	114.3	I.S.Q.
			17.4.36	111.5	General condition improving. Heart I.S.Q.

RHEUMATIC CARDITIS.

Grigaut[11] found normal cholesterol values in various cardiac conditions, while Maxwell[12] and Hurxthal[13] have shown that in congestive heart failure the blood cholesterol is usually within normal limits.

Valvular lesions.

The cholesterol values of eleven children with valvular disease are compared on Table 26 with eleven who did not display any cardiac lesion. The average figures for the two groups are

TABLE 26.

A comparison of the cholesterol values in subjects with and without cardiac lesions (22 cases).

No cardiac lesion

Case No.	Cholesterol mg.%
2	96.0
3	98.9
27	117.2
28	117.2
30	131.0
35	111.5
38	127.6
42	111.5
45	120.7
46	98.9
51	102.3
Av.	112.0

Cardiac lesion.

Case No.	Cholesterol mg.%
6	105.7
7	90.1
8	96.0
9	93.1
11	105.7
16	134.0
33	117.2
49	127.6
55	108.5
57	108.5
59	127.6
Av.	110.4

practically identical (110.4 mg.% and 112.0 mg.% respectively). Valvular disease of the heart, per se, would appear therefore to have little influence on the blood cholesterol.

Pericarditis (vide Table 27).

Determinations were made on six patients and low results were found in four. In one of them (No. 19) the cholesterol rose from 81.0 mg.% to 108.0 mg.% in three weeks. This increase was associated, however, with little change in the general condition, and the patient died a week later. The cholesterol was 140.0 mg.% the day before death. In the second fatal case (No. 18) the illness lasted much longer, and determinations made out over a period of ten weeks, demonstrated values between 93.1 mg.% and 98.9 mg.% throughout. The course of the cholesterol and the temperature in this case are compared in Chart 9 with Grigaut's case[11] of septic endocarditis. Grigaut's chart is reproduced to show the striking similarity between these two cases. In the other two subjects (Nos. 17 and 22) the cholesterol rose to a normal level as convalescence progressed. The cholesterol was within normal limits in the remaining two patients (20 and 21), but in both cases they had begun to recover before the cholesterol was estimated.

Chart 9.

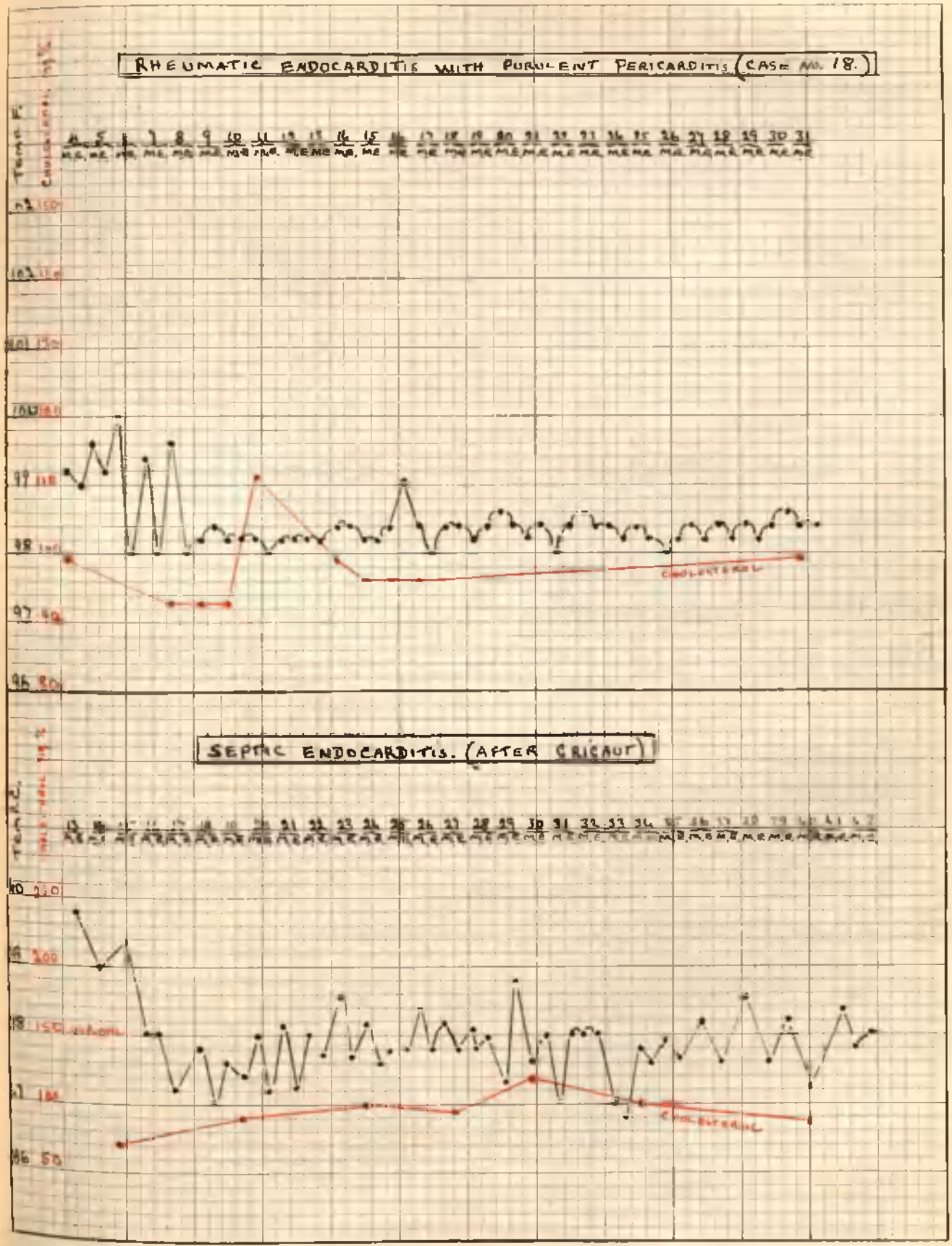

RHEUMATIC ENDOCARDITIS WITH PURULENT PERICARDITIS (CASE NO. 18.)
CHOLESTEROL
SEPTIC ENDOCARDITIS. (AFTER CRICAUT)

TABLE 27.

Pericarditis.

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
17	W.O.	$5\frac{6}{12}$	21.7.36	98.9	No history of rheumatism. V.S. and V.D. murmurs at apex. Friction 2 weeks ago.
			6.8.36	102.3	V.D. not audible, loud V.S. all over praecordium.
			12.8.36	98.9	General condition improving. V.S. as on 6.8.36.
			20.8.36	111.5	Much better, heart as on 6.8.36.
18	M.H.	8	12.12.35	117.2	Rheumatic endocarditis two years ago. General condition good. Aortic and mitral lesions.
			4.1.36	98.9	Fever for 7 days. Alveolar abscess incised on 2.1.36.
			8.1.36	93.1	Still some fever, abscess discharging.
			9.1.36	93.1	Afebrile. General condition not good.
			10.1.36	93.1	I.S.Q.
			11.1.36	111.5	Pulse very rapid (146 per min.)
			14.1.36	98.9	Abscess still discharging. General condition unchanged.
			15.1.36	96.0	I.S.Q.
			16.1.36	96.0	I.S.Q.
			17.1.36	96.0	Abscess healed. Poor general condition. Rapid pulse.
			31.1.36	98.9	Pallor and slight cyanosis. Corrigan's pulse and capillary pulsation present. V.S. & V.D. murmurs at apex.
			14.2.36	98.9	General condition slightly better.
			25.2.36	96.0	Condition improving.
			5.3.36	93.1	High fever for 4 days. Pericardial friction.
			23.3.36	-	Died.

Table 27 (Contd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Remarks.
19	D.S.	10	21.2.36	81.6	Rheumatic pains for 3 months, has mitral and aortic lesions. Nodules present. General condition poor.
			24.2.36	81.6	I.S.Q.
			26.2.36	90.2	General condition worse. Rapid pulse and oedema of limbs.
			2.3.36	90.2	Ascitis present. Nodules on elbow.
			5.3.36	102.3	I.S.Q.
			12.3.36	108.5	Slight cyanosis; oedema less.
			18.3.36	140.0	Much worse; oedema increasing.
			19.3.36	-	Died. Pericarditis found post mortem.
20	M.W.	$10\frac{10}{12}$	13.8.37	111.5	Acute rheumatism since 6.8.37. Pericardial friction, but condition is improving.
			16.8.37	117.2	Still some friction audible.
			24.8.37	102.3	No friction. General condition improving.
21	J.B.	$5\frac{6}{12}$	6.8.37	117.2	Acute rheumatism six months ago. Pericardial friction on 5.8.37. Condition improving.
			13.8.37	105.0	Still ill. Loud V.S. murmur at apex conducted to axilla.
			24.8.37	117.2	General condition improving.
			6.9.37	120.6	Much better. V.S. murmur at apex conducted to axilla.

Table 27 (Contd.)

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Remarks.
22	M.McG.	11	6.8.36	87.3	Ill for 2 weeks. Praecordial pain for 10 days. Pericardial friction and double murmur present. Marked dyspnoea.
			12.8.36	98.9	Dyspnoea much less. No friction.
			20.8.36	102.3	General condition much better. Heart sounds improving in quality.

TABLE 28.

Rheumatic endocarditis with cardiac failure.

Case No.	Name	Age in years	Date	Cholesterol mg.%	Remarks.
23	F.K.	18 12	16.4.37	93.1	This has been diagnosed as ? "rheumatic" endocarditis and the history is as follows. Oedema for 11 days. Examination of heart, lungs, abdomen, nervous system and urine negative.
			27.4.37	81.6	Afebrile. Trace oedema. V.S. murmur at apex conducted to axilla.
			30.4.37	-	Died. Autopsy report "Endocarditis, cardiac failure, terminal broncho-pneumonia."
24	C.G.	8	20.3.36	140.0	Healthy until 3 weeks ago, became tired and listless. Now acutely ill with rheumatic endocarditis and cardiac failure.
			(14.8.37	111.5	General condition good. V.D. & V.S. murmurs, latter conducted to axilla.) (Vide Table 33.)
25	M.G.	10	10.5.37	81.6	No previous history of rheumatism. Ill for 3 weeks with rheumatic endocarditis. Dyspnoea, double murmurs and capillary pulsation. Liver 3 fb.
			24.5.37	90.1	Still acutely ill.
			29.5.37	-	Dismissed irregularly and died afterwards.
26	C.M.	11 6 12	21.9.36	114.3	Onset of acute rheumatism 1 month ago. Now has aortic and mitral lesion.
			24.9.36	-	Died. Embolism before death. No post mortem examination permitted.

Rheumatic endocarditis with cardiac failure (vide Table 28).

There are four cases in this group. Three of them were fatal, and in two (Nos. 23 and 25) the cholesterol ranged between 80 mg.% and 90 mg.%. Embolism occurred before death in the third subject (No. 26) and a normal value was observed three days before death. In the remaining case (No. 24) the cholesterol was 140.0 mg.% when the child was acutely ill with cardiac failure, while seventeen months later, when the child had recovered and the general condition was good, the blood cholesterol was 111.5 mg.%.

Taking the results for pericarditis, and endocarditis with failure, together, values below 100 mg.% were found in 60 per cent of the patients. It will be remembered that a similar percentage of low values was observed in rheumatic arthritis.

One may conclude, therefore, that while cardiac disease per se produces little modification of the blood cholesterol, acute complications such as arthritis, pericarditis, and endocarditis with cardiac failure, are often associated with low values. Nevertheless, normal or slightly elevated values are sometimes found in cases of pericarditis and cardiac failure. It is thought that there may be considerable variability of the blood cholesterol in individual cases in these conditions.

Pulse.

(a) Bradycardia.

Abel and Faust[9] have shown that cholesterol derivatives have a powerful action on the heart akin to digitalis. One would

therefore expect hypercholesterolemia to be associated with bradycardia, and it might be suggested that the slow pulse rate often found in cases of jaundice, for example, is related to an accompanying hypercholesterolemia. Garrod et alii[10] state that a pulse rate of sixty is common in chorea after all active movements have ceased, and one might contend that this is the result of the high cholesterol values during convalescence. This is, of course, a mere conjecture. Nevertheless, if one accepts the findings of Abel and Faust, it would seem feasible that severe hypercholesterolemia might induce bradycardia.

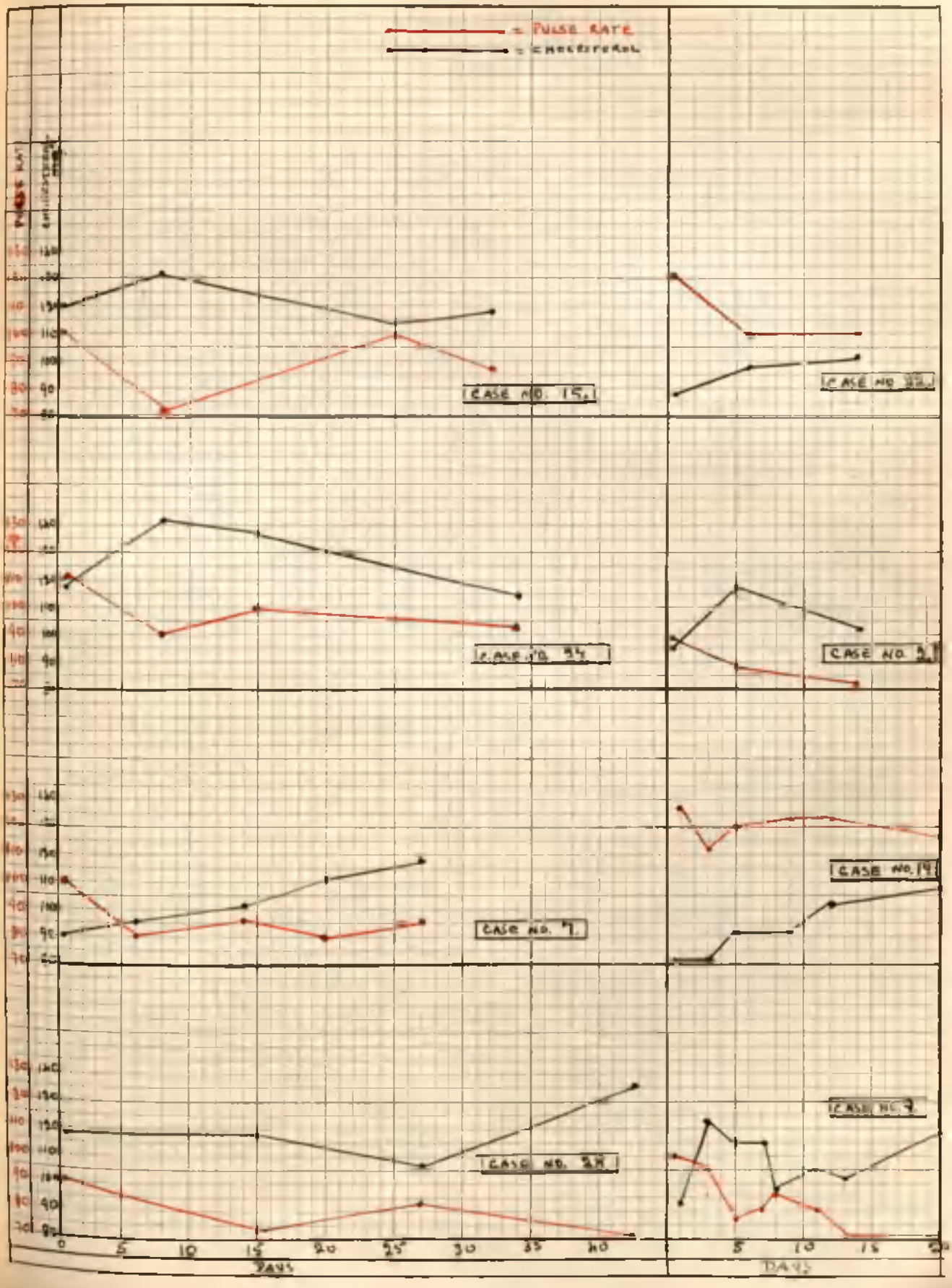
In the present investigation it was not possible to substantiate the above contention since none of the patients exhibited either a marked hypercholesterolemia, or a pulse rate of less than seventy.

(b) Tachycardia.

The relationship between tachycardia and the cholesterol value does not appear to have been discussed by any previous investigator.

In the present investigation a rapid pulse was associated, in the majority of cases, with a diminution of the blood cholesterol. Where serial estimations were made until both the cholesterol and the pulse rate became "normal," an inverse ratio was found in six out of eight cases (vide Chart 10).

Chart 10.


= PULSE RATE
= TEMPERATURE
CASE NO. 15.
CASE NO. 94
CASE NO. 9.
CASE NO. 24
0 5 10 15 20 25 30 35 40
DAYS
5 10 15 20
DAYS

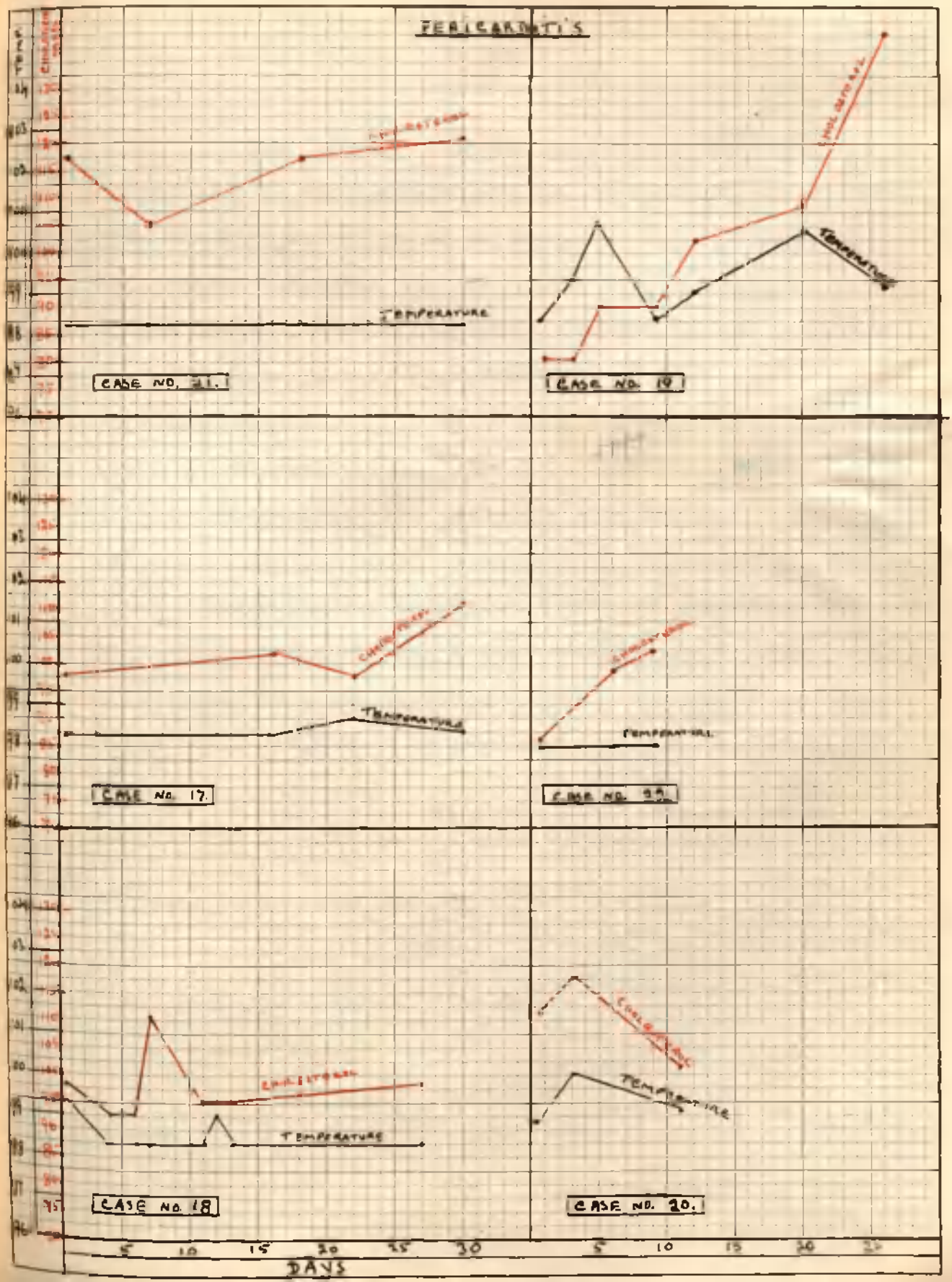
Temperature.

Some of the cases of articular rheumatism had fever of 100°F to 101°F for the first twelve to ninety six hours after admission. Other subjects had low fever of about 99°F for four or five days after admission to hospital. At the time of making the first determination of each series, described in the preceding pages, the temperature rarely exceeded 99°F, and in some patients this low fever recurred from time to time during the course of the illness. It is obvious, therefore, that fever was not an outstanding feature of any of these cases. The short duration of the fever was, of course, attributed to the administration of salicylates. The variations of temperature described above did not appear to disturb the cholesterol metabolism.

In pericarditis the fever was often of longer duration, and the following chart illustrates the lack of correlation between the variations of the cholesterol values and the temperature in six children with pericarditis.

One concludes, therefore, that there is no correlation between fever, per se, and the cholesterol values. This is in agreement with the findings of Stroesser[14] who estimated the blood cholesterol, before, during and after an artificial increase of the temperature in children.

Chart 11.


PERICARDITIS
CASE NO. 21.
TEMPERATURE
CASE NO. 19.
TEMPERATURE
CASE NO. 17.
TEMPERATURE
CASE NO. 18
TEMPERATURE
CASE NO. 20.
5
10
15
20
25
30
DAYS

Salicylate.

It was thought that the increase of the blood cholesterol in the convalescent period might be associated with the administration of salicylate. Accordingly, the cholesterol values of ten children who were receiving sodium salicylate were compared with ten who did not receive any salicylate mixture (see Chart 12). The patients receiving salicylate had acute articular rheumatism. Of those not receiving salicylate, seven had chorea, two had pericarditis and one had chronic rheumatism and was in poor general condition.

The cholesterol curves of the two groups are remarkably similar, there being a well marked rise in six, and a slight rise in three from each group. The absence of any significant difference between the cholesterol curves of these two groups leads one to conclude that the blood cholesterol is unaffected by the administration of salicylates.

Chart 12.

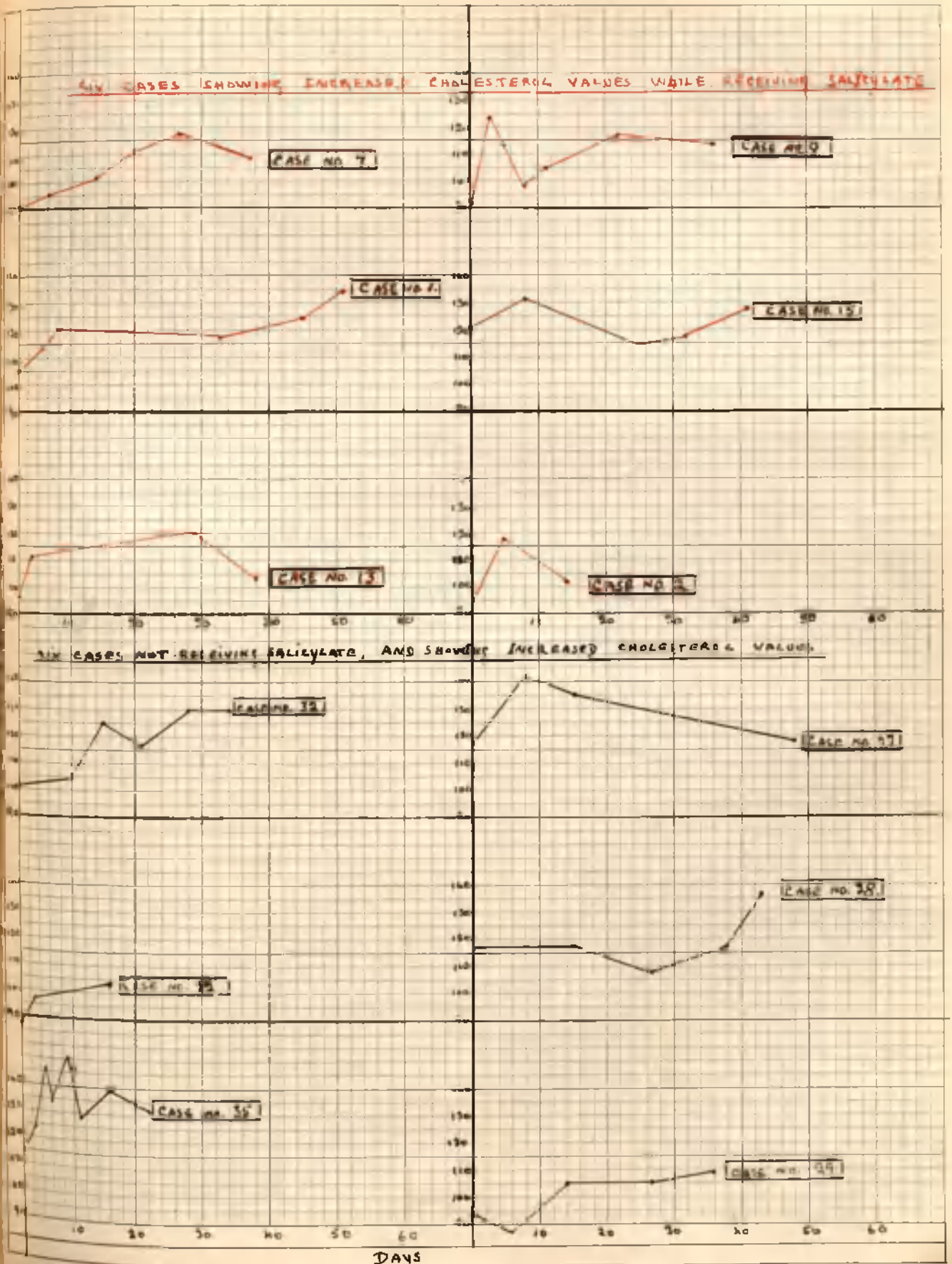
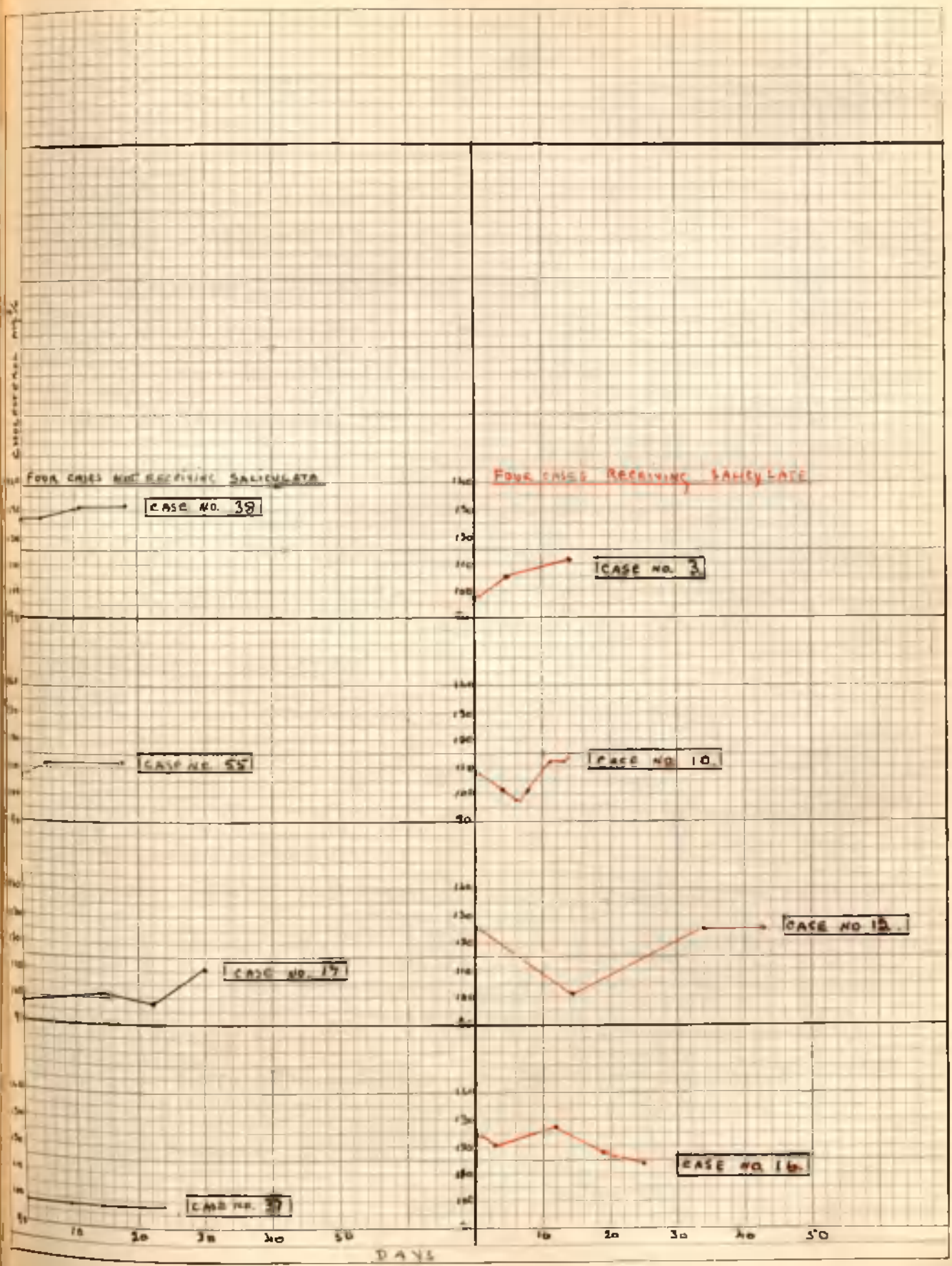

SIX CASES SHOWING INCREASED CHOLESTEROL VALUES WHILE RECEIVING SALICYLATE
CASE NO. 7.
CASE NO. 9.
CASE NO. 11.
CASE NO. 15.
CASE NO. 13.
CASE NO. 2.
SIX CASES NOT RECEIVING SALICYLATE, AND SHOWING INCREASED CHOLESTEROL VALUES.
CASE NO. 32.
CASE NO. 37.
CASE NO. 38.
CASE NO. 35.
CASE NO. 39.
DAYS

Chart 12 (Contd.)



CHOREA.

Lyons[15] demonstrated an emotional hypercholesterolemia in cats. Dobreff, Penef and Wittkower[16] conclude that emotional disturbances are accompanied by an increase of the blood cholesterol. They attribute this to the increased output of adrenalin. In the present investigation, however, adrenalin did not raise the cholesterol (vide page 232). Duncan[17] found a low serum cholesterol in patients with an excessive emotional reaction. Similar results have been obtained by Lockwood[18]. Hypocholesterolemia has been observed in some states of increased excitability of the nervous system such as hyperthyroidism and tetany, and it was thought that severe chorea, with its attendant emotional instability, might be associated with low cholesterol values.

Personal observations.

This group comprises twenty eight cases of chorea, of varying degrees of activity, in patients from two to twelve years of age. In eighteen subjects chorea was the first rheumatic manifestation to be observed.

Serial determinations were made in nineteen, and single determinations in nine patients. Few values below 100 mg.% were noted, although the cholesterol rose as convalescence progressed in about half of these subjects, and often reached a higher level than was ever observed in acute articular rheumatism.

Serial estimations.

The cases are divided into three sub-groups according to whether the cholesterol increased, remained more or less stationary, or decreased during the convalescent period.

(a) Increased values.

The results of this group are indicated in Table 29. Ten cases are included, and on the whole the cholesterol values differ little from those seen in many cases of acute rheumatism. In about half of them it fell a little towards the end of convalescence. In six patients the chorea had disappeared at the end of the period of observations, in the remaining four subjects it was much less active. It would appear, therefore, that the blood cholesterol rose during the period of recovery from chorea in ten out of nineteen patients on whom serial determinations were made. If, however, one examines these figures closely, it becomes obvious that the time of disappearance of the chorea did not coincide with the maximum cholesterol readings (vide Table 29). In the case of No. 27 the initial value was 117.2 mg.% and one week later it had risen to 143.7 mg.% but the chorea did not disappear until nine weeks afterwards, when the cholesterol had fallen to 120.7 mg.%. In three patients (Nos. 28, 29 and 30) the disappearance of the chorea was more or less coincident with the cholesterol increase. Subject No. 29 became ill with pericarditis about twelve weeks after the final cholesterol estimation. In two other cases the chorea subsided before the

cholesterol rose, and in one child (No. 35) the chorea remained unchanged in spite of a considerable increase of the blood cholesterol. This patient gave an initial value of 111.5 mg.%, the cholesterol rose gradually until a week later it reached its maximum of 150.6 mg.%. Thereafter it fell a little and the final reading was 111.5 mg.%. In the child R.R.(31) there was a history of acute rheumatism five weeks before the initial estimation, and the chorea had been active for two weeks. One week later the cholesterol was 10 mg.% higher and the chorea less active. Thereafter there was a coincident diminution in the activity of the chorea with a fall in the cholesterol values. This child was again observed ten months later with a second attack of chorea, and this time it was found that the cholesterol increased as the chorea diminished. Determinations before the onset of chorea are available in one child (No. 12) who was admitted on account of acute articular rheumatism, and the chorea appeared during the course of observation. The initial cholesterol value was 124.1 mg.%; three days later it was 117.2 mg.% and a fortnight after admission, when the chorea appeared, it had fallen to 102.3 mg.%. Thereafter it rose to 127.6 mg.% when the chorea became less active.

(b) Stationary values (vide Table 30).

There are four patients in this sub-group and the cholesterol values remained practically constant in every case. In two, 36 and 37, it remained at 98.9 mg.%. In one of them (37) the chorea subsided, while in the other it persisted. In the

latter case, however, the observations were only made over a period of six days. In case No. 38 the cholesterol remained between 127.6 mg.% and 131.0 mg.%, while the chorea was still active. Case No. 39 had mild chorea on admission and the cholesterol was 111.5 mg.%. Two months later, when the chorea had subsided, it was again 111.5 mg.%

(c) Diminished values.

This sub-group comprises five patients and their cholesterol values are indicated on Table 31. It is obvious from this table that there was a diminution of the blood cholesterol in every case, and the chorea became coincidently less active in four out of the five. In two children the initial values were somewhat high. One of them (40) was only observed over a period of three days, and the initial and final values were 160.9 mg.% and 134.0 mg.% respectively. There was, of course, no change in the chorea over this short period. In the other patient (44) the cholesterol fell gradually from 154.0 mg.% to 124.1 mg.% in the course of six weeks, while the chorea, which was very active when the first estimation was carried out, had completely subsided when the final estimation was made. It is interesting to note that the chorea was very active in these two patients with the highest cholesterol values. In another case (43) the cholesterol remained at 131.0 mg.% for about a month after admission, but fell to 114.3 mg.% two weeks later. During this time the chorea had gradually become less active.

In the remaining two children (Nos. 41 and 42) the cholesterol fell from 124.1 mg.% to 111.5 mg.%, and from 111.5 mg.% to 102.3 mg.%, respectively, and in both subjects the chorea had subsided when the final estimation was made.

It was impossible to carry out the cholesterol determinations in every case until the chorea had completely subsided, as some of them were sent to the country branch while the chorea was still slightly active.

In the following tables 29, 30, 31 and 32, the presence or absence of chorea is indicated thus:-

-	=	chorea absent
±	=	" slight.
+	=	" moderate.
++	=	" severe.

Cases showing an increase of the blood cholesterol during convalescence from chorea.

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Chorea	
12 (Table 24b)	R.W.	10	3.4.36	124.1	-	3.4.36. Has acute rheumatism which began six days ago.
			6.4.36	117.2	-	V.S. murmur at apex conducted to axilla.
			17.4.36	102.3	+	
			6.5.36	124.1	+	29.4.36. Follicular tonsillitis.
			15.5.36	124.1	+	4.6.36. Tonsillectomy.
			28.5.36	127.6	±	12.6.36. One nodule right elbow. V.S. murmur at apex,
			16.6.36	124.1	±	conducted to axilla.
27	P.C.	2	8.5.36	117.2	++	8.5.36. No history of rheumatism. Tonsillitis a few days
			16.5.36	143.7	+	ago. Severe chorea. Low fever.
			23.5.36	136.9	+	V.S. murmur at apex not conducted to axilla.
			28.5.36	124.1	+	25.6.36. Tonsillectomy.
			16.6.36	114.3	+	2.7.36. Dental extraction.
			26.6.36	117.2	-	6.8.36. General condition good. Heart sounds are pure.
			21.7.36	120.7	-	
			28.7.36	114.3	-	7.8.36. Transferred to convalescent home.
			6.8.36	105.7	-	
28	M.H.	5	5.2.36	117.2	++	5.2.36. No rheumatic history. Chorea for four weeks. Tonsils
			20.2.36	117.2	+	greatly enlarged and red.
			2.3.36	108.5	±	Heart sounds are pure.
			13.3.36	117.2	-	5.3.36. Tonsillectomy.
			18.3.36	136.0	-	18.3.36. General condition good. Heart sounds are pure.

Table 29 (Contd.)

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Chorea	
29	M.F.	5	27.1.37	93.1	±	27.1.37. Acute rheumatism. three months ago. Influenza
			2.2.37	87.3	±	five weeks ago. Chorea for four weeks.
			10.2.37	105.7	-	Tonsils greatly enlarged and septic. Double cardiac
			23.2.37	105.7	-	murmur.
			4.3.37	108.5	-	4.3.37. General condition good. V.S. murmur at apex conducted to axilla.
30	E.S.	8	20.10.36	131.0	±	20.10.36. Rheumatism four months ago. Chorea for ten
			16.11.36	140.3	-	weeks. Tonsils big. Afebrile. Heart sounds are
			7.8.37	105.7	-	pure. 16.11.36. General condition good. Heart sounds are pure. 7.8.37. Reported as out-patient. Very well. Heart sounds pure.
31 (1st attack)	R.R.	9	8.5.36	120.7	+	8.5.36. Rheumatism with arthritis five weeks ago,
			15.5.36	131.0	±	and irregular fever persisted until 23.4.36. Now afebrile
			23.5.36	124.1	±	No arthritis. V.S. murmur at apex, not conducted to
			28.5.36	102.3	±	axilla. 11.6.36. Tonsillectomy.
			16.6.36	98.9	-	16.6.36. General condition improved. No cardiac murmur.
(2nd attack)		10	10.3.37	105.7	±	10.3.37. Arthritis three weeks ago. Chorea for a
			19.3.37	108.5	-	week. Mitral and aortic lesions present.
			3.4.37	117.2	-	3.4.37. General condition very good. Heart I.S.Q.

Table 29 (Contd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Chorea	
32	C.C.	10	3.3.36	102.3	++	3.3.36. Healthy until 14.2.36 when chorea began.
			13.3.36	105.7	++	Severe chorea. Tonsils enlarged and red. Heart sounds
			18.3.36	126.7	++	are pure.
			24.3.36	117.2	++	14.3.36. to 18.3.36 temperature about 101°; Tonsillitis.
			31.3.36	131.0	+	24.3.36. Afebrile. Heart sounds pure.
			6.4.36	131.0	+	
			17.4.36	117.2	+	
			6.5.36	124.1	+	6.5.36. General condition moderately good. Heart sounds are pure.
33	M.B.	10	5.7.36	117.2	+	5.7.37. Acute rheumatism two years ago. Chorea for
			9.7.36	124.1	+	two weeks. Apical V.S. mur-
			21.7.36	117.2	+ -	mur conducted to axilla. 21.7.36. General condition better. Apical V.S. murmur conducted to axilla. 23.7.36. Dismissed to country branch.
34	M.R.	11	6.8.36	98.9	+	6.8.36. Acute rheumatism 2 months ago. Chorea for 3
			12.8.36	105.7	+	weeks. Tonsils very big and septic. Nodule on each
			20.8.36	102.3	-	elbow. V.S. murmur at apex conducted to axilla.
			22.10.36	131.0	-	22.10.36. General condition good. V.S. murmur at apex conducted to axilla.
35	E.D.	11	15.3.36	111.5	+	15.3.36. Chorea more or less constantly present for two
			18.3.36	124.1	+	years. General condition
			19.3.36	147.1	+	fair. Tonsils not enlarged.
			21.3.36	134.0	+	Heart sounds are pure.
			23.3.36	150.6	+	
			26.3.36	127.6	+	

Table 29 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Chorea	
35 (Ctd.)	E.D.	11	27.3.36	134.0	+	
			31.3.36	136.9	+	6.4.36. General condition improved. Heart sounds are pure.
			6.4.36	131.0	+	
			17.4.36	111.5	±	20.4.36. Dismissed to country branch.

TABLE 30.

Cases showing practically uniform values while in Hospital.

Case No.	Name	Age (yrs.)	Date	Cholesterol mg.%	Chorea	
36	A.S.	8	27.1.37	98.9	+	27.1.37. Rheumatism 18 months ago. Chorea for 2 months. Afebrile. V.S. murmur at apex conducted to axilla.
			2.2.37	98.9	+	
			(14.8.37	124.1	-)	14.8.37. Out-patient (see Table 33.)
37	N.McA.	9	23.2.37	98.9	+	23.2.37. Chorea for two weeks. Slight cough. Afebrile. V.S. murmur at apex not conducted to axilla. Rhonchi in chest.
			4.3.37	98.9	±	
			19.3.37	98.9	-	19.3.37. General condition better. Heart, V.S. at apex not well conducted to axilla.
38	I.H.	11	14.2.36	127.6	+	14.2.36. Scarlet fever three months ago. Chorea for six weeks. Tonsils red. Afebrile. Heart sounds are pure.
			18.2. 36	127.6	+	
			25.2.36	131.0	+	14.3.36. General condition improved. Heart sounds are pure.
			14.3.36	131.0	+	
39	M.S.	10	13.12.35	111.5	±	13.12.35. Acute rheumatism six months ago. V.S. murmur at apex conducted to axilla.
			1.2.36	117.2	-	
			13.2.36	111.5	-	13.2.36. General condition improved. Heart as on 13.12.35.

TABLE 31.

Showing a diminution of the blood cholesterol.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Chorea	
40	P.T.	7	28.12.35	160.9	±	28.12.35. Chorea for seven weeks. Good general condition V.S. murmur at apex not conducted to axilla. Afebrile. Chorea gradually becoming less active.
			30.12.35	134.0	±	
41	M.B.	7	28.8.36	124.1	+	28.8.36. Chorea for 6 weeks. Tonsils big. Heart sounds pure. Afebrile.
—			17.9.36	111.5	-	17.9.36. General condition good. Soft V.S. murmur at apex not conducted.
42	M.H.	9	26.6.36	111.5	++	26.6.36. Chorea for two months Tonsils big. Afebrile. Heart sounds are pure.
			4.7.36	105.7	+	9.7.36. General condition good. Heart sounds are pure.
			9.7.36	102.3	-	
43	P.H.	9	17.4.36	131.0	+	17.4.36. Acute rheumatism eight months ago. Low fever. Tonsils enlarged and red. Heart sounds are pure.
			8.5.36	131.0	±	
			15.5.36	131.0	±	8.5.36. Afebrile. Nodule on each elbow. V.S. murmur at apex not conducted to axilla.
			23.5.36	124.1	±	
			28.5.36	114.3	±	28.5.36. General condition better. Short V.S. murmur at apex not conducted.
44	H.B.	10	27.5.36	154.0	++	27.5.36. Tonsillitis two months ago. Chorea for three weeks. Basal V.S. murmur not conducted.
			16.6.36	131.0	+	
			25.6.36	127.6	+	3.7.36. Tonsillectomy.
			9.7.36	124.1	-	9.7.36. General condition better. V.S. murmur not conducted to axilla and not heard when sitting up.

Single estimations.

Single estimations were made on nine patients, and the results, which are tabulated below, do not suggest any correlation between the actual cholesterol value and the activity of the chorea.

TABLE 32.

Case No.	Date	Name	Age (yrs)	Cholesterol mg.%	Chorea	
45	14.5.36	S.H.	4	120.7	±	No history of rheumatism Chorea for four months. No cardiac lesion.
46	11.5.36	M.A.	7	98.9	±	Chorea two months ago. Rheumatism two weeks ago. No cardiac lesion.
47	20.12.35	J.D.	7	143.7	±	Chorea for six months. Basal systolic murmur, not conducted.
48	6.5.36	S.D.	8	131.0	+	No history of rheumatism. Chorea for one week. Heart sounds pure.
49	21.3.36	A.B.	9	127.6	+	Chorea a year ago and again six months ago. Presystolic murmur and V.S. at apex conducted to axilla.
50	6.8.37	F.McM.	11	111.5	+	Indefinite rheumatic pains 4 months ago. Chorea for six weeks. No cardiac lesion.
51	4.12.35	E.G.	12	102.3	+	First attack of chorea nine months ago, second attack four days ago. Heart - sounds pure.
52	22.10.36	M.R.	12	117.2	+	Chorea three years ago. Second attack began three months ago. V.S. murmur at apex, not conducted to axilla.
53	13.5.36	M.S.	12	117.2	++	Chorea a year ago. Second attack began seven weeks ago. Heart sounds are pure.

It is evident from the preceding tables that the patients with the most active chorea did not display the lowest cholesterol values. In two of the most severe cases, the cholesterol values were 102.3 mg.% and 154 mg.% respectively.

The children exhibiting the greatest cholesterol increase do not necessarily make the most rapid recovery. In the case of No. 35 the cholesterol rose from 111.5 mg.% to 150.6 mg.%, while during this period the chorea remained unchanged. In another case, No. 37, the cholesterol was 98.9 mg.% both when the chorea was moderately severe and after it had ceased.

These results, therefore, show conclusively that there is no apparent correlation between the level of the blood cholesterol and the severity of the chorea.

CHRONIC RHEUMATISM.

Ward[3], and Kaiser and Gray[4] found increased cholesterol values in chronic juvenile rheumatism with definite cardiac damage. The results of the present investigation are not, however, in agreement with these findings.

There are fifteen subjects in the present series, and their ages range from five to twelve years. This group comprises children who have had recurrent chorea or acute rheumatism not less than four months previously, and who had well established cardiac lesions. All were afebrile and in moderately good health, and they were not confined to bed. Some were out-patients attending the cardiac clinic, on whom previous determinations had been made. The results are indicated on Table 33, and they show remarkable uniformity. In all cases, the cholesterol is well within normal limits, and exhibits a very limited range of values, the highest being 127.6 mg.% and the lowest 108.5 mg.%. These results differ from those observed in acute rheumatism, where the highest value was 134.0 mg.% and the lowest 81.6 mg.%. Serial determinations were made on three cases but no significant variations were observed. A history of more than one attack of acute rheumatism or the presence of an aortic lesion in addition to the mitral lesion, did not appear to have any influence on the blood cholesterol. In view of the low values sometimes found in pericarditis (vide page 106) it is interesting to note that one child (No. 17) had a blood cholesterol of 111.5 mg.%, one year after recovery from this complication.

The uniformity of the cholesterol values in this group may possibly be attributed to the absence of any acute infection, and to the comparatively good general condition of these patients.

TABLE 33.

Chronic Rheumatism.

Case No.	Name	Age	Date	Cholesterol mg.%	
54	J.McA.	10	7.7.36	108.5	Acute rheumatism 2 years ago and again 4 months ago. General condition good. Apical V.S. murmur, poorly conducted to axilla. Condition complicated by mediastinal tuberculosis.
55	E.G.	$5\frac{11}{12}$	4.7.36	108.5	Acute rheumatism 9 months ago. General condition fairly good. V.D. and V.S. murmurs, latter conducted to axilla.
			9.7.36	111.5	General condition better. Heart as on 4.7.36.
			21.7.36	111.5	I.S.Q.
			28.7.36	108.5	I.S.Q.
			6.8.36	111.5	General health much better. V.S. murmur at apex conducted to axilla.
56	C.G.	$5\frac{10}{12}$	28.8.37	111.5	Acute rheumatism on 4.6.36. General condition good. Apical V.D. & V.S. murmurs, latter conducted to axilla
57	A.McA.	6	9.11.35	108.5	Acute rheumatism 4 months ago. General condition moderately good. Rheumatic nodules R. elbow. V.S. murmur at apex conducted to axilla.

Table 33 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	
58	C.P.	7	14.8.37	124.1	Acute rheumatism 3 years ago. General condition fairly good. Loud V.S. best heard at apex and conducted to axilla.
59	T.C.	9	22.5.36	127.6	Acute rheumatism 5 months ago. Slight recurrence on 18.5.36. Nodule on elbow and knee. Apical V.S. murmur conducted to axilla.
			28.5.36	111.5	Nodules still present. Heart I.S.Q
			25.6.36	117.2	Condition improved generally. Nodules and heart I.S.Q.
60	J.H.	10	13.12.35	124.1	Severe chorea from 1.11.35 until 6.12.35. V.S. and V.D. murmurs at apex, former conducted to axilla.
			17.12.35	124.1	
61	F.F.	12	28.8.37	111.5	Acute rheumatism 8 years ago and again 2 years ago. General condition good. V.D. & V.S. murmurs, former conducted down the sternum and the latter to the axilla.
62	M.D.	$10\frac{6}{12}$	7.7.36	127.6	Acute rheumatism a year ago. Vague pains since then. V.S. murmur apex not conducted.
			28.8.36	111.5	Basal V.S. barely audible at apex. General condition fairly good.
63	E.C.	10	28.8.37	108.5	Acute rheumatism 8 months ago. General condition now good. Apical V.S. murmur conducted to axilla. Afebrile.
*13 (Table 24b)	H.R.	$12\frac{9}{12}$	4.9.37	114.2	Acute rheumatism 18 months ago. General condition good. V.S. murmur at apex conducted to axilla.

Table 33 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	
*17 (Table 27)	W.O.	$5\frac{6}{12}$	20.8.37	111.5	Pericarditis a year ago. General condition now very good. Loud V.S. murmur best heard at apex and conducted to axilla.
*24 (Table 28)	C.G.	8	14.8.37	111.5	Acute rheumatism 18 months ago. V.D. and V.S. murmurs, latter conducted to axilla. General condition good.
*34 (Table 29)	M.R.	$11\frac{11}{12}$	14.8.37	114.3	Acute rheumatism a year ago. General condition good. Apical V.S. conducted to axilla.
*36 (Table 30)	A.S.	9	14.8.37	124.1	Chorea 8 months ago. General condition good. V.S. murmur at apex conducted to axilla.

* For previous determinations on these cases, see appropriate tables.

Rheumatic nodules.

The close association of nodules with carditis led one to tabulate the blood cholesterol values of eighteen children, nine of whom had nodules. The remaining children, though they had rheumatic manifestations had not at any time exhibited nodules. The figures are shown on Table 34 and the average for one group is 103.9 mg.% and for the other 107.0 mg.%.

This series of cases, therefore, does not show any correlation between rheumatic nodules and the blood cholesterol.

TABLE 34.

Without nodules.

Case No.	Cholesterol mg.%
3	98.9
4	105.7
8	96.0
14	105.7
17	98.9
22	87.3
31	120.7
39	111.5
55	108.5
Av.	103.9

With nodules.

Case No.	Cholesterol mg.%
7	90.1
11	105.7
12	124.1
13	96.0
19	81.6
37	98.9
44	131.0
58	108.5
60	127.6
Av.	107.0

Tonsils.

Ward[3] did not find any correlation between infected tonsils and cholesterol in acute rheumatism.

In the present investigation very little difference was observed between the cholesterol values of children with enlarged tonsils and recurrent sore throat, and children having had tonsillectomy performed several years previously. The cholesterol values for thirteen children with considerably enlarged and inflamed tonsils are compared in Table 35 with the figures for ten children who had tonsillectomy performed one or more years previously. There is no significant difference between figures for the two groups (109.4 mg.% and 107.3 mg.%).

TABLE 35.

Tonsils absent		Tonsils +++	
Case No.	Cholesterol mg.%	Case No.	Cholesterol mg.%
5	108.5	7	90.1
6	105.7	10	108.5
9	93.1	13	96.0
11	105.7	15	120.7
14	105.7	22	87.3
24	140.0	28	117.2
35	111.5	31	102.3
37	98.9	45	120.7
54	108.5	49	127.6
62	117.2	51	102.3
		55	108.5
		56	105.7
		57	108.5
Av.	109.4	Av.	107.3

Seasonal variations of the blood cholesterol in acute rheumatism and chorea.

Kaiser and Gray observed a seasonal variation of the blood cholesterol in both healthy and rheumatic children. Estimations made in the summer were slightly lower than those made in the winter.

Personal observations.

Estimations were made on 13 children whose rheumatism commenced between November and April and in 14 cases whose rheumatism commenced between May and October (vide Table 36a). The average figures for the two groups are 108.2 mg.% and 102.4 mg.% respectively. The difference between the winter and summer results was not considered sufficiently definite to be of any significance.

TABLE 36.

(a) Acute rheumatism.

Commencing between May & Oct.

Case No.	Cholesterol mg.%
2	96.0
3	98.9
4	105.7
8	96.0
11	105.7
13	96.0
15	120.7
17	98.9
20	111.5
21	117.2
22	87.3
25	81.6
26	114.3
56	105.7
Av.	102.4

Commencing between Nov. & April.

Case No.	Cholesterol mg.%
1	105.7
5	108.5
6	105.7
7	90.1
9	93.1
10	108.5
12	124.1
14	105.7
16	134.0
18	117.2
19	81.6
23	93.1
24	140.0
Av.	108.2

Similar observations were made on twenty eight cases of chorea, and a difference of only about 2 mg.% was found between the figures for the summer and winter months (vide Table 36b). In the present series of normal children referred to on page 23 no seasonal variation was found.

TABLE 36.

(b) Chorea

Commencing between May and October.		Commencing between November and April.	
Case No.	Cholesterol mg.%	Case No.	Cholesterol mg.%
27	117.2	12	124.1
30	131.0	28	117.2
31	120.0	29	93.1
33	117.2	32	102.3
34	98.9	35	111.5
41	124.1	36	98.9
42	111.5	37	98.9
44	154.0	38	127.6
45	120.5	39	111.5
46	98.9	40	160.9
48	131.0	43	131.0
50	111.5	47	143.9
53	117.2	49	127.6
		51	102.3
		52	117.2
Av.	119.4	Av.	117.8

General Conclusions.

1. Rheumatic arthritis, pericarditis, and endocarditis with cardiac failure, were attended in fifty per cent of cases by low cholesterol values.

2. The blood cholesterol was increased in amount during the course of an uneventful convalescence, in practically every case of acute rheumatism.

3. Oscillations of the cholesterol values during the course of articular rheumatism were usually associated with some complication. Variability of this sort was not observed in cases recovering from chorea; few, however, had complications.

4. There was no difference between the cholesterol values of children suffering from their first or second attack of acute rheumatism.

5. The blood cholesterol was not significantly affected by fever or by the administration of salicylates.

6. No correlation was found between the blood cholesterol and the activity of the chorea.

7. The blood cholesterol in chronic rheumatism with well established cardiac lesions was within normal limits in every case.

SECTION 3.

RENAL DISEASE.

In view of the fact that both the maximum and minimum values for blood cholesterol have been observed in renal disease, it is surprising that this subject has incited so few investigators. Both Campbell[1] and Maxwell[2] have commented upon our lack of knowledge of the blood cholesterol in nephritis.

High values are found in chronic parenchymatous nephritis, and the blood cholesterol in acute nephritis and in chronic interstitial nephritis is the subject of dispute. Gardner[3] believes that hypercholesterolemia occurs only when nephritis is complicated by the so-called nephrotic syndrome, a view which is supported by Trumper and Cantarow[4].

The majority of workers agree that hypocholesterolemia occurs in uraemia, and very low results have been reported. Cantarow and McCool[5] have, however, pointed out that low values are found in a variety of "terminal states", and may not therefore be "specific for uraemia."

The cause of these variations in the blood cholesterol is unknown. Disturbed fat metabolism, diminution of the serum proteins and renal degeneration, are a few of the apparently inadequate explanations which have been formulated.

A. ACUTE NEPHRITIS.

The association of cholesterol variations with infective processes has been indicated in the earlier part of this work; and the important rôle of a streptococcal infection in the etiology of nephritis is well known[6][7]. Fleming[8] attributes the increased cholesterol values during convalescence in two of her cases to the subsidence of an infection.

Personal observations.

Serial determinations were made on twenty five subjects, and single determinations were made on eighteen. These cases have been studied with special reference to the rôle of oedema and infection, in the cholesterol variations in nephritis.

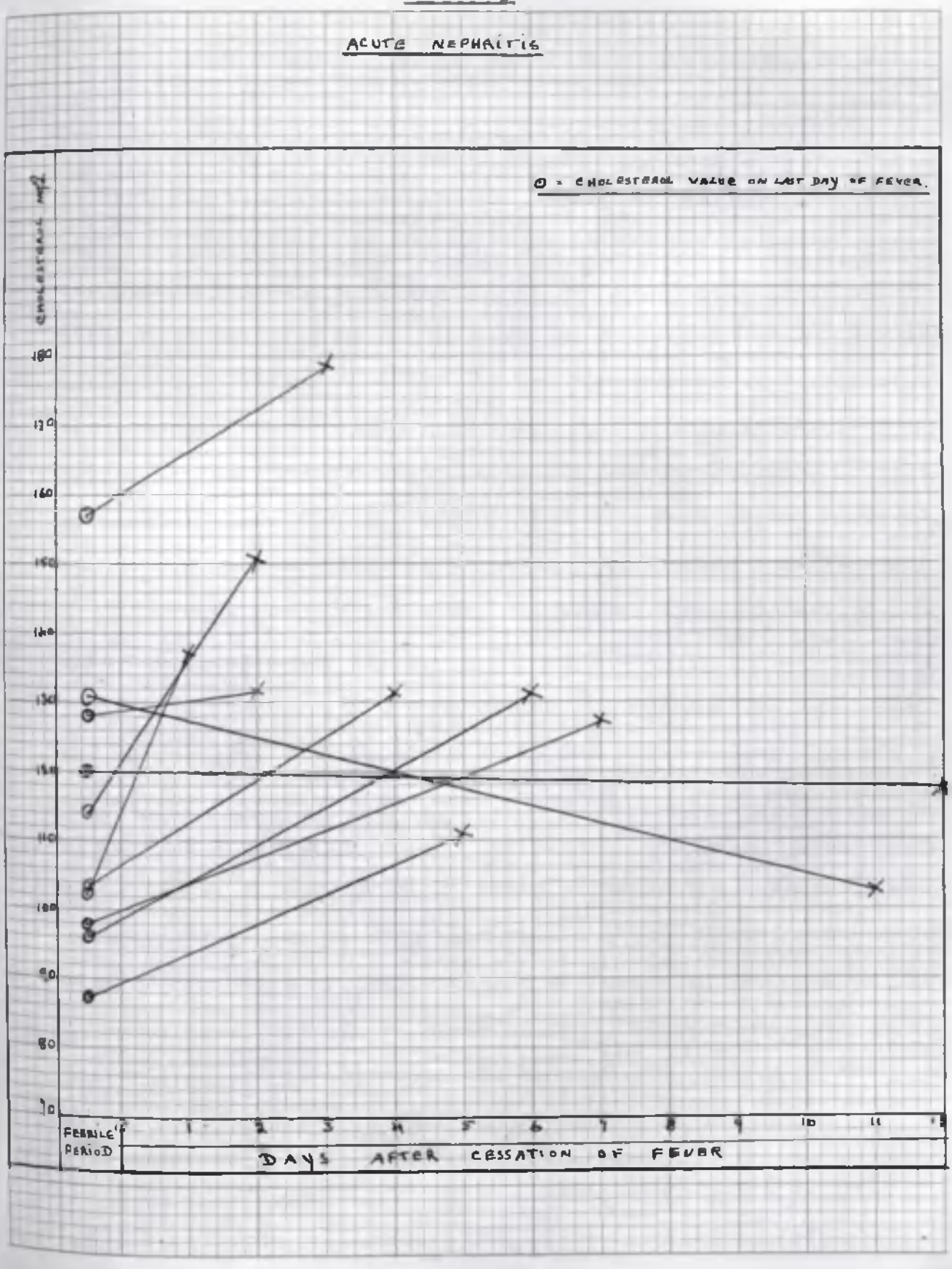
Infection.

A history of infection was obtained in all but two children, and fever was actually present when the initial determinations were made in ten cases. The figures for these ten cases with fever are tabulated below.

TABLE 37. (Vide chart 13.)
Showing an increase within 7 days of the cessation of fever.

Case No.	Temp.	Cholesterol mg.%		Days after fever.
		During fever	After cessation of fever	
1	99.4	102.3	136.9	1
2	100.0	131.0	105.7	11
6	99.0	98.9	127.6	7
8	99.4	128.1	131.0	2
11	100.6	102.5	131.0	4
17	99.6	157.4	178.1	3
19	102.2	114.3	150.6	2
21	100.4	120.7	117.2	15
22	99.0	96.0	131.0	6
23	100.0	87.3	111.5	5

Chart 13.


ACUTE NEPHRITIS
⊙ = CHOLESTEROL VALUE ON LAST DAY OF FEVER.
CHOLESTEROL mg%
180
170
160
150
140
130
120
110
100
90
80
70
FEBRILE PERIOD
1
2
3
4
5
6
7
8
9
10
11
DAYS AFTER CESSATION OF FEVER

It is evident from the above table that normal or low cholesterol values were obtained in nine out of the ten cases.

Another infection occurring during the course of the illness was also found to produce a fall in the cholesterol. In case No. 12 (vide Table 40) an alveolar abscess producing fever was associated with a diminution of the blood cholesterol from 124.1 mg.% to 111.5 mg.%. In case No. 3 (vide Table 39) a moderately severe attack of diarrhoea was accompanied by a fall of the cholesterol from 164.3 mg.% to 111.5 mg.% within twenty four hours. In case No. 14 (vide Table 40) the occurrence of an upper respiratory infection was accompanied by a fall of the cholesterol from 131.0 mg.% to 117.2 mg.% and the temperature rose to 102.0°F.

These results indicate, therefore, that hypercholesterolemia and pyrexia are seldom found together.

It has already been shown in the sections on pneumonia and rheumatism, that an increase in the blood cholesterol occurred during convalescence from these infections. It is not, therefore, altogether surprising that an increase of the blood cholesterol was obtained in many of these cases of nephritis. Referring again to Table 37 it can be seen that when the cholesterol was estimated within seven days of the cessation of fever, an increase was noted in every case. It can be observed from Tables 38-40 that this post infective rise was followed by a gradual return of the cholesterol values to within normal limits in all cases.

Oedema.

Maxwell in 1928[2] made observations on both adults and children and found increased cholesterol values in every case exhibiting oedema. Fleming[8], in 1931, found that the oedema was not proportionate to the amount of cholesterol in the blood. Sylvestre[9] found hypercholesterolemia almost constantly present in children with acute nephritis, though low values were found in gravely ill patients. This author did not, however, find any correlation between the oedema, albuminuria or haematuria and the blood cholesterol. Peters and Van Slyke[10] believe the co-existence of oedema and lipaemia in nephritis to be only a coincidence, because oedema is found in other conditions without any alteration of the blood lipoids.

The results of the present investigation are in agreement with the contention of Peters and Van Slyke.

In the serial determinations indicated on Tables 38, 39 and 40 oedema was present in twenty one subjects at the time of making the initial estimation, and there was a history of oedema, or at least puffiness, in all but one case.

Severe oedema was present in only two subjects, and the results are indicated in Table 38. It is apparent from the table that the cholesterol variations during the course of the illness in these two subjects do not differ markedly from what has been found in pneumococcal and rheumatic infections. The maximum figures for these two subjects were 147.2 mg.% and 131.0 mg.% respectively. The absence of high values in these two cases exhibiting marked oedema is noteworthy.

Oedema was absent when the initial determination was made in four children (vide Table 39) and the maximum values for each case were 204.0 mg.%, 178.1 mg.%, 164,3 mg.% and 136.9 mg.%, respectively. It is interesting to note that the highest value of the series was found im this group.

The remaining nineteen children (vide Table 40) had slight or moderate oedema and only six of them displayed a parallel fall of the blood cholesterol with the subsidence of the oedema. In two subjects (Nos. 22 and 23) values of 90.2 mg.% and 84.5 mg.%, respectively, were found and these low values associated with oedema are noteworthy. The maximum cholesterol values exceeded those observed during convalescence from pneumonia in only two instances.

In a series of eighteen single estimations indicated on Table 41, the absence of any correlation between the blood cholesterol and oedema is apparent.

TABLE 38.

Cases with marked oedema.

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
1	J.D.	9	21.11.35	102.3	++	99.4	History - Sore throat 7 days ago. Oedema since then. Has numerous septic spots on skin. Urine contains red blood cells and casts. 25.11.35 - B.P. 154/90. 1.12.35 - B.P. 114/80. 6.12.35 - B.P. 111/70. 17.12.35 - General condition much better. Urine still contains some red blood cells and casts. 17.1.36 - Dismissed to country branch.
			22.11.35	147.2	++	99.0	
			23.11.35	143.7	++	99.0	
			24.11.35	136.9	+	-	
			25.11.35	139.3	+	-	
			26.11.35	139.3	+	-	
			27.11.35	134.0	+	-	
			28.11.35	120.8	±	-	
			29.11.35	124.1	±	-	
			30.11.35	128.1	-	-	
			2.12.35	134.0	-	-	
			3.12.35	131.0	-	-	
			9.12.35	131.0	-	-	
			19.12.35	131.0	-	-	
			30.12.35	128.1	-	-	
2	E.G.	11	20.6.37	131.0	++	100.0	History - Abdominal pain and vomiting 3 weeks ago. 5.7.37 - Increasing ascites and oedema. Albumen and blood in urine. Irregular fever from 4.6.37 to 24.6.37. 8.9.37.- Very well; no oedema; urine clear.
			5.7.37	105.7	+	-	
			9.7.37	117.2	+	-	

TABLE 39.

Cases without oedema.

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
3	J.M.	3	30.9.36	160.8	-	-	History - Vomiting and fever 10 days ago.
			6.10.36	164.3	-	-	Face puffy on 29.9.36. Urine contains red
			7.10.36	111.5	-	-	blood cells and casts.
			16.10.36	136.9	-	-	7.10.36 - moderately severe diarrhoea. Dismissed "well" on 30.10.36.
4	T.O'B.	5	28.4.36	204.0	-	-	History - Face said to have been puffy for
			6.5.36	150.6	-	-	3 weeks. Urine contains red blood cells
			12.5.36	131.0	-	-	and casts. 12.5.36 - only a few red cells in urine. Dismissed "well" on 5.6.36.
5	R.J.	7	28.4.36	131.0	-	-	History - Right otitis media 10 days ago.
			6.5.36	120.7	-	-	Urine contains blood and casts.
			12.5.36	120.7	-	-	22.5.36 - General condition very good;
			18.5.36	136.9	-	-	urine clear.
			22.5.36	178.1	-	-	
6	E.O'D.	9	23.1.36	98.9	-	99.0	History - Oedema 5 days ago. V.S. murmur
			24.1.36	98.9	-	99.0	at apex not conducted to axilla.
			31.1.36	127.6	-	-	23.1.36 - B.P. 132/92. Urine contains red
			6.2.36	131.0	-	-	blood cells and casts. Dismissed "well" on
			12.2.36	136.9	-	-	12.2.36.

TABLE 40.

Cases with moderate oedema.

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
7	J.S.	2	20.1.36	108.5	±	-	History - Stiff neck a week ago. Temperature 102°0 4 days ago. Tonsils enlarged and inflamed. Urine contains a few red blood cells and casts.
			22.1.36	102.3	±	-	
			23.1.36	105.7	-	-	
			24.1.36	108.5	-	-	
			30.1.36	131.0	-	-	31.1.36 - Child very well. Occasional red blood cells and casts in urine.
			31.1.36	131.0	-	-	
8	J.H.	3	21.12.35	128.1	±	99.4	History - Oedema for 4 days. Tonsils acutely inflamed, and rhonchi all over left side of chest. Urine contained blood and casts. Dismissed irregularly on 16.1.36.
			23.12.35	131.0	±	-	
			3.1.36	111.5	-	-	
9	M.H.	3	12.2.36	157.4	+	-	History - No history of recent infection. Oedema for 4 days. Tonsils enlarged and red. Coarse râles all over chest. Urine contains albumen +++, casts and blood +++. 13.2.36 - N.P.N. = 21.6 mg.%. 16.2.36 - B.P. = 96/64. 19.2.36 - Urine still contains red blood cells and casts. 15.3.36 - Urine clear. Dismissed "well" on 21.3.36.
			13.2.36	131.0	+	-	
			14.2.36	143.7	+	-	
			15.2.36	143.7	±	-	
			19.2.36	136.9	-	-	
			20.2.36	120.7	-	-	
			21.2.36	120.7	-	-	
			24.2.36	117.2	-	-	
			25.2.36	124.1	-	-	
			5.3.36	124.1	-	-	
			15.3.36	111.5	-	-	

Table 40 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
10	C.B.	4	15.3.36	117.2	±	-	History - Fever and oliguria for 2 days.
			16.3.36	140.0	±	-	Temp. of 101.0 on the 14/3/36.
			18.3.36	153.0	±	-	15.3.36 - Urine contains red blood cells & casts
			23.3.36	150.0	-	-	27.3.36 - There are still a few red blood
			25.3.36	131.0	-	-	cells on microscopic examination of urine.
			27.3.36	136.9	-	-	3.4.36 - Urine clear. Was dismissed "well"
			3.4.36	120.7	-	-	on 15.4.36.
11	A.W.	4	27.2.36	102.5	±	100.6	History - Oedema for 2 days. Urine contains
			2.3.36	131.0	±	-	blood and casts.
			7.3.36	136.9	-	-	7.3.36 - red blood cells in urine on microscopic examination. Dismissed "well" on 11.3.36.
12	A.McL.	5	30.1.36	136.9	+	-	History - Oedema for 10 days. Vomiting for 2
			1.2.36	131.0	±	-	days. Tonsils are greatly enlarged and
			3.2.36	124.1	±	-	septic. Urine contains abundant blood
			12.2.36	111.5	-	99.4	and casts.
			15.2.36	150.6	-	-	2.2.36 - B.P. = 96/80.
			21.2.36	114.3	-	-	12.2.36 - Alveolar abscess.
			22.2.36	111.5	-	-	23.2.36 - Still a few red blood cells and casts in urine.
			24.2.36	105.7	-	-	6.3.36 - General condition fairly good. Dismissed to country branch
			3.3.36	117.2	-	-	

Table 40 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
13	D.D.	5	25.7.36	120.7	±	-	History - oedema for 6 days. No history of acute infection. 25.7.36 - Urine contains blood and casts. 19.8.36 - Urine clear. Child dismissed "well" on 4.9.36.
			3.8.36	143.6	-	-	
			6.8.36	105.7	-	-	
			12.8.36	105.7	-	-	
			19.8.36	117.2	-	-	
14	D.H.	6	9.9.36	131.0	±	-	History - Oedema for 5 days. Urine contains red blood cells and casts. Upper respiratory infection from 18.9.36 to 23.9.36. Dismissed "well" on 23.10.36.
			22.9.36	117.2	-	102.0	
15	B.C.	6	13.5.37	133.4	±	-	History - Oedema for 9 days. Tonsils enlarged and septic. Urine contains red blood cells and casts. Dismissed "well" on 10.6.37.
			26.5.37	124.1	-	-	
16	W.McK	6	12.10.36	108.5	±	-	History - Face puffy for 4 days. Tonsils big and septic. Urine much albumen and a few red blood cells. Dismissed "well" on 6.11.36.
			29.10.36	105.7	-	-	
17	M.G.	6	3.4.36	157.4	+	99.0	History - Oedema for 1 week. Oliguria for 5 days. Tonsils greatly enlarged and pus in crypts. Short V.S. murmur at apex not conducted to axilla. B.P. 134/104. Urine contains blood and casts. N.P.N. 46.4 mg.
			6.4.36	178.1	+	-	
			8.4.36	131.0	+	-	
			17.4.36	136.9	±	-	
			22.4.36	140.0	-	-	

Table 40 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
17	M.G. (Ctd.	6	6.5.36	134.0	-	-	8.4.36 - General condition improving.
			9.5.36	140.0	-	-	13.5.36 - Much better. Dismissed "well" on 29.5.36
			13.5.36	131.0	-	-	
18	W.R.	7	3.4.37	131.0	+	-	History - Oedema for 1 wk. Temp. 101.0 from 30.3.37
			5.4.37	117.2	±	-	to 2.4.37. Urine contains blood and casts. Dismiss-
			7.4.37	117.2	-	-	ed "well" on 14.4.37.
19	C.P.	7	20.2.36	114.3	±	102.2	History - Oedema for 2 weeks. The urine contains
			22.2.36	150.6	-	-	abundant blood and casts. 23.2.36 -B.P. 100/60.
			24.2.36	140.0	-	-	3.3.36 - The urine contains
			25.2.36	143.7	-	-	occasional red blood cells. Child was dismissed "well"
			26.2.36	124.1	-	-	on 31.3.36.
			27.2.36	120.7	-	-	
			28.2.36	120.7	-	-	
			3.3.36	120.7	-	-	
			15.3.36	120.7	-	-	
			27.3.36	124.1	-	-	
20	M.L.	8	19.8.36	196.6	+	-	History - Oedema for 8 days. Tonsils acutely in-
			21.8.36	108.5	+	-	flamed. Urine contains casts and red blood cells.
			1.9.36	124.1	±	-	Dismissed "well" on 2.10.36.
21	E.M.	8	28.4.36	120.7	±	100.4	History - Oedema for 3 days. Rhonchi all over
			13.5.36	117.2	-	-	chest. Urine contains red blood cells & casts.
			28.5.36	111.5	-	-	Dismissed "well" on 3.7.36.

Table 40 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
22	T.B.	9	9.11.35	131.0	±	99.0	History - oedema for 1 week. There is slight oedema of limbs & face is puffy. There is a short V.S. murmur at the apex, not conducted to axilla. B.P. 140/90. Urine contains blood and a few casts. From the 25th until the 30th the urine was free from casts but a few blood corpuscles were found on microscopic examination. The child made a good recovery and was dismissed on 17.1.36.
			10.11.35	96.0	±	99.0	
			11.11.35	98.9	±	-	
			12.11.35	90.2	±	-	
			13.11.35	94.2	-	-	
			14.11.35	98.9	-	-	
			16.11.35	131.0	-	-	
			18.11.35	128.1	-	-	
			19.11.35	124.1	-	-	
			20.11.35	124.1	-	-	
			21.11.35	124.1	-	-	
			22.11.35	117.2	-	-	
			2.12.35	105.7	-	-	
			9.12.35	124.1	-	-	
			19.12.35	124.1	-	-	
			30.12.35	120.8	-	-	
23	A.W.	9	29.11.35	93.1	±	100.0	History - Tonsillitis 2 weeks ago. Oedema for 1 week. There is slight oedema of the lumbo-sacral region. B.P. = 160/94. The urine contains red blood cells & casts. 30.12.35 - The urine still contains casts & a few red blood cells on microscopic examination. 15.3.36 - Urine clear. The child made a good recovery & was dismissed on 31.3.36.
			30.11.35	87.3	±	100.0	
			1.12.35	87.3	±	-	
			2.12.35	84.5	±	-	
			3.12.35	90.2	±	-	
			4.12.35	93.1	±	-	
			5.12.35	111.5	-	-	
			8.12.35	108.6	-	-	
			9.12.35	108.6	-	-	
			12.12.35	124.1	-	-	
			19.12.35	108.6	-	-	
			30.12.35	102.3	-	-	
			15.3.36	98.9	-	-	

Table 40 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Oedema	Fever	
24	M.O'H.	10	22.1.36	134.0	±	-	History - Vomiting a week ago, ill since then. Prolonged convulsion on 19.1.36. Tonsils septic. Moist rales left base. B.P.= 148/120. Urine contains blood and casts. 12.2.36 - No casts, but very occasional red blood cell. 10.3.36 - General condition good; urine clear.
			31.1.36	136.9	-	-	
			5.2.36	140.0	-	-	
			12.2.36	143.7	-	-	
25	C.M.	10	29.7.36	105.7	+	-	History - Oedema for one week. Tonsils septic. Urine contains red blood cells & casts 6.8.36 - Urine clear. Dismissed "well" on 21.8.36.
			6.8.36	124.1	-	-	
			11.8.36	114.2	-	-	

TABLE 41.

Single determinations on 18 cases of acute nephritis.

Case No.	Name	Date	Age in yrs.	Cholesterol mg.%	N.P.N. mg.%	Fever	Urine		Oedema	Duration of Oedema.
							Casts	Blood		
26	A.M.	6.4.36	5	181.5	29.7	100.0	+	+	-	-
27	J.C.	29.1.36	3	164.3	84.0	-	+	+	±	5 days
28	M.D.	11.2.36	8	154.0	-	-	±	±	±	11 "
29	J.McL.	31.5.37	5	143.7	57.5	-	+	+	±	2 "
30	F.C.	30.8.37	5	143.7	100.0	101.8	+	+	±	7 "
31	D.McC.	25.2.36	2	136.9	28.4	-	±	±	±	8 "
32	W.P.	24.4.36	5	136.9	25.0	-	+	+	±	4 "
33	J.S.	21.1.36	3	131.0	26.0	-	+	+	-	-
34	D.H.	21.4.36	4	131.0	41.3	100.0	+	+++	++	10 days
35	D.H.	9.9.36	6	131.0	44.7	-	+	+	±	5 "
36	M.McM.	21.10.36	3	127.5	61.7	101.4	+	+	-	-
37	J.C.	13.9.37	4	126.5	28.9	-	+	+	±	8 days
38	W.W.	9.9.36	6	124.1	55.7	99.8	+	+	+	5 "
39	M.F.	30.6.36	2	124.1	-	-	±	±	-	-
40	F.McK.	28.8.36	8	111.5	27.3	-	±	±	+	10 days
41	W.McA.	8.4.37	3	111.5	28.4	-	+	+	±	4 "
42	N.M.	5.2.36	3	105.7	-	-	+	+	-	-
43	J.Y.	11.3.37	4	98.9	-	-	+	+	+	7 days

In Table 42 the concomitant changes in the blood cholesterol and the body weight are indicated in twelve children. Loss of weight was associated with a diminution of the cholesterol in five, and an increase in five subjects. There was a coincident increase in weight and rise of the cholesterol in one patient. The absence of any correlation is therefore apparent.

The oedema was of recent onset in every child and it is therefore impossible to say whether or not there is any correlation between the duration of the oedema and the blood cholesterol values. Case No. 4, however, displayed the maximum value of the series and also gave the longest history; oedema having been present for three weeks before admission to hospital.

It will be remembered that Maxwell[2] found hypercholesterolemia in all cases of acute nephritis exhibiting oedema, and it is interesting to note that in his subjects the oedema was of considerably longer duration. It is thought that the presence of infection, and the short duration of the oedema, may be associated with the lower values of the present series.

In view of the contention of some authors that there is a close relationship between cholesterol and oedema, it is interesting to note, at this point, that in the present investigation the blood cholesterol was not increased in five cases of oedema from other causes. In one case of congenital oedema the cholesterol was as low as 58.6 mg.% (vide Table 43). These results therefore give support to the contention that there is no correlation between the blood cholesterol and oedema.

TABLE 42.

Acute nephritis.

(a) Showing a general tendency for a parallel between the loss of weight and the fall of the blood cholesterol in 5 cases.

Case No.	Date	Cholesterol mg.%	Weight in kilos.
1	21.11.35	102.3	29.2
	22.11.35	147.2	29.2
	23.11.35	143.7	28.4
	24.11.35	136.9	27.4
	25.11.35	139.3	26.7
	26.11.35	139.3	25.6
	27.11.35	134.0	25.1
	28.11.35	120.8	25.0
	29.11.35	124.1	25.1
	30.11.35	128.1	24.6
	2.12.35	134.0	24.2
	3.12.35	131.0	24.2
	9.12.35	131.0	25.0
	19.12.35	131.0	24.1
	30.12.35	128.1	24.6
3	30.9.36	160.8	14.4
	6.10.36	164.3	14.0
	7.10.36	111.5	14.0
	16.10.36	136.9	13.8

Table 42 (Contd.)

Case No.	Date	Cholesterol mg.%	Weight in kilos.
5	28.4.36	131.0	21.3
	6.5.36	120.7	21.1
	12.5.36	120.7	20.0
	18.5.36	136.9	21.8
	22.5.36	178.1	22.0
9	12.2.36	157.4	15.0
	13.2.36	131.0	15.5
	14.2.36	143.7	14.4
	15.2.36	143.7	13.5
	19.2.36	136.9	12.5
	20.2.36	120.7	12.7
	21.2.36	120.7	12.7
	24.2.36	117.2	13.1
	25.2.36	124.1	13.1
	5.3.36	124.1	13.1
	15.3.36	111.5	13.2
19	20.2.36	114.3	23.0
	22.2.36	150.6	22.2
	24.2.36	140.0	21.9
	25.2.36	143.7	21.2
	26.2.36	124.1	21.1
	27.2.36	120.7	20.8
	28.2.36	120.7	20.6
	3.3.36	120.7	20.6
	15.3.36	120.7	20.8
	27.3.36	124.1	21.8

TABLE 42.

(b) Showing a general tendency towards an inverse ratio between the loss of weight and the cholesterol values in 5 cases.

Case No.	Date	Cholesterol mg.%	Weight in kilos.
6	23.1.36	98.9	22.4
	24.1.36	98.9	22.2
	31.1.36	127.6	22.1
	6.2.36	131.0	22.2
	12.2.36	136.9	22.4
11	27.2.36	102.5	14.2
	2.3.36	131.0	12.8
	7.3.36	136.9	12.0
17	3.4.36	157.4	23.8
	6.4.36	178.1	21.5
	8.4.36	131.0	20.6
	17.4.36	136.9	21.2
	22.4.36	140.0	20.0
	6.5.36	134.0	21.0
	9.5.36	140.0	20.8
	13.5.36	131.0	21.6

Table 42 (Contd.)

Case No.	Date	Cholesterol mg.%	Weight in kilos.
23	29.11.35	93.1	24.0
	30.11.35	87.3	23.8
	1.12.35	87.3	22.8
	2.12.35	84.5	22.4
	3.12.35	90.2	22.0
	4.12.35	93.1	21.4
	5.12.35	111.5	21.0
	8.12.35	108.6	20.6
	9.12.35	108.6	20.3
	12.12.35	124.1	20.0
	19.12.35	108.6	21.4
	30.12.35	102.3	21.2
25	29.7.36	105.7	25.2
	6.8.36	124.1	20.8
	11.8.36	114.3	21.2
(c)	Two cases without oedema at the time of making the determinations.		
4	28.4.36	204.0	15.0
	6.5.36	150.6	15.1
	12.5.36	131.0	15.8
7	22.1.36	102.3	10.7
	23.1.36	105.7	10.9
	24.1.36	108.5	11.0
	30.1.36	131.0	11.6
	31.1.36	131.0	11.7

TABLE 43.

Case No.	Name	Age	Cholesterol mg.%	Diagnosis
44	F.K.	18/12	93.1	Cardiac failure with oedema
45	J.N.	13/12	105.7	Nutritional oedema.
46	J.McP	2	105.7	Nutritional oedema.
47	L.	3/52	90.2	Congenital oedema.
48	C.G.	10/12	58.6	Congenital oedema.

Nitrogen retention.

Fleming[8] and others,[11] have been unable to demonstrate any correlation between the blood urea and the blood cholesterol, and their findings have been confirmed in the present series. Referring again to Table 41, the highest cholesterol value (181.5 mg.%) is displayed in case No. 26, with a non-protein nitrogen value of 29.7 mg.%. In case No. 30 the non-protein nitrogen was 100.0 mg.%, while the blood cholesterol was 143.7 mg.%. Again case No. 36 had a non-protein nitrogen value of 61.7 mg.% when the cholesterol was 127.5 mg.%.

Table 44 indicates clearly the complete absence of any correlation between the blood pressure and the cholesterol.

TABLE 44.

Showing the relation between the blood pressure and the blood cholesterol in 10 subjects.

Case No.	Date	Cholesterol mg.%	Blood pressure	
			Systolic	Diastolic
19	22.2.36	150.6	100	60
9	15.2.36	143.7	94	60
1	25.11.35	139.3	154	90
32	24.4.36	136.9	130	65
24	22.1.36	134.0	132	104
33	21.1.36	131.0	92	60
40	28.8.36	111.5	126	84
7	22.1.36	102.3	104	74
6	23.1.36	98.9	132	92
"	24.1.36	98.9	130	80
"	31.1.36	127.6	96	50
23	30.11.35	87.5	126	80
"	1.12.35	87.5	118	80

B. URAEMIA.

The majority of investigators find low values in uraemia. Ashe and Bruger[12] quote the literature on the subject indicating that in nephritis the blood cholesterol usually falls as uraemia becomes evident. These authors believe that hypocholesterolemia with marked nitrogen retention predicts in many cases a fatal termination. Henes[13] also found low values in fatal cases. Grigaut[14] observed hypocholesterolemia in uraemia and he states that during the course of convalescence the blood cholesterol increases as the nitrogen retention diminishes. Gainsborough[15], on the other hand, does not believe that determination of the blood cholesterol is of any prognostic value. He states that a decrease of the cholesterol, to either a normal or a low figure, may be associated either with recovery in the purely nephrotic type, or progression towards sclerosis and a fatal termination.

In the present investigation uraemia occurred in two subjects with acute nephritis (vide Table 45a). The cholesterol values during the acute phase were 81.6 mg.% and 93.1 mg.% respectively. The blood urea in the first case was 31.0 mg.% and in the second case the non-protein nitrogen was 22.5 mg.%. Both children made good recoveries.

Uraemia was observed in three patients with chronic nephritis (vide Table 45b). Marked hypocholesterolemia was found in No. 51, the initial value being 64.3 mg.% and it rose to 93.1 mg.% before death. In this case the pathologist made

the following interesting note on the supra-renals, "the adrenal glands are small and there is complete absence of cholesterol storage in their cortices." In case No. 52 the cholesterol was 251.0 mg.% the day before death. In another subject, No. 53, the blood cholesterol was 159.1 mg.% a few hours before death. The blood cholesterol was not, therefore, of any prognostic value in these cases. The increased values in Nos. 52 and 53 are noteworthy since they are in disagreement with the results of many of the authors quoted.

With regard to the low values in cases Nos. 49 and 50, it has already been shown that the blood cholesterol variations in acute nephritis differ little from those in other infections and it is not therefore surprising to find low values in the acute stage of the illness. Cantarow and McCool[5] have pointed out that hypocholesterolemia is found in the terminal phases of many illnesses, and may not therefore be specific for uraemia.

TABLE 45.

Uraemia.

(a) Acute nephritis.

Case No.	Name	Age in yrs.	Date	Cholesterol mg.%	
49	A.B.	7	6.11.36	81.6	History - Oedema for 3 days. Convulsion yesterday. B.P. 140/116. Blood urea - 31.0 mg.% Child drowsy. Urine contains blood and casts. Child made a good recovery and was dismissed on 11.1.37.
50	J.H.	7	17.11.36	93.1	History - Oedema of face 4 days ago. Headache and drowsiness yesterday. Very drowsy and has severe vomiting. No oedema. N.P.N. 22.5 mg.%. Urine contains blood and casts. Child made a good recovery and was dismissed on 11.1.37.

TABLE 45.

Uraemia.

(b) Chronic nephritis.

Case No.	Name	Age in yrs.	Date	Cholesterol mg.%	
51	J.M.	8	5.5.37	64.3	History - Acute nephritis 3 yrs. ago.
			6.5.37	75.9	5.5.37 - B.P. 175/110. Acutely ill. Urine contains albumen but no blood. Frequent convulsions from 4.5.37 until 26.5.37.
			11.5.37	93.1	
			18.5.37	93.1	6.5.37 - N.P.N. 177.6 mg.%
			26.5.37	Died	Autopsy report - "Advanced secondary contracted kidney. Adrenal glands small & complete absence of cholesterol storage in their cortices."

Table 45 (Contd.)

Case No.	Name	Age in yrs.	Date	Cholesterol mg.%	
52	J.S.	10	17.11.35	239.0	History - "Kidney trouble" 6 yrs. ago. Child remained well until a month ago - began to have frequent attacks of cramp. 17.11.35 - Undersized child. No oedema. Optic neuritis present. Urine contains albumen +++ and a few red blood cells. 22.11.35 - N.P.N. 625.0 mg.% Post-mortem report - "Kidneys small and capsules slightly adherent. Surface mottled, yellowish areas being intermingled with zones of congestion. On cutting the kidney substance the cortex is narrowed and the markings irregular. Both renal arteries show some hypertrophy."
			22.11.35	251.0	
			23.11.35	Died	
53	M.C.	8	26.11.35	183.4	History - Recurrent vomiting for a month. 26.11.35 - Severe retinitis. B.P. 210/180; N.P.N. = 30.1 mg.%. Autopsy report - "Chronic nephritis, hypertrophy of the heart, tabes mesenterica."
			8.12.35	159.1	
			8.12.35	Died	

C. NEPHROSIS.

Much work has been done on the blood cholesterol in nephrosis but the cause of the hypercholesterolemia in this condition remains unknown.

Calvin and Goldberg[16] review the relationship between the blood cholesterol and oedema in renal disease, and state briefly the views of different workers. Schwarz and Kohn[17] give a résumé of the literature on the subject, with special reference to children under one year.

The following are some of the explanations formulated by different investigators.

Oedema.

Some authors[17][18] do not find any correlation between the blood cholesterol and oedema, stating that the cholesterol remains high even in the oedema free periods. Other workers[19] find higher values in the presence of oedema than in the free periods.

Serum proteins.

A slight but inconstant ratio between the blood cholesterol and the serum proteins has been observed by some[17] and contradicted by other workers.[19] Some investigators[20] find that high cholesterol values are, in the majority of cases, associated with low serum protein values, while others[21] do not find any close proportionality between the two values. Cowie et alii[18] suggested that there might be a ratio between the amount of protein lost in the urine and the blood cholesterol increase.

Schwarz and Kohn[17], while noting the lack of uniformity of the cholesterol-protein ratio, conclude that the increased blood cholesterol does not replace the protein lost from the blood. Leiter[22] reduced the serum proteins to 3 gm.% below normal, by bleeding animals, and found a coincident fall of the cholesterol. Cessation of the depletion was followed by a sharp rise of the cholesterol.

Diet.

It has been suggested that a dietetic regimen might have some beneficial effect in this condition. Fat free and other diets have, however, been shown to have no effect on the blood cholesterol in nephrosis[16,19,23].

Metabolism.

The metabolic rate is low in many cases of nephrosis, and Epstein and Lande[24] thought that it was inversely proportional to the blood cholesterol. Recent workers have, however, been unable to demonstrate any correlation between the blood cholesterol and the metabolic rate[17][23].

A few authors[27] have reported beneficial results following thyroid administration, The majority of workers, however, find the condition unaffected by this extract[23].

Bruger[25] found that the cholesterol excretion in the urine was parallel to the protein excretion in nephrosis.

Personal observations.

This group comprises seven cases which did not all exhibit precisely the same clinical picture. The majority of them may be classified as subacute nephritis, or what is commonly called chronic parenchymatous nephritis or nephrosis. General anasarca of a chronic nature, and abundant albuminuria occurred in all patients. Blood was absent from the urine in three subjects, scanty red blood cells were found after spinning in three, and haematuria occurred in the remaining child. The blood pressure showed a decided increase in only one subject.

Hypercholesterolemia occurred in every case, and the oscillations of the blood cholesterol did not appear to be related to any known factor (vide Table 46).

In case No. 54 the cholesterol values were followed out for five months, and during this period the readings varied between 300 mg.% and 600 mg.%. Schally[26] found that liver extract caused a diminution of the cholesterol in nephrosis; therefore campolon 2 c.c. daily was tried in this case. During the first six days of treatment there was a steady increase from 482.7 mg.% to 618.8 mg.%. Three days after this the child was placed on a salt free diet, and the blood cholesterol gradually diminished, until after thirteen days on this diet it had fallen from 607.9 mg.% to 439.1 mg.%. Thereafter it oscillated between 300 mg.% and 575 mg.%. This child's condition gradually deteriorated and twelve days before death the blood cholesterol was 308.0 mg.%.

In case No. 55 the majority of readings were between 200 mg.% and 300 mg.% over a period of six months. After being

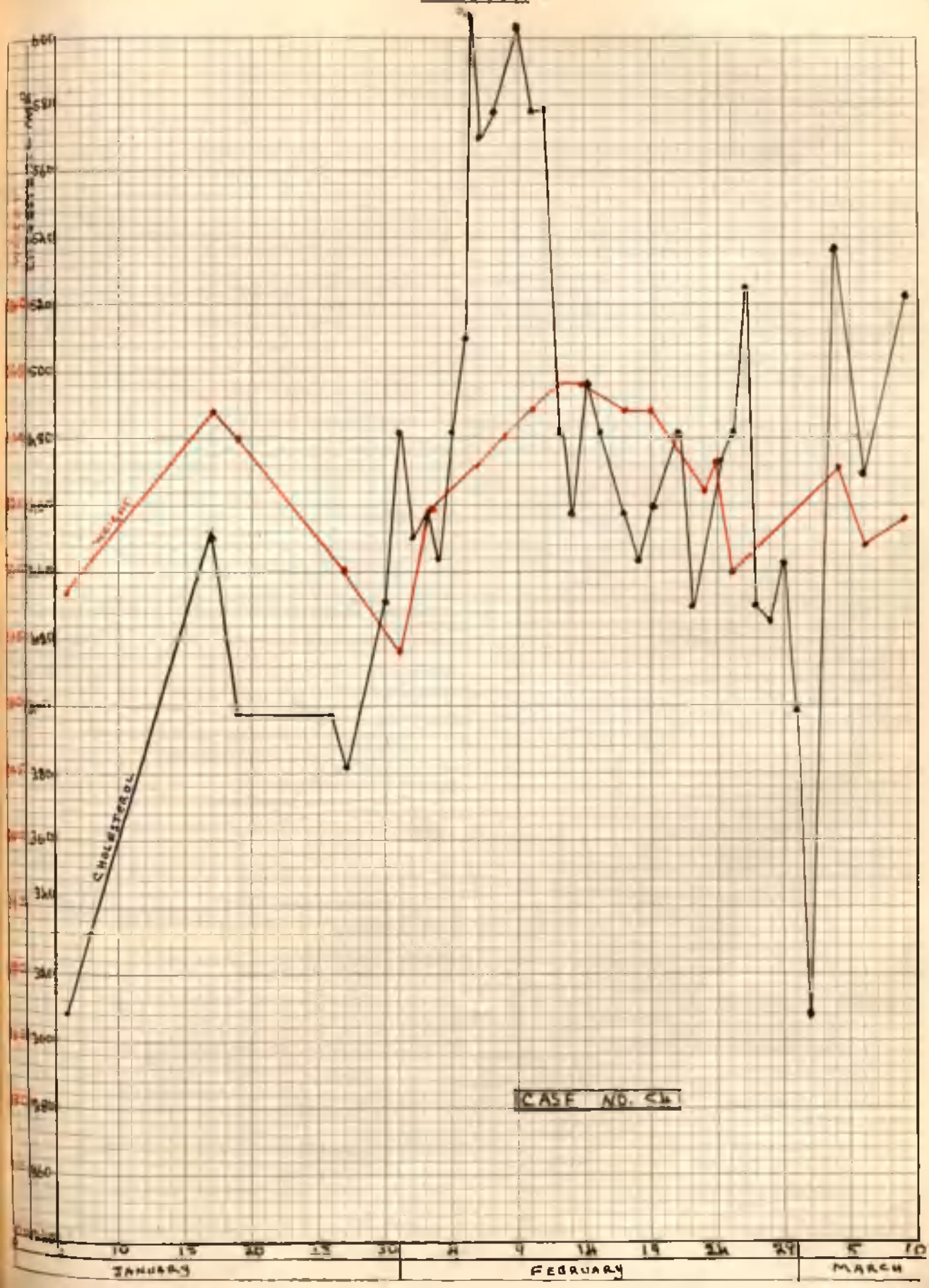
placed on a salt free diet the cholesterol gradually fell from 260.0 mg.% to 164.3 mg.%. This diminution may however have been associated with the gradual deterioration which occurred in the patient's general condition during this period. The increase in weight and the fall of the cholesterol values in the terminal stage of the illness is noteworthy.

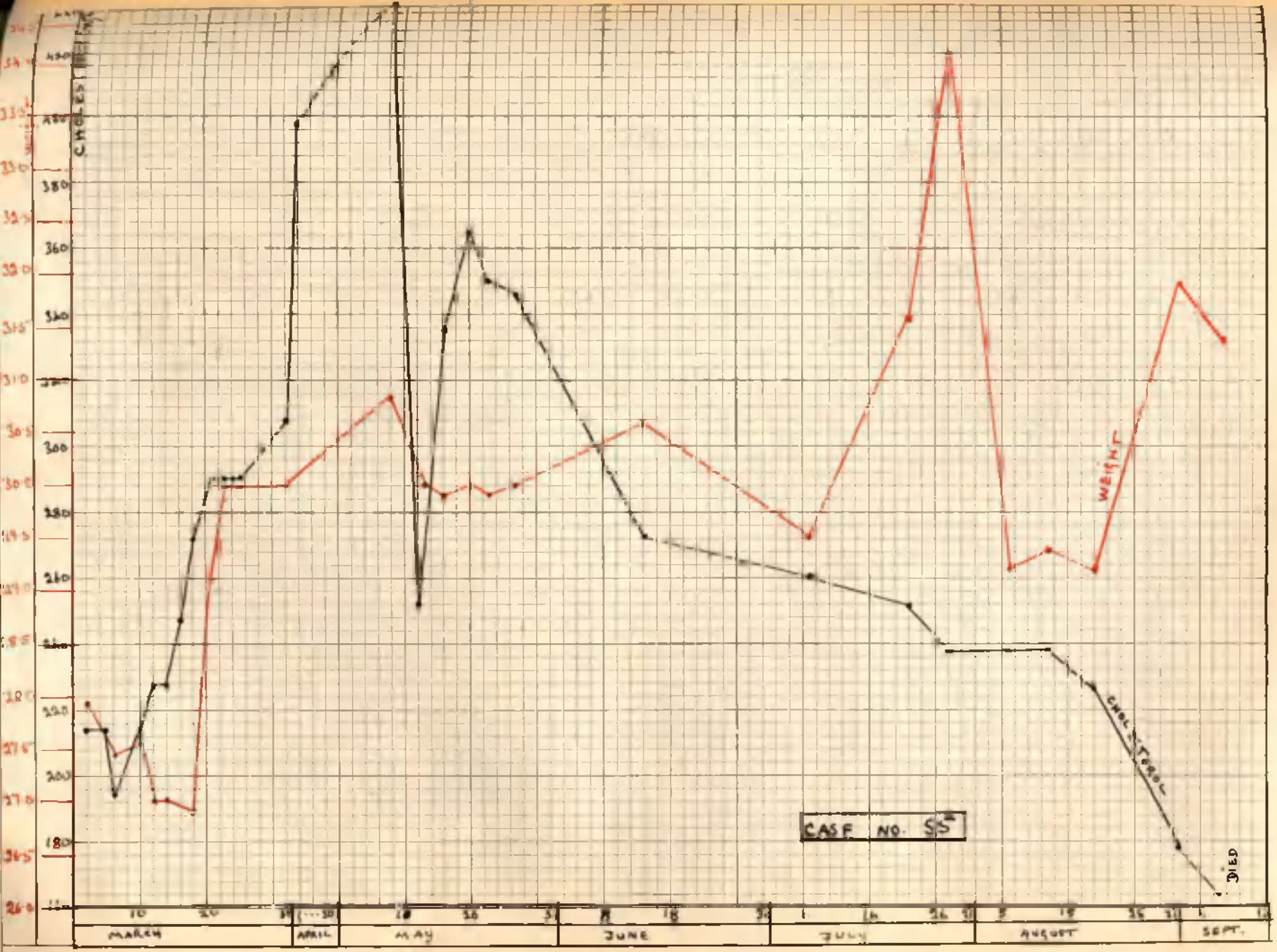
In case No. 56 observations were made both during an oedema free period and during a period of oedema. This child was admitted to hospital with severe general anasarca. Oedema persisted for three months and during the period the cholesterol values ranged from 193.1 mg.% to 421.8 mg.%. Determinations made during an oedema free period gave values ranging from 87.3 mg.% to 308 mg.%. From this case it would appear that the presence or absence of oedema has little influence on the blood cholesterol.

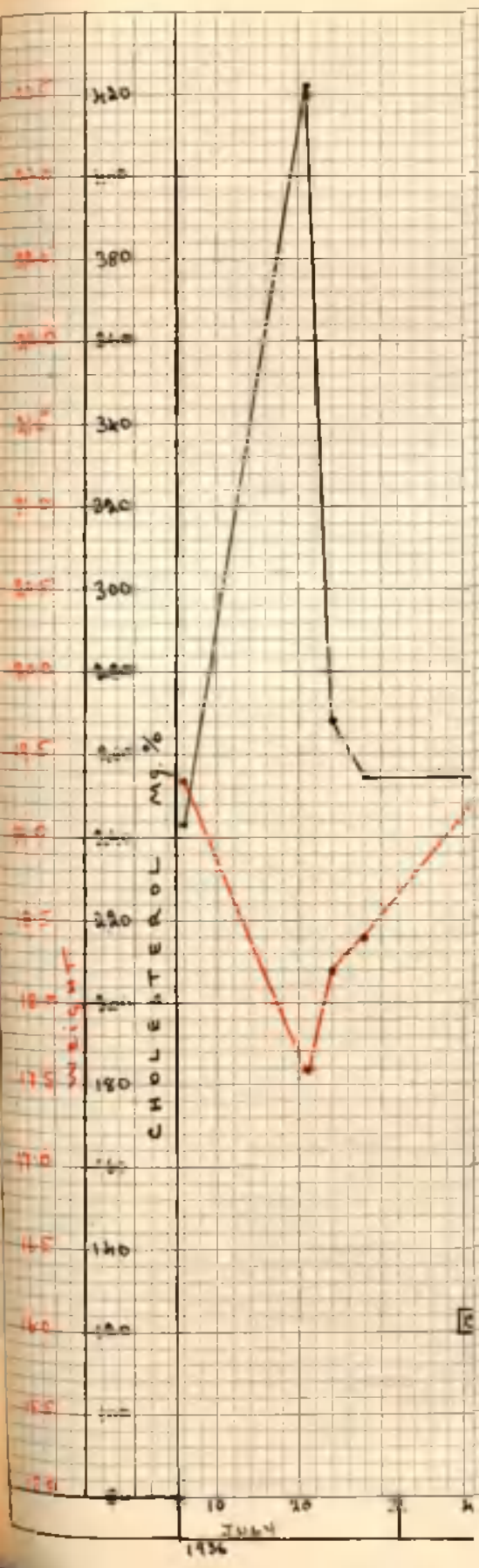
In chart 14 a comparison is made between the variations in the blood cholesterol and the changes in the body weights of cases 54, 55 and 56. At some periods of the illness the two curves are more or less parallel but this relationship is not, however, sufficiently definite to suggest that the cholesterol values are related to the oedema.

It may be said, therefore, that this small series of cases show consistently high values which cannot be correlated with any of the biochemical or physical findings (vide Table 46).

Chart 14.




CHOLESTEROL
WEIGHT
CHOLESTEROL
DIED
CASE NO. 55
MARCH
APRIL
MAY
JUNE
JULY
AUGUST
SEPT.


420
380
340
300
260
220
180
140
100
60
20
Mg. %
CHOLESTEROL
10
20
30
4
June
1936

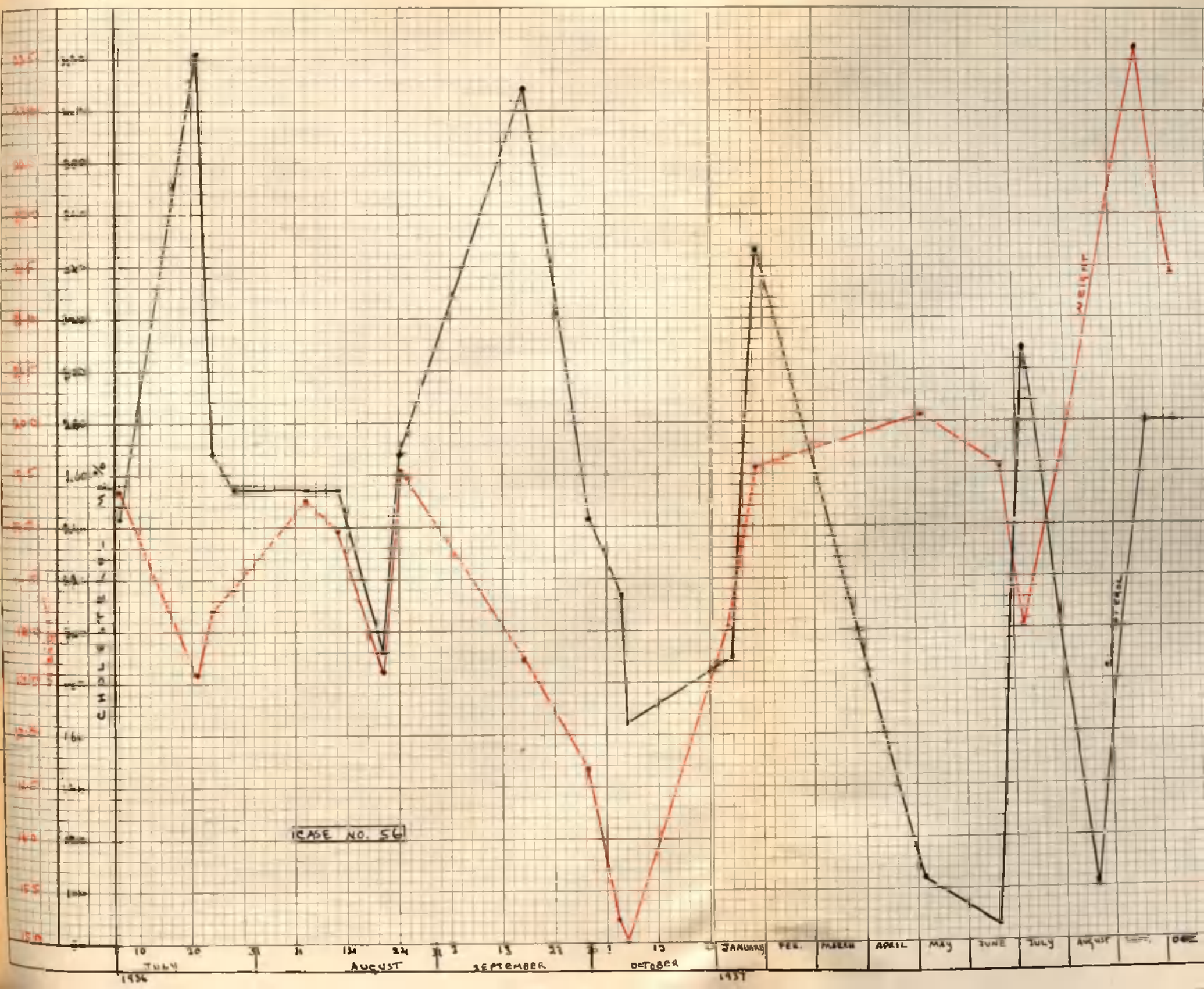

CASE NO. 56
CHOLESTEROL mg %
WEIGHT
JULY
AUGUST
SEPTEMBER
OCTOBER
JANUARY
FEB.
MARCH
APRIL
MAY
JUNE
JULY
AUGUST
1936
1937

TABLE 46.

Case No.	Name	Age	Date	Cholesterol mg.%	Weight in kilos.	
54	M.M.	8	6.1.36	308.0	21.84	History - apart from whooping
			17.1.36	451.0	23.20	cough at 2 years of age and
			19.1.36	398.9	23.0	measles at 3 years of age,
			26.1.36	398.9	-	health was good until onset
			27.1.36	382.7	22.0	of present illness 9 days ago.
			30.1.36	433.3	-	28.12.35 - Face puffy.
			31.1.36	482.7 c.	21.4	1.1.36 - Puffiness worse, vomiting and oliguria present.
			1.2.36	451.7	-	
			2.2.36	457.4	22.46	6.1.36 - Marked oedema of face limbs and lumbo-sacral region.
			3.2.36	444.8	-	B.P. 108/88. Afebrile. Urine - Albumen +++ and casts.
			4.2.36	482.7	22.6	17.1.36 - N.P.N. = 63.8 mg.% Total protein = 4.443 gm.%
			5.2.36	510.2	-	
			6.2.36	618.8	22.8	18.1.36 - Ascitis present and general oedema very marked.
			7.2.36	571.0	-	31.1.36 - Start campolon 2 c.c. daily (c)
			8.2.36	579.0	23.0	6.2.36 - Start salt free diet (s.f.d.)
			9.2.36	607.9 s.f.d	-	15.2.36 - Stop campolon (s.c.)
			10.2.36	579.0	23.2	16.2.36 - Little change in general condition.
			11.2.36	579.0	-	
			12.2.36	482.7	23.4	24.2.36 - Complained of abdominal pain. Irregular fever persisted until 4.3.36.
			13.2.36	457.0	-	
			14.2.36	496.5	23.4	
			15.2.36	482.1 s.c.	-	
			17.2.36	457.4	23.2	
			18.2.36	444.8	-	

Table 46 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Weight in kilos.	
54 (Ctd.	M.M.	8	19.2.36	459.1	23.2	On 29.2.36 there was no change in the oedema.
			21.2.36	482.7	-	
			22.2.36	439.1	22.6	5.3.36 - N.P.N. = 41.2 mg.%
			24.2.36	476.4	22.8	14.3.36 - Had 1 novurit suppository on 13.3.36 followed by frequent loose stools.
			25.2.36	482.7	-	Oedema and ascitis unchanged.
			26.2.36	525.0	22.0	16.3.36 - N.P.N. = 87.7 mg.%. Total proteins = 5.14 gm.%
			27.2.36	437.0	-	
			28.2.36	433.3	-	9.5.36 - General condition practically unchanges; oedema of legs less but ascitis I.S.Q
			29.2.36	444.8	-	
			1.3.36	398.9	-	21.5.36 - Child greatly emaciated; oedema and ascitis less.
			2.3.36	308.4	-	9.6.36 - Died.
			4.3.36	538.1	22.8	Post-mortem permit refused.
			6.3.36	470.0	22.2	
			9.3.36	523.1	22.4	
			11.3.36	470.0	22.6	
			13.3.36	523.0	22.6	
			15.3.36	575.0	23.2	
			18.3.36	575.0	-	
			8.5.36	346.0	-	
			12.5.36	239.0	19.8	
			16.5.36	299.9	-	
			23.5.36	299.9	18.2	
			27.5.36	308.0	20.0	

Table 46 (Contd.)

Case No.	Name	Age in yrs	Date	Cholesterol mg.%	Weight in kilos.	
55	S.K.	8	2.3.36	214.9	27.8	History - Intermittent otorrhoea since infancy. Urine of dark colour since January 1936. On 4.2.36 face puffy. On 12.2.36 severe vomiting and marked oedema.
			5.3.36	214.9	-	
			6.3.36	196.5	27.4	
			7.3.36	196.5	-	
			10.3.36	214.9	27.6	2.3.36 - Marked oedema and ascitis present. N.P.N. = 78.1 mg.%. Serum protein = 6.03 gm.%.
			12.3.36	227.5	27.0	
			14.3.36	227.5	27.0	B.P. 120/84. Urine contains albumen +++, blood +++ and casts.
			16.3.36	247.1	-	
			18.3.36	272.4	26.8	7.3.36 - Still gross oedema and haematuria.
			21.3.36	290.0	29.2	30.3.36 - General anasarca persists with slight haematuria.
			23.3.36	290.0	30.0	
			24.3.36	290.0	-	20.4.36 - Papular rash present.
			25.3.36	294.2	30.0	
			31.3.36	308.0	30.0	3.5.36 - Condition unchanged.
			1.4.36	398.9	-	26.6.36 - Oedema slightly less; dulness and impairment of R.M. at left base.
			8.5.36	444.8	30.8	8.7.36 - Low salt diet.
			12.5.36	252.0	30.0	16.7.36 - Tonsillectomy.
			16.5.36	335.6	29.8	19.7.36 - Profuse double otorrhoea.
			20.5.36	366.6	30.0	7.9.36 - Oedema +++++ generalised; respiration laboured.
			23.5.36	356.2	29.8	8.9.36 - Condition worse.
			27.5.36	346.0	30.0	10.9.36 - Died.
			16.6.36	272.0	30.6	Autopsy report - 'Sub-acute nephritis. Generalised anasarca, early acute pericarditis.'
			7.7.36	260.0	29.5	
			22.7.36	255.1	31.6	
			28.7.36	239.0	34.1	

Table 46 (Contd.)

Case No.	Name	Age in yrs	Date	Cholesterol mg.%	Weight in kilos.	
55 (Contd.)	S.K.	8	6.8.36.	239.0	29.2	
			12.8.36	239.0	29.4	
			19.8.36	226.5	29.2	
			1.9.36	178.1	31.8	
			7.9.36	164.3	31.4	
56	J.McD.	4	6.7.36	243.0	19.32	History - Healthy until oedema appeared 2 wks. ago. No history of an acute infection.
			21.7.36	421.8	17.6	
			24.7.36	268.4	18.2	6.7.36 - Severe general anasarca. Tonsils small and unhealthy. Blood urea 28.3 mg.%. Total serum protein = 4.939 gm.%. Urine - albumen ++, casts + and a few red blood cells.
			28.7.36	255.1	18.4	
			6.8.36	255.1	19.28	
			12.8.36	255.1	18.94	
			21.8.36	193.1	17.6	23.7.36 - Oedema increased.
			24.8.36	268.4	19.52	15.8.36 - Oedema less.
			17.9.36	404.5	17.72	17.9.36 - Oedema considerably increased.
			30.9.36	243.0	16.68	
			6.10.36	214.9	15.2	5.10.36 - Only slight oedema; severe diarrhoea with blood and mucus in stool; recovered after a few days.
			7.10.36	164.3	15.0	
			15.1.37	189.9	18.08	15.1.37 - Very slight oedema. Dismissed to country branch.
			31.1.37	346.0	19.58	3.3.37 - Whooping cough. Dismissed to fever hospital.
			3.5.37	105.7	20.1	
			25.6.37	87.3	19.52	3.5.37 - Out-patient. Very well. No oedema. Made excellent recovery from whooping cough.
			9.7.37	308.0	18.0	
			21.8.37	102.3	-	14.6.37 - Readmitted to hospital with history of increasing oedema of 12 days' duration. Has marked oedema. Blood
			26.9.37	280.0	23.60	
			1.10.37	280.0	21.40	

Table 46 (Contd.)

Case No.	Name	Age	Date	Cholesterol mg.%	Weight in kilos.	
56 (Contd.)	J.McD.	4				urea = 36.5 mg.% 25.6.37 - General condition much improved; no oedema. 8.7.37 - Slight oedema. Serum proteins 8.2 gm.%. General condition good. 9.7.37 - Transferred to country branch. 13.8.37 - Dismissed home. 21.8.37 - Out-patient. Very well. No oedema. 21.9.37 - Readmitted to hospital. No oedema until 10 days ago, gradually increased since then. Now has gross oedema and ascitis. 1.10.37 - Oedema entirely gone. Looks well.
57	R.McC.	3	8.4.36 8.5.36	569.8 299.9		History - Oedema and albuminuria for 3 months. 8.4.36 - Severe anasarca, ascitis ++ and fluid at base of both lungs. B.P. 100/?. Urine - albumen +++, a few hyaline and granular casts, no blood. N.P.N. 23.5 mg.%. Serum proteins 7.868 gm.%. Condition remained practically unchanged until death on 9.5.36.
58	F.D.	8	3.6.36	991.0		History - Oedema of face and legs and abdomen for 4 years. Basal systolic murmur audible. Tonsils enlarged and red. Urine contains albumen ++, no blood. B.P. 117/80. Afebrile. N.P.N. 38.7. Serum protein 6.375 gm.%.

Table 46 (Contd.)

Case No.	Name	Age in yrs	Date	Cholesterol mg.%	
59	L.C.	4	27.3.37	239.0	History - Oedema for 2 weeks. Marked oedema and some ascitis. Urine contains albumen +++ and a few red blood cells. N.P.N. = 23.5 mg.%. Total protein = 4.700 gm.%. B.P. = 122/82.
60	J.S.	9	8.11.37	214.9	History - Oedema for 5 months. Moderate oedema. Urine contains red blood cells & casts. B.P. 150/132. N.P.N. = 24.3 mg.%.

The blood cholesterol in some other affections of the renal system.

The blood cholesterol was low in renal dwarfism and congenital cystic disease of the kidney (vide Table 47). A case of hyperpiesis had a normal cholesterol value.

TABLE 47.

Case No.	Name	Age in yrs.	Cholesterol mg.%	Diagnosis
61	A.S.	12	98.9	Renal dwarfism
62	M.W.	7	90.3	Renal dwarfism
63	W.T.	18/52	98.9	Congen. cystic disease of kidney.
64	E.D.	10	120.6	Chronic nephritis hyperpiesis. (B.P. 200/60)

Summary.

Normal or low cholesterol values were found in the majority of the children with acute nephritis. The cholesterol, however, increased during convalescence in many of these subjects, and showed variations very similar to what has been observed in pneumonia, in rheumatism and in other infections during the convalescent period.

It has been suggested that infection may play an

important part in the cholesterol variations in acute nephritis. Fever was accompanied by low values in the majority of cases. Consistently high values were only found in subjects presenting the so-called "nephrotic syndrome".

In acute nephritis, no correlation was found between the blood cholesterol and the blood pressure, or between the blood cholesterol and the nitrogen retention.

The absence of any correlation between the blood cholesterol and oedema, both in acute and chronic nephritis, has been demonstrated. Increased values were not found in cardiac, nutritional, or congenital oedema. These findings are in agreement with many of the authors quoted.

The blood cholesterol in uraemia was not found to be of any prognostic value. Low results were noted in the two cases that recovered. Of the three fatal cases the cholesterol was high in two, and very low in one. These results are in disagreement with many of the workers already quoted who believe that low values are usually found in fatal cases.

All the cases of acute nephritis made a good recovery, and it is therefore impossible to give any definite opinion respecting the prognostic value of the blood cholesterol. Nevertheless, it is probably significant that this good recovery was associated with a return of the blood cholesterol to a normal level in twenty four out of twenty five cases on whom serial determinations were made.

The blood cholesterol was low in two children with renal dwarfism and in one with congenital cystic disease of the kidney.

SECTION 4.

SOME DISEASES OF THE LIVER AND BLOOD TOGETHER WITH OBSERVATIONS ON THE HISTAMINE TEST OF LIVER FUNCTION.

Rôle of the liver and gall-bladder in cholesterol metabolism - a review of the literature.

Much has been written on the rôle of the gall-bladder in cholesterol metabolism, and the conclusions arising therefrom show a considerable lack of unanimity. Some believe that the gall-bladder secretes cholesterol; some think it absorbs cholesterol, while others deny that it takes any active part in cholesterol metabolism. In the year 1898 Naunyn[1] and his school thought that cholesterol was secreted by the mucosa of the biliary passages, while in 1936 Mackey[2] concluded that the gall-bladder probably absorbs cholesterol. It is not proposed, however, to do more than mention this aspect of the subject which has been reviewed recently by Mackey.

Many investigators believe that the liver either secretes or excretes cholesterol, and that the blood cholesterol value depends on the functional activity of the liver cells. Hence arises the idea that the blood cholesterol level might be an index of liver efficiency.

As early as 1862 Flint[3] wrote an instructive article on the "new excretory function of the liver." He believed that cholesterol was separated from the blood by the liver, and finally discharged into the alimentary tract together with the bile. He came to these conclusions after investigating the cholesterol values in various diseases, and performing experimental work on dogs. Sperry[4] in 1926 concluded that cholesterol was secreted

by the liver as a waste product for excretion into the faeces, and he quotes the results of a large number of workers in support of his beliefs. Borgatti[5] thought that the liver not only excreted but produced cholesterol. Thannhauser[6] is of the opinion that the liver is the regulator not only of the blood cholesterol, but also of the relation between the free and ester cholesterol.

A. CATARRHAL JAUNDICE.

The etiology of this condition is uncertain but most authors agree that biliary obstruction plays some part in its causation[7][8]. The majority of workers[9,10,11,12] find that the blood cholesterol is increased in cases of biliary obstruction, but exactly why this increase occurs is the subject of much controversy. It has been suggested that the increased cholesterol values are due to regurgitation of the cholesterol, together with the bile salts, into the circulation. This suggestion has, however, been contested by several investigators. Heinlein[13] believes that hypercholesterolemia occurring in obstructive jaundice is due to diminished storage by the liver. Rothschild and Felsen[14] consider that the cholesterol metabolism is regulated by the liver, and that the blood cholesterol is kept constant by excretion into the bile. Any obstruction to this outflow would therefore produce hypercholesterolemia.

Chauffard *et alii*[15] found that the blood cholesterol was more or less proportional to the bile retention in obstructive jaundice, and in catarrhal jaundice the cholesterol, bilirubin and bile elements in the blood ran a parallel course, diminishing progressively during the convalescent period. This latter finding is in agreement with the results of the present investigation. Ottenberg[10] has found the blood cholesterol increased in catarrhal jaundice, and he considers the cholesterol value to be a useful aid in differentiating between catarrhal jaundice and acute yellow atrophy of the liver.

Personal observations.

This group comprises eighteen children with catarrhal jaundice, between the ages of five months and eleven years.

Serial determinations were made during the course of the illness in ten subjects (see Table 48). The initial estimation was made within a week of the appearance of the jaundice in every case. The initial values showed without exception either definite hypercholesterolemia, or high normal values. The maximum figures were obtained at the first determination in all but three instances, the maximum results in these cases were however noted, one, two and three days later, respectively. Thereafter in all but one subject the blood cholesterol gradually diminished coincidently with the disappearance of the jaundice, and of the bile pigments from the urine. There was, however, no absolute parallel, for the bile pigments often disappeared from the urine before the blood cholesterol had fallen to a normal level. The same thing occurred in respect of the disappearance of the jaundice. In Case No. 4 for example, the jaundice disappeared while the blood cholesterol was still 218.0 mg.%, and in No. 9 there was definite jaundice when the cholesterol had fallen to 124.1 mg.%. In the majority of subjects, however, the highest initial cholesterol values were found in the most deeply jaundiced children. There would appear therefore to be a more or less definite parallel, subject to notable exceptions in a few cases, between the bile pigments in the blood and the cholesterolemia. A very similar relationship is indicated in the cases of catarrhal jaundice in Table 50

between the bilirubinemia and the cholesterolemia. There is only one notable exception (Case No. 10) in this table. These results are in close agreement with the findings of Chauffard et alii in catarrhal jaundice[15].

The blood cholesterol rose during the convalescent period in one case (No. 7). This subject was not, however, observed after the jaundice had completely disappeared. Owing to infection in the ward it became necessary to dismiss the child at a somewhat early date, and it is possible that had a determination been made at a later date, a diminution of the blood cholesterol would have been found.

Fever (Vide Tables 48 and 49).

The cholesterol values in catarrhal jaundice are apparently an exception to the general rule that pyrexia is accompanied by hypocholesterolemia. Fever was present in seven subjects and five of them had cholesterol values of over 170 mg.%. In one case fever of 101.8 was associated with a blood cholesterol of 251.0 mg.%.

A series of single determinations on eight subjects are shown on Table 49 and two of them exhibit normal values. One, No. 11, gave a reading of 102.3 mg.%, this child of five months was in extremely poor general condition and had conjunctivitis followed later by a corneal ulcer. The other child (No. 16) was eleven years of age and was only faintly jaundiced.

It is apparent from both the serial and single determinations indicated on Tables 48 and 49 that there is no correlation between the blood cholesterol and the duration of the jaundice.

In this series of eighteen cases there was a remarkable inverse proportion between the ages of the children and the cholesterol values. Of the seven children under four years of age, four displayed results of over 250 mg.% and of the remaining three, two had cholesterol values of over 200 mg.%, i.e. six out of the seven children had values of over 200 mg.%. Of the eleven children over four years of age, all except two displayed values of less than 200 mg.%.

In conclusion it may be said that the blood cholesterol was increased in catarrhal jaundice, and that it returned to a normal level during the convalescent period.

High values were observed even in the presence of fever.

TABLE 48.

10 cases of catarrhal jaundice.

Case No.	Name	Age (yrs)	Date	Cholestgrol mg.%	Jaundice	Urine	Stools.	
1	A.H.	6/12	11.8.36	251.0	+	Bile	Clay	History - Jaundiced for 4 wks. Motions clay coloured for 2 wks. Exam.- Marked jaundice, liver 4 fb., spleen not palpable. Blood picture normal. Van d. Bergh biphasic - indirect - 12.0 units. Temp. 99-101° from 10.8.36 to 17.8.36. Condition improved slowly while in hospital and was dismissed "well" on 1.9.36.
			15.8.36	181.4	++	Bile	Clay	
			21.8.36	143.7	±	-	Normal	
			1.9.36	111.5	-	-	Normal	
2	M.L.	19/12	13.10.37	268.0	±	Bile	Pale	History - Jaundiced for 6 days. Liver 3 fb. and spleen 2 fb. Slight fever on 14th & 16th. On the 18th the general condition was much better and on 22nd was dismissed to country branch.
			14.10.37	208.0	±	Bile	Normal	
			16.10.37	164.3	-	-	Normal	
			18.10.37	131.0	-	-	Normal	
3	J.C.	2	4.1.36	255.1	+	Bile	Clay	History - Convulsion 1 week ago followed by left sided paralysis. Jaundiced and stools pale for 3 days. Exam. - No paralysis; moderate jaundice. Temp. 102°. 5.1.36 - Jaundice increased 6.1.36 - Fever still present, jaundice I.S.Q. 7.1.36 - Afebrile. Jaundice almost gone. Dismissed "well" on 24.1.36.
			6.1.36	275.9	+	Bile	Clay	
			8.1.36	255.1	±	Bile	Clay	
			9.1.36	211.4	±	Bile	Clay	
			10.1.36	154.0	-	Bile	Clay	
			11.1.36	127.6	-	-	Clay	
			13.1.36	127.6	-	-	Normal	
			14.1.36	111.5	-	-	Normal	
			15.1.36	124.1	-	-	Normal	
			16.1.36	120.7	-	-	Normal	

Table 48 (Contd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Jaundice.	Urine	Stools	
4	G.B.	3	7.9.36	218.0	±	Bile	Clay	History - Listlessness and fever for 8 days.
			8.9.36	290.0	±	-	Clay	Exam. - Slight jaundice. Tonsils enlarged and red.
			9.9.36	235.0	±	-	Clay	Liver 2 fb. Temp. 99.4°.
			10.9.36	218.0	-	-	Clay	7.9.36 - Temp. 99.2°. Condition I.S.Q.
			11.9.36	218.0	-	-	Pale	8.9.36 - Afebrile, liver still enlarged.
			12.9.36	208.0	-	-	Pale	14.9.36 - General condition very good. Dismissed
			14.9.36	143.7	-	-	Pale.	
5	B.S.	5	6.10.36	160.8	±	±	Pale	History - Sore throat 2 weeks ago. Jaundice for
			8.10.36	124.1	-	-	Normal	1 week.
			19.10.36	143.7	-	-	Normal	Exam. - Afebrile. Liver 3 fb. Does not look ill. 9.10.36 - Van d. Bergh - biphasic, indirect 1.0 units 20.10.36 - Dismissed "well"
6	S.McP.	5	18.3.36	197.0	++	Bile	Clay	History - Jaundiced 1
			19.3.36	181.5	+	Bile	Clay	month ago; cleared up in a week and returned 1 week ago.
			21.3.36	235.0	+	Bile	Normal	Exam.- Temp 99°. Liver
			23.3.36	223.0	±	-	Normal	enlarged. Van d. Bergh - direct - biphasic, indir-
			25.3.36	193.1	±	-	Normal	ect - 12.0 units. Tonsils enlarged and red.
			26.3.36	140.0	±	-	Normal	20.3.36 - Still fever of 99° 21.3.36 - Afebrile.
			27.3.36	120.7	-	-	Normal	27.3.36 - Temp. 103°. 30.3.36 - Afebrile; gener-
			30.3.36	111.5	-	-	Normal	al condition much better.
			31.3.36	127.6	-	-	Normal	1.4.36 - Dismissed "well".
7	J.S.	7	10.10.36	185.0	+	Bile	Clay	History - Severe vomiting, epigastric pain 1 wk. ago.
			12.10.36	178.1	+	Bile	Clay	Exam. - Intermittent fever
			13.10.36	280.0	±	-	Normal	of 99. Van d. Bergh - direct - biphasic, indirect 6.0 units. 14.10.36 - General condition much improved. Dismissed.

Table 48 (Contd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Jaundice	Urine	Stools	
8	M.B.	7	8.11.37	164.3	++	Bile	Clay	History - Jaundiced for 6 weeks.
			29.11.37	133.9	++	Bile	Clay	Exam. Deeply jaundiced liver 1 fb. V.d.Bergh: direct - biphasic: indirect - 36.0 units. 18.2.38 - Dismissed "well". This child had a protracted convalescence; the jaundice cleared very slowly.
9	W.McG.	9	30.6.36	150.6	+	Bile	Clay	History - Abdominal pain, fever and vomiting 8 days ago. Jaundiced for 3 days.
			1.7.36	124.1	+	Bile	Clay	
			2.7.36	120.7	±	Bile	Normal	Exam. - Afebrile. Liver enlarged; urobilin in urine; blood picture normal. 4.7.36 - Dismissed "well"
			4.7.36	108.5	-	-	Normal	
10	J.D.	11	23.2.37	143.7	+	Bile	Clay	History - Jaundiced for 1 week.
			6.3.37	105.7	±	-	Normal	Exam. - Afebrile. Liver 3 fb. Van den Bergh direct - biphasic; indirect 22.0 units. 6.3.37 - General condition improving. 26.3.37 - Dismissed "well".

TABLE 48.

Single determinations in 8 cases of catarrhal jaundice.

Case No.	Name	Age (yrs)	Cholesterol mg.%	Duration of jaundice	Fever	Urine	Stools	
11	J.McP.	5/12	102.3	4 weeks	99.2	Bile	Clay	Photophobia, conjunctivitis. General condition poor; markedly undernourished, and septic spots on face and neck.
12	M.B.	3	231.0	2 days	Afebrile	Bile	Clay	V. d. Bergh delayed direct 1.5 units.
13	H.McQ.	3	263.0	6 days	99.0	Bile	Clay	Tonsils inflamed
14	G.B.	5	174.0	1 day	Afebrile	Bile	Clay	Urobilinuria. Blood normal.
15	M.F.	7	181.9	5 days	Afebrile	Bile	Pale	-
16	C.W.	11	114.2	5 days	99.0	Bile	Pale	-
17	A.B.	9	157.4	10 days	Afebrile	Bile	Pale	-
18	C.S.	10	196.5	5 days	Afebrile	Bile	Clay	V. d. Bergh - direct - biphasic, indirect - 8.0 units.

TABLE 50.

Showing the relation between bilirubinemia and cholesterolemia in 14 subjects.

Case No.	Name	Cholesterol mg.%	Van den Bergh	Diagnosis.
1	A.H.	251.0	12.0	Catarrhal jaundice.
24	A.Y.	208.0	11.0	Congenital obliteration of bile ducts.
6	S.McP.	197.0	12.0	Catarrhal jaundice.
7	J.S.	185.0	6.0	Catarrhal jaundice.
20	J.S.	171.0	8.0	Pneumonia, jaundice.
9	W.McG.	150.6	5.0	Catarrhal jaundice.
10	J.D.	143.7	22.0	Catarrhal jaundice.
23	A.L.	140.9	24.0	Congenital obliteration of bile ducts.
5	B.S.	124.1	1.0	Catarrhal jaundice.
40	E.P.	117.2	3.0	Banti's disease.
21	J.H.	93.1	12.0	Septicaemia.
44	R.P.	90.2	4.0	Icterus gravis.
45	O.D.	87.3	44.0	Icterus gravis.
19	D.C.	81.5	22.3	Pneumonia, jaundice.

B. JAUNDICE ASSOCIATED WITH SOME OTHER CONDITIONS.

Toxaemic jaundice (4 cases).

The results in these subjects tend to be either increased or decreased (vide Table 51). Diminution of the blood cholesterol has already been found in acute infections, and it is thought that the increased values in the above cases may have been associated with a slight catarrhal infection sufficient to produce some degree of biliary stasis.

TABLE 51

Toxaemia.

Case No.	Name	Age in years	Cholesterol mg.%	Diagnosis
19	D.C.	12/52	81.5	Pneumonia.
20	J.S.	3	171.2	Pneumonia.
21	J.H.	9/52	93.1	Septicaemia
22	H.G.	7/52	140.3	Meningitis.

Congenital atresia. (4 cases)

In three subjects there was a definite increase of the blood cholesterol to about 200 mg.%; two of them had congenital atresia of the bile ducts, while one had atresia of the duodenum. The remaining case had a high normal value.

TABLE 52.

Congenital atresia.

Case No.	Name	Age in yrs.	Cholesterol mg.%	Diagnosis
23	A.L.	1/12	140.9	Atresia of bile ducts
24	A.Y.	6/52	208.0	Atresia of bile ducts
25	B.	2/52	193.1	Atresia of bile ducts
26	W.McC	4/365	204.0	Atresia of duodenum.

It will be shown later (vide page 193) that the blood cholesterol is often low in haemolytic jaundice.

One may conclude from the preceding results that there is no correlation between jaundice per se and the blood cholesterol. The findings suggest, however, that the cholesterol values increase proportionately with the degree of biliary obstruction. These results are in agreement with those of the majority of workers who have investigated the blood cholesterol in obstructive and catarrhal jaundice.

C. THE HISTAMINE TEST OF LIVER FUNCTION.

The statement that the blood cholesterol curve after giving histamine, might be a useful aid in the diagnosis of liver diseases, led one to investigate the effect of this drug on the blood cholesterol of normal and jaundiced children.

Hypercholesterolemia has been produced in dogs by the introduction of hydrochloric acid into the duodenum,[11][16] and also by giving histamine. This is thought to be the result of stimulation of the sensory nerve endings in the alimentary canal, and this interpretation is in conformity with the results of many workers[17] who believe that stimulation of the parasympathetic nervous system produces hypercholesterolemia.

Stephanutti[18] found that in normal subjects 1 mg. of histamine produced a rise preceded by a preliminary fall of the blood cholesterol which returned to normal within forty minutes. In patients with hepatitis and catarrhal jaundice the curves were exactly reversed, while subjects with profound liver damage exhibited hypercholesterolemia which slowly returned to normal. Uniform results after histamine have not, however, been obtained by all investigators. Goebel[19] noted a rise, while Cornell[20] observed a fall of the blood cholesterol, after histamine and after food, and after both histamine and food.

Personal observations.

This group comprises ten children exhibiting jaundice, and ten who were not suffering from any acute illness and who were in good general condition. The latter form the control group.

Histamine 0.1 mg. per 10 kilos. was injected subcutaneously and the blood cholesterol was estimated before, and 6, 14, 20, 30 and 40 minutes afterwards.

Control group (vide Table 53).

Three of these children had recovered from an acute illness. None of them were confined to bed, and at the time of making the observations they did not display any evidence of disease. Histamine was followed by increased cholesterol values in eight subjects. The rise varied from 9 mg.% to 40 mg.%, the average increase for the eight cases was 16 mg.%. In two of these children there was a preliminary fall of the cholesterol and in four of them it had returned to the initial value 40 minutes afterwards. The remaining two cases displayed a fall of the cholesterol, and it is interesting to note that they were two of the three children giving a history of a recent acute illness, one having had chorea and the other nephritis. In the former case the cholesterol fell only 7 mg.%, while the latter showed a very decided fall of 43 mg.%. The urine was clear in the latter case; there was no oedema, and the child appeared to have made a complete recovery from the attack of acute nephritis.

TABLE 53.

Cholesterol curves after histamine
0.1 mg. per 10 kilos. body weight.

(a)Control children showing increased values.

Case No.	Name	Age (yrs)	Before	Cholesterol mg.% after histamine.					Remarks.
				6	14	20	30	40	
						mins.			
27	A.G.	5	136.9	143.7	143.7	143.7	143.7	155.0	Enuresis - urine clear.
28	A.G.	6	136.9	136.9	147.3	136.9	136.9	-	Healthy child.
29	J.B.	7	111.5	102.3	124.1	120.6	117.2	124.1	Epilepsy.
30	C.M.	8	114.3	98.9	114.3	115.5	124.1	117.2	Pulm. Tub. General condition very good.
31	M.S.	8	105.7	111.5	124.1	117.2	120.6	105.7	Optic neuritis, cause unknown.
32	A.C.	10	131.0	136.9	136.9	143.7	131.0	131.0	Epilepsy.
33	M.R.	11	131.0	136.9	157.4	150.6	136.9	171.2	Chorea, recovered.
34	M.L.	12	155.0	164.3	164.3	143.7	155.0	155.0	Pyuria, urine contains only a few pus cells.
			(b) Control children showing diminished values.						
35	E.S.	8	131.0	124.1	124.1	124.1	131.0	131.0	Chorea, recovered.
36	C.D.	10	131.0	105.7	98.9	87.3	98.9	114.3	Nephritis, recovered.

One may conclude from the above results that histamine produces an increase of the blood cholesterol in the majority of healthy children.

Jaundice.

The cholesterol curves following histamine in eight children with catarrhal jaundice are indicated in Table 54.

The blood cholesterol rose in four subjects, and in one, the rise was preceded by a slight fall, while in three of these four cases the cholesterol was above the initial level at the end of forty minutes.

A diminution was observed also in four patients, but it was not preceded by a rise in any of them. Three of the subjects displayed a return of the cholesterol to the initial level at the end of forty minutes.

It is apparent from Table 54 that when the initial cholesterol is high, histamine frequently produces a diminution of the value, while if it is low, histamine causes an increase.

A deviation from what appeared to be the normal curve after histamine was found, therefore, in half of the patients in this group. It is difficult to assess the significance of this finding since so little is known of the pathology of catarrhal jaundice. Soffer and Paulson[21] have shown, however, that impairment of hepatic function often follows catarrhal jaundice.

Histamine was also given to a case of pneumonia with jaundice, and to a child with Hanot's cirrhosis. A fall, and a slight increase, respectively, followed the histamine in these two cases.

TABLE 54.

Cholesterol curves after histamine 0.1 mg. per 10 kilos. in 10 cases of jaundice.

Case No.	Name	Age (yrs)	Before	Cholesterol mg.% after histamine.					Remarks.
				6	14	20	30	40	
						(mins.)			
16	C.W.	11	114.2	136.9	136.9	150.0	126.9	117.2	Catarrhal jaundice.
18	C.S.	10	196.5	211.0	219.4	227.0	234.0	214.9	" "
5	B.S.	5	143.7	160.8	178.1	150.6	157.4	164.3	" "
14	G.B.	5	174.6	171.2	160.8	160.8	174.6	181.5	" "
17	A.B.	9	157.4	143.7	155.0	143.7	143.7	155.0	" "
7	J.S.	7	280.0	239.0	247.1	223.0	223.0	251.0	" "
12	M.B.	3	223.0	223.0	196.5	204.0	208.0	219.3	" "
2	M.L.	1½	208.0	211.0	208.0	200.0	185.0	214.9	" "
37	M.S.	10	96.0	105.7	102.3	96.0	96.0	98.9	Hanot's cirrhosis.
20	J.S.	3	171.2	160.8	164.3	154.0	168.3	171.2	Pneumonia, jaundice.

Histamine did not produce any change in the blood cholesterol values of two cases of coeliac disease.

TABLE 55.

Coeliac disease.

Case No.	Name	Age	Cholesterol mg.% after histamine.				
			Before	6	14	20 mins.	30	40
38	C.C.		105.7	114.2	105.7	105.7	105.7	105.7
39	M.S.		96.0	96.0	93.1	93.1	93.1	96.0

In conclusion it may be said that although histamine produced a rise of the blood cholesterol in the majority of healthy children in this series, the results in disease are manifestly inconsistent and do not give any justification for the use of histamine as a liver function test.

D. DISEASES OF THE BLOOD.

(i) Anaemias.

Muller[22] gives a most comprehensive review of the cholesterol metabolism in anaemia. He has collected many cases from the literature showing the cholesterol variations in haemolytic, pernicious and the so-called "secondary" anaemias. Frequent reference will be made to this work in the next few pages.

Haemolytic anaemia.

Investigators have found the blood cholesterol either diminished[23] or within normal limits[15] in this condition. Hypercholesterolemia has not been reported by any author.

Biscons and Rouzaud[24] collected eight cases of haemolytic jaundice and found hypocholesterolemia in every one. Muller[22] discovered thirty seven cases in the literature and hypocholesterolemia was reported in 67.5 per cent of them.

Govaerts[25] found higher cholesterol values and a lower incidence of icterus in infants who did not have their vernix washed off. He attributes this to the antihaemolytic action of cholesterol. Sperry[26] on the other hand, did not find any correlation in his series between physiological icterus and the total cholesterol.

McNee[7] believes that in haemolytic jaundice there is over-activity of the reticuloendothelial system especially the

spleen, and consequently excessive blood destruction takes place. Muller[22] draws attention to the fact that there is no correlation between the severity of the anaemia and the blood cholesterol values in these cases.

There does not appear therefore to be any general agreement respecting the rôle of the blood cholesterol in the haemolytic anaemias.

Splenic anaemia.

In the present investigation there were two cases of splenic anaemia, and the cholesterol was within normal limits in one (No. 40) and very low in the other (No. 41). In No. 40 the blood cholesterol displayed little variation during the first six weeks in hospital, remaining about 120 mg.%. At the end of this period splenectomy was performed and three days afterwards the cholesterol had fallen to 98.9 mg.%. Thereafter it rose, gradually to a maximum of 181.5 mg.% fifty two days after the operation. Eight months later it had fallen to 131.0 mg.%. In No. 41 the initial cholesterol value was 64.3 mg.%, and after almost a month in hospital the child's general condition had improved, but the blood cholesterol was only 70.0 mg.%. Splenectomy was then performed, and twenty two days afterwards the cholesterol had increased to 98.9 mg.%. Seven weeks later, however, the cholesterol was only 93.1 mg.% (vide Table 56).

A definite increase of the blood cholesterol after splenectomy was observed therefore in both cases, and these results are in agreement with the findings of other workers,[22,27,28,29] who

TABLE 56.

Splenic anaemia.

Case No.	Name	Age in yrs.	Date	Cholesterol mg.%	
40	E.P.	10	15.1.36	114.3	History - Small premature baby jaundiced at birth, cleared slowly but never completely. Jaundice varies from time to time.
			17.1.36	117.2	
			20.1.36	111.5	Exam. - Well nourished child with definite jaundice of skin and conjunctivitis. Liver and spleen 1½ fb. Urine - trace of urobilin, no bile.
			21.1.36	124.1	
			24.1.36	117.2	
			30.1.36	120.7	16.1.36 - Urine - urobilin +
			31.1.36	117.2	17.1.36 - Urine - urobilin +++ V. d. Bergh; direct - biphasic; indirect - 3.0 units.
			1.2.36	120.7	
			6.2.36	117.2	4.2.36 - Jaundice persists. General condition good. Spleen and liver 2 fb.
			13.2.36	117.2	
			21.2.36	98.9	18.2.36 - Splenectomy.
			27.2.36	111.5	27.3.36 - Very well.
			3.3.36	124.1	10.4.36 - " "
			4.3.36	124.1	4.12.36 - " "
			27.3.36	143.7	
			10.4.36	181.5	
			4.12.36	131.0	
41	E.H.	4	29.1.37	64.3	History - Healthy until 4 days ago had abdominal pain and vomited about half a pint of blood.
			24.2.37	70.0	
			16.3.37	98.9	Exam. - Spleen is 1½ fb. and urine contains no urobilin.
			3.5.37	93.1	
					25.2.37 - Splenectomy.
					16.3.37 - General condition much improved.
					3.5.37 - Very well.

observed hypercholesterolemia followed by a gradual return of the blood cholesterol to a normal level. This hypercholesterolemia has not been satisfactorily explained by any author. MacAdam and Shiskin[27] state that there is no evidence as to what extent, and in what way, this hypercholesterolemia is related to the question of splenic function.

There was only one case of acholuric jaundice in this series and the blood cholesterol was 75.9 mg.%, showing a well marked hypocholesterolemia.

Case No.	Name	Age	Cholesterol mg.%	Diagnosis
42	A.C.	2	75.9	Acholuric jaundice.

Icterus Gravis (vide Table 57).

There are four cases of icterus gravis and the blood cholesterol was low in three, and markedly increased in one of them. The three subjects having low values died, and the child exhibiting marked hypercholesterolemia recovered. The high figure in No. 46 may probably be accounted for by the presence of biliary thrombi which are common in neonatal anaemias[30]. It has already been observed that biliary obstruction is associated with increased values.

TABLE 57.

Icterus gravis.

Case No.	Name	Age	Cholesterol mg.%	Remarks
43	A.B.	8 days	90.2	Icterus gravis. Died.
44	R.P.	2/52	90.2	Icterus gravis. Died.
45	O'D	1/365	87.3	Icterus gravis. Died.
46	D.B.	11/365	255.1	Icterus gravis. Recovered.
47	R.B.	14/365	98.9	Physiological icterus.

Aplastic anaemia.

Muller[22] states that the blood cholesterol is normal or increased in severe aplastic anaemia. Only one case was observed in the present investigation and gradually diminishing values were observed during the course of the illness (vide Table 58).

TABLE 58.

Aplastic anaemia.

Case No.	Name	Age	Date	Cholesterol mg.%	Hb %	R.B.C. in millions	Remarks
48	R.G.	7	22.5.36	96.0	30	1¾	Bleeding of gums 18 days ago. Petechiae and ecchymosis are present & child is acutely ill. W.B.C. = 3700. Dismissed 14.8.36, slightly improved.
			27.5.36	87.3	38	1¾	
			6.8.36	70.0	-	-	

Nutritional anaemia.

In Table 59 the results in five subjects with nutritional anaemia are noted.

Although somewhat low values were observed in every case a marked degree of hypocholesterolemia was not observed in any of the children.

TABLE 59.

Nutritional anaemia.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Hb %	R.B.C. in millions	Remarks
49	D.D.	10/12	7.5.36	105.7	43	3½	General condition poor.
50	T.McA	16/12	7.5.36	98.9	62	4½	Small, poorly nourished child.
	"	"	22.5.36	117.2	68	4¾	General condition much better.
51	H.O.	2	14.5.36	87.3	28	3¼	Rickets. Heart - V.S. murmur at base
52	R.L.	2	1.7.36	108.5	40	3½	Heart - V.S. murmur at base.
53	C.M.	3	12.7.37	98.9	35	3¼	Radiographic exam. revealed severe rickets.

Anaemia resulting from haemorrhage.

Feigl[31] found high values after severe post-operative haemorrhage in comparatively healthy men. The increase was less marked in patients in poor general condition, and the maximum figures were obtained forty eight hours after the haemorrhage. Other workers have noted increased cholesterol values in experimental anaemia in animals[32].

Loss of serum protein, mobilisation of fat from the tissues, lack of red cells and consequent diminished oxidation, are a few of the explanations which have been offered for this hypercholesterolemia.

In the present investigation the cholesterol was determined in an apparently healthy adult male before, and again twenty four hours after withdrawing 500 c.c. of blood for a transfusion. The two values were identical (111.5 mg.%). The blood cholesterol was also estimated in seventeen children before and twenty four hours after operation. A diminution of the blood cholesterol occurred in fourteen patients and the remaining three subjects displayed only an insignificant increase. It is interesting to note the complete absence of hypercholesterolemia in these cases.

TABLE 60.

The blood cholesterol before and after operation.

Case No.	Name	Age (yrs)	Cholesterol mg.%		Diagnosis.
			Before	After	
65	D.M.	11/12	98.9	93.1	Hernia.
66	C.McI.	1	93.1	90.7	Prolapse of bladder.
67	D.B.	1	105.7	98.9	Hernia.
68	D.McL.	2	111.5	98.9	Hirschsprung's disease.
69	J.H.	2	117.2	105.7	Talipes.
70	C.H.	2	120.6	102.3	Congenital dislocation of the hip joint.
71	P.O'N.	3	102.3	90.7	Hernia.
72	J.C.	3	131.0	105.7	Torticollis.
73	H.F.	3	98.9	102.3	Hernia.
74	J.H.	6	111.5	117.2	Congenital dislocation of the hip joint.
75	C.S.	7	98.9	93.1	Tenotomy.
76	J.McK.	7	111.5	102.3	Osteotomy.
77	G.D.	10	111.5	117.2	Tenotomy.
78	D.McL.	12	96.0	93.1	Tenotomy.
79	R.S.	7	108.5	98.9	Hypospadias.
80	C.P.	8	131.0	117.2	Chronically inflamed appendix.
81	A.B.	7	108.5	98.9	Chronically inflamed appendix.

(11) Leukaemia.

Muller observed hypocholesterolemia in thirteen out of fifteen cases of myelogenous leukaemia. Uniform results have not, however, been observed in the present investigation. Hypocholesterolemia occurred in two cases, the cholesterol was normal in one, while the last subject displayed a slight degree of hypercholesterolemia.

TABLE 61.

Leukaemia.

Case No.	Name	Age	Date	Cholesterol mg.%	Hb %	R.B.C. in millions	Remarks
54	I.W.	2	8.4.36 16.4.36	154.0 Died	71	4¼	Child has severe dyspnoea and is acutely ill. X-ray exam. shows consol. both lungs. Temp. 103.° W.B.C. = 124,200. Film contains a large number of primitive white cells mostly mononuclears.
55	A.McK	5	3.12.36	105.7	55	2	W.B.C. = 230,000 cells mainly lymphocytes. Child dismissed irregularly on 11.12.36.
56	N.M.	5	29.7.36 4.8.36	81.6 Died	28	1¼	W.B.C. = 14,500. Fever of 100° to 101.8°. Diagnosed aleukaemic leukaemia.
57	A.McK	6	15.3.37 23.3.37	64.3 Died	43	2	W.B.C. = 1,600. Platelets almost absent from the blood film. Reticulocytes < 1%.

(iii) Purpura.

The cholesterol in five out of the seven cases in the present series was well within normal limits. A somewhat low figure (98.9 mg.%) was noted in No. 62, while in No. 63 the cholesterol was a little above the normal limit.

In the present small series of cases, therefore, the blood cholesterol did not display any marked deviation from the normal values.

TABLE 62.

Purpura.

Case No.	Name	Age	Date	Cholesterol mg.%	Remarks
58	A.H.	2	20.1.36 22.1.36 24.1.36	114.3 120.7 105.7	Diffuse purpuric rash. No swelling or tenderness of joints. R.B.C. = 4,120,000; W.B.C. = 13,600; Hb = 74%. Child made a good recovery and was dismissed on 24.1.36.
59	R.B.	4	25.6.37	105.7	Henoch's purpura. Blood in stools and purpuric eruption. Moderately ill. R.B.C. = 4,240,000. Hb = 87%. W.B.C. = 9,400. Platelets 674,000. Dismissed "well" on 13.7.37.
60	J.G.	5	14.10.36	114.3	Purpura 2 months ago; still has slight petachial rash. Hb = 90%. R.B.C. = 5,160,000 Platelets 20,640. General condition good.
61	D.McK.	11	11.1.37	111.5	History of pain and swelling of ankles for 2 weeks. Has generalised purpuric rash. Dismissed "well" on 19.3.37.

Table 62 (Contd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Remarks.
62	J.C.	10	12.2.37	98.9	Purpuric rash fading. R.B.C. = 3,760,000. Hb = 75%. W.B.C. = 38,000. Platelets 94,000. Made good recovery after somewhat prolonged convalescence and was dismissed on 30.4.37.
63	H.K.	7	16.11.35	150.6	Henoch's purpura. Abdominal pain and vomiting 6 days ago. Thin child with fading purpuric rash. Hb. 93%. R.B.C. = 4,130,000; W.B.C. = 10,400. Platelets 444,000. Dismissed on 29.11.35 to country branch.
64	C.M.	11	13.2.37	117.2	Henoch's purpura. Fading haemorrhagic papules on skin and thighs. Blood in stools. W.B.C. = 28,000. R.B.C. = 4,680,000. Platelets 238,680.

E. MALIGNANT TUMOURS.

(i) Sympathicoblastoma (vide Table 63).

In two children the initial values were normal, but the cholesterol fell as the patients' condition deteriorated. In No. 83 a severe hypocholesterolemia was observed. This child was acutely ill and he had a very severe anaemia.

TABLE 63.

Sympathicoblastoma.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Remarks.
82	A.G.	1	2.10.36	117.2	Child acutely ill. Abdomen greatly distended, and large mass palpable. Hb - 38%. R.B.C. = 2,295,000; W.B.C. = 5,300.
			14.10.36	96.0	
			9.11.36	Died	
83	J.R.	2	1.11.35	41.2	Child acutely ill. Liver greatly enlarged. Spleen 2 fb Hb - 15%. R.B.C. = 1,460,000.
			3.11.35	33.8	
			5.11.35	Died	
84	E.L.	2	16.1.37	124.1	X-ray examination shows multiple bone lesions. Hb - 64.7%. W.B.C. = 12,800; R.B.C. = 4,195,000.
			19.1.37	105.1	
			5.2.37	Died	

(11) Lymphadenoma (vide Table 64).

Low values were found in the two cases observed. The increase to 120.6 mg.% in No. 85 was noted after he had received a blood transfusion.

TABLE 64.

Lymphadenoma.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Remarks.
85	D.McG.	6	13.5.36	120.7	History - Swelling of right side of neck began about January 1935 and has gradually increased in size.
			12.11.36	87.3	
			8.1.37	81.6	18.5.36 - Hb. 55%. R.B.C. = 3,810,000. W.B.C. = 6,700.
			27.1.37	96.0	
			5.7.37	87.3	13.11.36 - Having fever of 100° to 102° from time to time. Had deep X-ray therapy on 5.11.36. Glands are smaller and child seems a little better.
			13.10.37	120.6	
			16.11.37	Died	18.10.37 - Child's condition gradually deteriorated. Had blood transfusion on 12.10.37. Autopsy report - "Lymphadenoma, pericardial and pleural effusions; ascites, severe anaemia".
86	A.W.	7	7.1.36	98.9	History - Admitted to hospital 3 months ago with considerable glandular swelling especially of cervical group. Child moderately ill with fever of 103.0° from time to time. General condition gradually deteriorating.
			8.4.36	Died	

Summary.

1. Hypercholesterolemia was found in catarrhal jaundice, congenital atresia of the bile ducts, atresia of the duodenum and in one case of icterus gravis, i.e., in subjects with some degree of biliary obstruction.

2. Hypocholesterolemia was noted in anaemia, and the lowest results occurred in grave anaemias proceeding to a fatal termination. There was not, however, any definite correlation between the red cell count and haemoglobin percentage, and the blood cholesterol.

3. Little disturbance of the cholesterol values was found in purpura.

4. A post operative fall of the blood cholesterol occurred in the majority of the children.

5. Lymphadenoma and sympathicoblastoma did not appear to produce any characteristic change in the blood cholesterol.

THE BLOOD CHOLESTEROL IN DISEASES OF THE NERVOUS SYSTEM.

Some investigators believe that the nervous system plays an important part in cholesterol metabolism (vide page 11), but this view is not supported by many workers. Nevertheless, nervous tissue contains a large percentage of cholesterol and it is conceivable that a lesion of this system might produce some disturbance of the blood cholesterol.

Duncan[1] found hypercholesterolemia in cases of psychosis with gross organic lesions, and Lolli[2] found marked disturbances of the cholesterol in cerebral haemorrhage, tumour and meningitis.

Convulsions.

McQuarrie et alii[3] quote the literature on the blood cholesterol in epilepsy, showing a definite lack of uniformity in the results of different authors. In their own cases they have not found any constant relationship between the cholesterol values and the seizures. Nevertheless, hypocholesterolemia was present in the majority of severe epileptic patients. In some of their cases the convulsions were reduced in number after the blood cholesterol had been increased by the giving of a ketogenic diet. Rampini[4] observed hypercholesterolemia in twelve out of twenty epileptic subjects and in all cases of tetany. Varone[5] found the blood cholesterol increased in rickets and tetany.

In the present investigation there were only four cases of epilepsy (vide Table 65). The lowest value, 81.6 mg.% in case No. 1, was observed about two hours after a convulsion, while a high normal value, 143.7 mg.% was found in No. 3, twelve hours after a seizure. In the remaining two children the cholesterol was 98.9 mg.% and 131.0 mg.%, two, and four days, respectively, after the last convulsion.

In this small series of cases it is impossible to express any opinion respecting the relationship between the blood cholesterol values and the seizures in epilepsy.

TABLE 65.

The blood cholesterol in epilepsy.

Case No.	Name	Age	Date	Date of last convulsion.	Cholesterol mg.%	Remarks
1	W.M.	$3\frac{2}{12}$	27.4.37	26.4.37	81.6	Epilepsy.
"	"	"	19.5.37	16.5.37	124.1	"
"	"	"	2.6.37	16.5.37	114.3	"
2	J.W.	$6\frac{10}{12}$	25.3.36	21.3.36	131.0	"
3	A.H.	$10\frac{6}{12}$	28.3.36	27.3.36	143.7	Daily convulsions. Cerebral tuberculoma.
4	A.L.	8	1.2.37	29.1.37	98.9	Epilepsy.

TABLE 66.

The blood cholesterol in tetany.

Case No.	Name	Age	Date	Cholesterol mg.%	Serum Calcium mg.%	Remarks
5	J.McL.	11/52	20.3.36	120.0	6.7	Craniotabes
6	W.C.	8/12	14.4.37	81.6	6.2	Rickets +
"	"	"	23.4.37	124.1	-	Very well.
"	"	"	10.5.37	108.5	-	Not so well (boils). No evidence of tetany.
7	W.McD.	8/52	15.1.37	87.3	6.5	
"	"	"	20.1.37	105.7	-	Improving.
"	"	"	1.2.37	101.8	-	Well.
8	J.McF.	5/12	30.3.36	96.0	7.1	Died 30.3.36
9	J.F.	12/52	28.12.36	64.3	7.4	
10	I.B.	8/12	7.4.37	90.1	8.1	Rickets.
11	W.R.	15/12	10.3.37	98.9	7.0	Nutritional oedema.

Tetany.

The results in tetany are much more definite than in epilepsy, for low values were noted in six out of seven subjects. Serial determinations were made in two of them. The initial values were 81.6 mg.% and 87.3 mg.%, respectively, and in both cases the cholesterol rose during the convalescent period to over 100 mg.% (Nos. 6 and 7). In one child the cholesterol was as low as 64.3 mg.%, and the remaining subjects had values of 90.1 mg.%, 96.0 mg.% and 120 mg.%.

Wade[6] noted an inverse ratio between the serum calcium and the blood cholesterol. On the other hand, Goebel[7] found that intravenous calcium raised the blood cholesterol. In the present series an inverse ratio was not observed between the cholesterol and the serum calcium (vide Table 66).

TABLE 67.

The blood cholesterol in convulsions associated with acute infections.

Case No.	Name	Age	Date	Date of last convulsion.	Cholesterol mg.%	Remarks
12	D.M.	$1\frac{11}{12}$	14.1.36	14.1.36	102.3	Tonsillitis.
13	J.D.	2	7.4.37	7.4.37	87.3	"
14	M.McA.	$\frac{9}{52}$	30.3.36	30.3.36	120.7	Acute gastro-enteritis.
15	C.S.	$1\frac{10}{12}$	21.11.35	20.11.35	87.3	Dysentery.
16	W.B.	$\frac{7}{12}$	10.3.37	10.3.37	105.7	Acute iliocolitis.

Convulsions from divers causes.

It will be shown when discussing diabetes that low cholesterol values were found in all cases of hypoglycaemic coma.

The values in convulsions associated with acute infections and in convulsions of unknown origin are indicated on Tables 67 and 68 respectively. There is considerable variability of the results, and there does not appear to be any correlation between the cholesterol level and the occurrence of convulsions in these subjects.

Anterior poliomyelitis.

At the acute onset of this illness Inglessi[8] found slight hypocholesterolemia, having no relation to the temperature. When paralysis became established hypercholesterolemia resulted and lasted a long time. He suggests that the increased cholesterol values are due to the breaking down of nervous tissue and the setting free of cholesterol.

There are only three cases of poliomyelitis in the present series and the blood cholesterol did not show any significant variation from the normal values for children of the same age groups (Nos. 25, 26 and 27 in Table 69).

Other lesions of the nervous system (Vide Table 69).

The highest figure - 154.0 mg.% - was found in a case of cerebral thrombosis with oedema of the brain, and the lowest value - 90.1 mg.% - occurred in a case of cerebral tumour. The remaining cases, which include spastic diplegia, cerebellar ataxia, and hydrocephalus, were within normal limits.

TABLE 68.

The blood cholesterol in convulsions of unknown origin.

Case No.	Name	Age	Date	Date of last convulsion.	Cholesterol mg.%	Remarks
17	C.N.	$1\frac{10}{12}$	28.8.36	26.8.36	96.0	Serum Calcium 11.1 mg.%.
18	J.A.	$8\frac{11}{12}$	19.8.36	No recent convulsions	120.6	-
19	E.G.	$2\frac{1}{12}$	11.11.35	8.11.35	105.7	W.B.C. 57,400 (no infection present.)
20	J.B.	$7\frac{3}{12}$	3.4.36	No recent convulsions	154.0	Choroiditis.
21	J.F.	$2\frac{9}{12}$	14.5.37	"	111.5	Acidosis.
22	M.B.	$2\frac{5}{12}$	13.1.37	12.1.37	98.9	Serum Ca = 11.2
	"	"	16.1.37	13.1.37	102.3	? Mentally defective
23	D.McR	3	24.5.37	24.5.37	104.3	Microcephaly.
	"	"	28.5.37	25.5.37	111.5	Cerebral diplegia.
24	J.A.	1	10.6.37	10.6.37	81.6	Serum calcium 11.3 mg.%.

TABLE 69

The blood cholesterol in some lesions of the nervous system.

Case No.	Name	Age	Cholesterol mg.%	Diagnosis
25	E.F.	1	111.5	Poliomyelitis (onset 3 wks. ago).
26	N.McC.	2	102.3	Poliomyelitis (onset 4 wks. ago).
27	C.L.	4	124.1	Poliomyelitis (onset 2½ yrs. ago).
28	M.S.	8	90.1	Cerebral tumour.
29	R.M.	8	114.3	Cerebral tumour.
30	J.O.	11	131.0	Cerebral tumour.
31	M.T.	3	124.1	(Encephalitis) spastic hemiplegia.
32	O.P.	5	105.7	Spastic diplegia.
33	E.W.	11	105.7	Spastic diplegia.
34	J.McB.	7/12	102.3	Hydrocephalus.
35	J.H.	1	111.5	Microcephaly. Optic atrophy.
36	I.B.	4	120.7	Cerebellar ataxia.
37	I.F.	3	105.4	Cerebellar ataxia (mentally defective.)
38	J.H.	9/12	127.6	Facial paralysis.
39	D.Y.	9	111.5	Disseminated sclerosis.
40	J.S.	2	143.7	Cerebral thrombosis. Oedema of brain.
"	"	"	154.0	Second determination made 4 days after the first.

Serial determinations were made on a case of polyneuritis (vide Table 70). This child was afebrile for the first five weeks of the illness, but from the fifth to the eleventh week he had frequent attacks of fever and his temperature sometimes rose to 101.0 or 102.0. The initial cholesterol value was 120.7 mg.% and it fell 9 days later to 105.7 mg.%. Thereafter the blood cholesterol gradually rose and it was 157.4 mg.% seven days after the cessation of the final attack of fever. The cholesterol then returned slowly to the initial level in the fourth month of the illness and the final reading was 111.5 mg.%.

It is apparent that the cholesterol variations in this case are similar to what has been observed during the course of acute infections such as pneumonia.

Summarising the results, one may say that normal values were noted in the majority of the nervous cases on which determinations were made. Low values were observed in tetany but the blood cholesterol was not found to be consistently low in convulsions from other causes.

TABLE 70.

Serial determinations in a case of polyneuritis.

Case No.	Name	Age	Date	Cholesterol mg.%	
41	R.C.	11	4.3.36	120.7	History - Healthy until 3 days ago he complained of weakness of limbs, which has gradually become worse. Exam. - Paralysis of leg and foot and small muscles of the hand. Mantoux and Schick tests negative; Pandy: positive. 20.5.36 - Definite improvement in the paralysis. 13.6.36 - Child very well, paralysis improving. 6.8.36 - Improving steadily.
			13.3.36	105.7	
			17.4.36	131.0	
			6.5.36	157.4	
			19.5.36	143.7	
			12.6.36	111.5	
			27.6.36	124.1	
			6.8.36	111.5	

THE BLOOD CHOLESTEROL IN DIABETES, HYPOTHYROIDISM AND COELIAC DISEASE, WITH OBSERVATIONS ON THE EFFECT OF SOME ENDOCRINE PREPARATIONS ON THE BLOOD CHOLESTEROL.

A. Diabetes.

The probable causes of the disturbed lipoid metabolism in diabetes are still disputed by authorities on the subject. Degeneration of the tissues setting free lipoids has been suggested by some, while others think that the mobilisation of fat from the tissues is the most probable cause. Hemoconcentration has been suggested by Man and Peters[1]. Joslin[2] supports the view that the hypercholesterolemia is due to faulty fat combustion, resulting from the derangement of the carbohydrate metabolism. Accepting this explanation, one would expect the blood cholesterol to be an index of the efficiency of the carbohydrate metabolism. This assumption is in conformity with the findings of Rabinowitch[3] who showed that the subsequent course of patients with a normal cholesterol and a normal blood sugar, was more tranquil than that of patients with a high cholesterol and a normal blood sugar. This is also in agreement with Joslin (1937), who emphasizes the importance of estimating the blood cholesterol in juvenile diabetics. The following is a quotation from his recent book.

> "It is as important to know the blood cholesterol value of juvenile diabetics as it is to know their blood-sugar values, because diabetes is often more severe in the child than in the adult and because uncontrolled diabetes has a higher incidence in children. Cholesterol values are a more accurate index of the diabetic condition than is the blood-sugar value. Glycosuria and glycaemia, which respond so promptly to insulin therapy, do not always suggest the gravity of an uncontrolled diabetic condition. A high blood cholesterol is reliable evidence that a diabetic is uncontrolled. Its existence indicates that dangers are present or imminent and that immediate action to control the diabetic condition should be taken."

Chaikoff et alii[4] on the other hand do not believe that the blood cholesterol is a reliable index of the degree of control of the diabetic patient. Their principal argument in favour of their view is the absence of marked hypercholesterolemia in acidosis. Both schools of thought appear to produce equally convincing evidence in favour of their divergent views.

It will be shown later in this investigation that high cholesterol values are seldom found in cases of short duration even when severe acidosis is present, but that they are found where the disease has been present for one or more years. Hypercholesterolemia apparently develops slowly.

It is suggested that the blood cholesterol values may be an index of the duration of the inefficiency of the carbohydrate metabolism.

Personal observations.

Thirty juvenile diabetics were observed during 1936 and 1937, and I have had access to the figures for 1934 and 1935. The results are indicated in Table 76.

(a) Hypercholesterolemia. Cholesterol values of more than 200 mg.% were observed at some period of the illness in seven children and four of them had to be readmitted from time to time for stabilisation of diet and insulin. In all the above patients the cholesterol fell gradually to the normal level during the succeeding two or three years of insulin and dietetic treatment. In twelve subjects the blood cholesterol was under 140 mg.% and ten of them remained balanced without readmission to hospital.

It would appear therefore that children with hypercholesterolemia tend to be more difficult to stabilise than children with lower values. This is in agreement with the findings of Joslin[2] and Rabinowitch[3]. Lange and Schoen[5], working with mice, and Liu Shih-Hao and Mills[6], working on nephrosis, found that high cholesterol values inhibited the action of insulin. It is possible that this may explain the difficulty of stabilising some diabetics with hypercholesterolemia.

(b) Hypocholesterolemia. Joslin[2] considers that a blood cholesterol of 90 mg.% or less is a serious and rare finding. He found that 40% of such cases died within five weeks. These low results were practically always associated with infection.

In the present investigation values below 100 mg.% were observed in eight children. In five of them this occurred before their diet and insulin had been stabilised, hypoglycaemia being present in two, while other two had had recent hypoglycaemia. Thus four out of eight cases were associated with hypoglycaemia. Severe pyuria was a complication in another case. The remaining three children were attending the out-patient clinic and appeared

TABLE 71.

Low cholesterol values.

Case No.	Name	Cholesterol	Sugar	Duration of disease (yrs)	Infection.	Initial Cholesterol	Remarks.
22	R.F.	81.6	24.4	3/52	-	114.3	Hypoglycaemic coma
"	"	93.0	76.0	1 10/12	-	-	General condition good.
15	E.McC.	93.0	71.4	1/12	-	105.0	Slight hypoglycaemia (drowsy).
4	C.D.	87.3	64.5	2/12	-	134.0	General condition good. Has been refusing diet.
24	J.McN.	96.0	-	6/52	-	126.7	General condition fair.
8	H.K.	96.0	55.0	2/12	-	-	Irritable and refuses food.
11	H.McI.	98.9	41.6	2/12	Pyuria ++	150.0	Temp. 101° and looks ill.
17	T.D.	98.9	62.5	2	-	-	General condition very good.
23	J.H.	98.9	76.0	6/12	-	-	General condition very good.

to be in good health (vide Table 71). In this small series of cases the majority of the low values would appear to be independent of any infective process. On the other hand five of these patients gave a comparatively short history of diabetes and it is conceivable that the onset may have been associated with some infection,

two of the subjects having a definite history of a febrile illness. In every case however the cholesterol was well within normal limits on admission, and there was no fever. Hypocholesterolemia followed insulin treatment and dietetic restriction in each of the above mentioned subjects. One may exclude, therefore, the infective process as a cause of the hypoglycamie in these cases. Though it is inadvisable to draw conclusions from such a small number of cases, the above results are definitely suggestive of some correlation between hypocholesterolemia and hypoglycaemic coma. It is interesting to note here that Lewin[7] found that high cholesterol values prevented hypoglycaemic convulsions in animals and he suggests that cholesterol has a protective action in preventing hypoglycaemia. Other authorities already quoted[5][6], have shown that high cholesterol values inhibit the action of insulin in experimental work on animals and in nephrosis.

Diabetic coma.

Joslin (1937)[2] indicates in his series of 94 cases of coma that there is no definite correlation between the height of the blood cholesterol and the severity of the acidosis. Chaikoff et alii[4] have found similar results in children. The figures for the present small series of cases are in agreement with the findings of the above authorities. Four cases are included and the maximum cholesterol value was only 17 mg.% above the highest normal figure. In one of the cases the blood sugar was 1081.1 mg.% while the cholesterol was 114.3 mg.%.

The following table indicates that in this small series the blood cholesterol was not dependent on the degree of acidosis.

TABLE 72.

Diabetic coma.

Case No.	Name	Age (yrs)	Cholesterol	Sugar	Insulin	Coma
9	R.K.	6	157.4	-	-	+
8	H.K.	$2\frac{6}{12}$	98.9	952.4	-	+
22	R.F.	$10\frac{6}{12}$	114.3	1081.1	-	+
11	H.McI	4	150.6	196.1	40 units	+

It is interesting to note here that determinations were made on four subjects with acidosis from other causes, and the results did not show any deviation from the normal values.

TABLE 73.

Acidosis in non-diabetic subjects.

Case No.	Name	Age yrs	Cholesterol mg.%	Blood CO_2 vols.%	Remarks
31	D.	$\frac{4}{365}$	98.9	18.02	Congenital cardiac condition.
32	A.C.	$\frac{7}{12}$	102.3	25.01	-
33	N.R.	5	111.5	35.18	-
34	H.B.	8	102.3	36.46	-

Blood sugar and cholesterol.

Though there appears to be an association between hypoglycaemic coma and hypocholesterolemia, a low blood sugar is not always accompanied by a low cholesterol value, nor are hyperglycaemia and hypocholesterolemia often found together (vide Table 76). On the other hand more or less parallel changes occurred in three cases where frequent serial estimations of the blood sugar and cholesterol were made over a period of several weeks (vide Chart 15). These results are probably a better index of the carbohydrate metabolism than the determinations made at longer intervals, which are shown in Table 76.

Diet and insulin.

Most authorities quoted by Joslin (1937)[(2)] agree that in normal and diabetic persons, alimentary lipemia produces little change in the blood cholesterol. The results of the present investigation are in agreement with this statement.

The effect of insulin and food on the blood sugar and cholesterol has been studied in ten children. In nine cases the estimations were made before and immediately after insulin and food, and the blood cholesterol remained practically unchanged in every case. There was therefore no parallel between the blood sugar and the cholesterol where the immediate action of the insulin and diet was studied (vide Table 74). In Case No. 29

Chart 15.

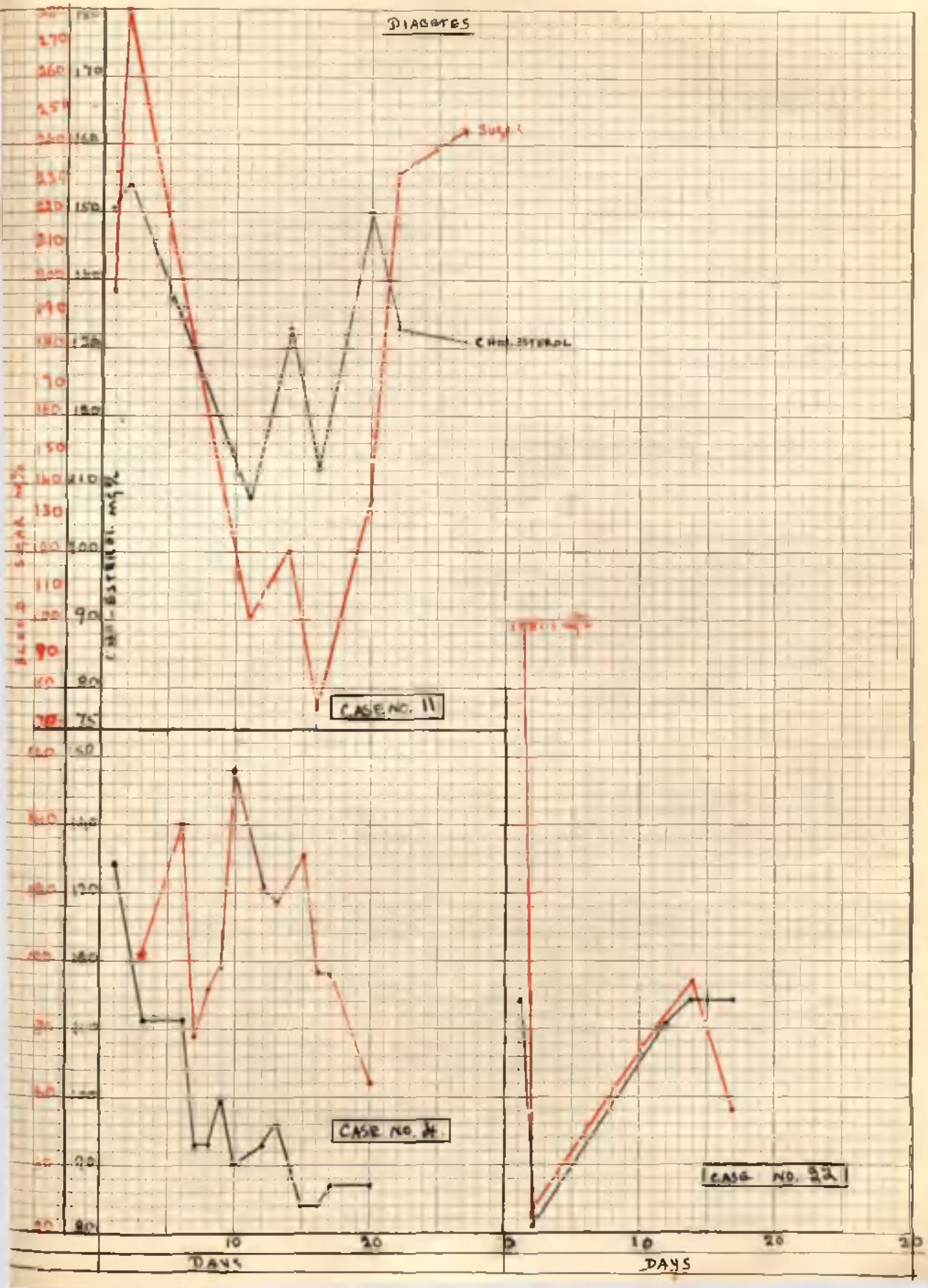

DIABETES
SUGAR
CHOLESTEROL
CASE NO. 11
CASE NO. 24
CASE NO. 22
DAYS
DAYS

TABLE 74.

(a) Determinations of the blood cholesterol and sugar before and after Insulin and Diet.

Case No.	Name	Age (yrs)	Cholesterol mg.%		Blood sugar	
			Before	After	Before	After
17	T.D.	11	124.1	124.1	102.0	147.0
30	M.D.	15	160.9	164.3	208.3	285.7
12	A.G.	15	120.7	127.5	90.5	131.5
20	V.G.	14	131.0	127.5	172.4	370.3
13	J.L.	11	117.2	114.3	180.1	266.6
26	H.M.	14	143.7	143.7	175.4	224.7
18	A.McL.	9	127.5	127.5	80.0	121.8
14	J.P.	16	120.7	120.7	204.0	281.6

(b) Case No. 29.

	Fasting	Hours after insulin & diet.					Diet in "lines"		Insulin in units.
		1	2	3	4	5	Red	Black	
Cholesterol mg.%	131.0	124.1	124.1	131.0	131.0	131.0	3	3	5
Sugar mg.%	74.6	82.6	82.6	80.0	74.1	71.4	-	-	-

observations were made before and hourly for five hours afterwards. During this period the blood sugar and the cholesterol displayed little variation.

Insulin in non-diabetic subjects.

Bruger and Mosenthal (1934)[8] give a review of the literature on the effect of insulin on the blood cholesterol. They state that an increased blood cholesterol following the administration of insulin was not observed by any worker. No reference is made, however, to the action of insulin in children. The authors, themselves, found that insulin produced no change in the majority of the blood cholesterol values of their diabetic and non-diabetic patients.

Personal observations.

Nine fasting non-diabetic children were given 5 or 6 units of insulin four hours after food. A definite fall of the blood cholesterol occurred in every case, the lowest value being observed usually one or one and a half hours after the insulin. Both the sugar and the cholesterol were estimated on the same specimen of blood and the two curves were more or less parallel, the cholesterol showing a definite lag. One concludes, therefore, that insulin lowers the cholesterol in children and that it acts on the cholesterol more slowly than on the sugar (vide Table 75 and Chart 16).

It is interesting to observe that, although somewhat low blood sugar values were found in some of these cases, none of the children displayed any evidence of hypoglycaemia.

Chart No. 16.

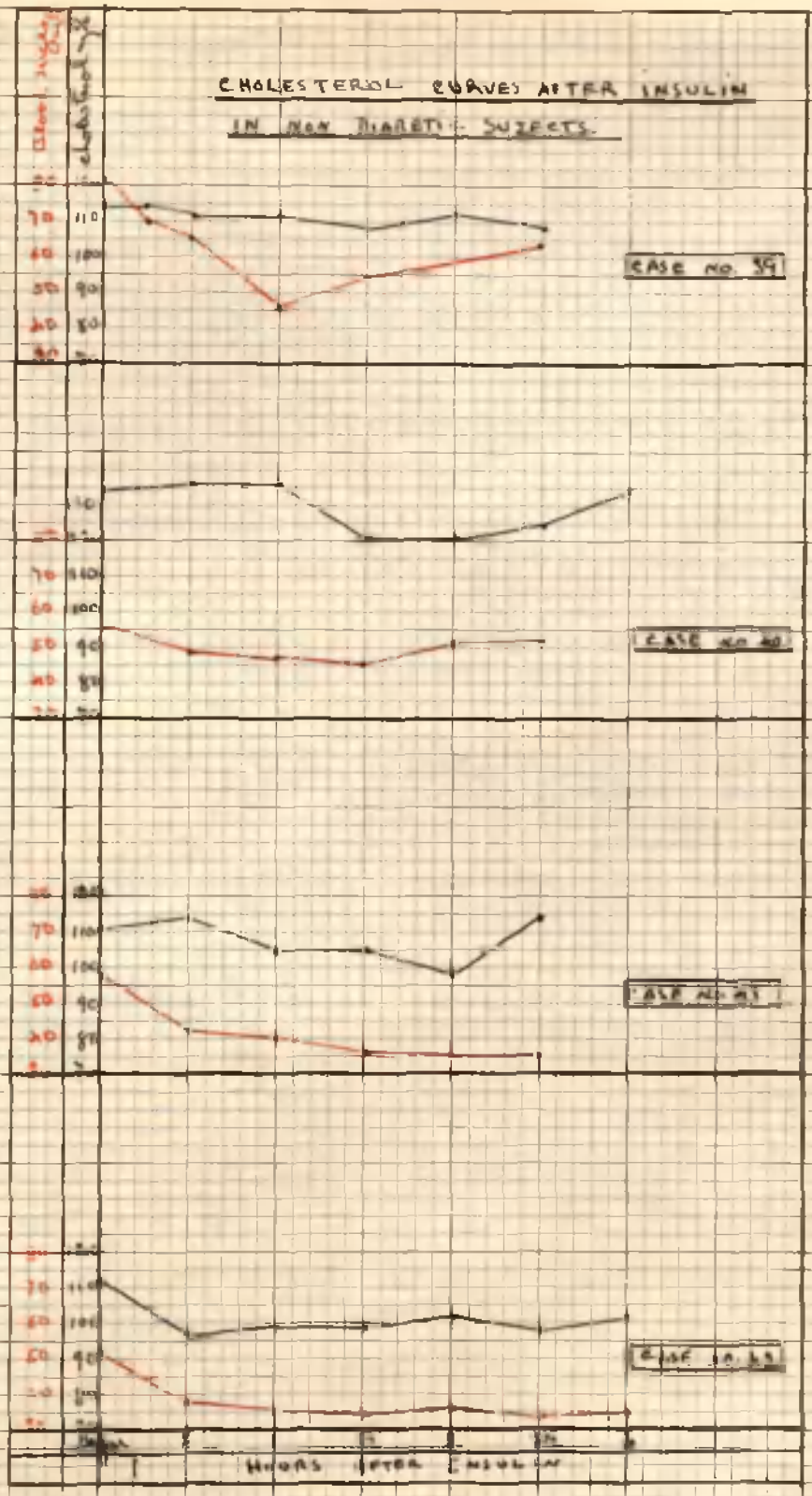

CHOLESTEROL CURVES AFTER INSULIN
IN NON DIABETIC SUBJECTS.
CASE NO. 59
CASE NO. 40
CASE NO. 41
CASE NO. 43
HOURS AFTER INSULIN

TABLE 75

Cholesterol curves after 6 units of Insulin in 9 Non Diabetic Subjects

Case No.	Name	Age (yrs)	Blood sugar and Cholesterol	Cholesterol mg.%.								
				Before	15	30	60	90	120	150	180	mins
35	J.M.	10	Cholesterol	116.2	102.3	102.3	98.9	96.0	98.9	96.0	105.7	
36	R.M.	8	Cholesterol	108.6	-	108.6	87.3	96.0	98.9	98.9	102.3	
37	M.S.	10	Cholesterol	111.5	111.5	96.0	87.3	105.2	111.5	108.6	114.8	
38	M.M.	11	Cholesterol	124.1	117.2	102.3	111.5	111.5	114.3	-	-	
39	B.McK.	7	Cholesterol	114.1	114.1	111.5	111.5	108.5	111.5	108.5	-	
			Sugar	81.9	70.4	66.6	46.2	54.5	-	69.4	-	
40	T.B.	7	Cholesterol	134.0	-	136.9	136.9	120.8	120.8	124.1	134.0	
			Sugar	56.8	-	48.3	46.9	45.4	52.3	52.3	-	
41	F.C.	6	Cholesterol	111.5	-	114.3	105.7	105.7	98.9	105.7	-	
			Sugar	58.8	-	42.7	41.6	36.9	35.2	35.0	-	
42	C.M.	10	Cholesterol	114.3	-	111.5	114.3	98.9	102.3	108.5	102.3	
			Sugar	51.6	-	42.3	41.7	41.0	33.3	35.2	30.7	
43	C.McG.	12	Cholesterol	111.5	-	96.0	98.9	98.9	102.3	98.9	102.3	
			Sugar	52.1	-	37.9	35.7	34.5	35.2	33.1	33.3	

Age of onset.

The illness began before attaining the age of two years in two patients, and the maximum cholesterol value observed was 157 mg.%. Fifty six determinations were made on nine children between two and five years of age, and the three highest values were 360, 394 and 200 mg.% respectively. Between six and ten years there were also nine children, and in this group the highest results were 410, 404 and 377 mg.% respectively. Thirty nine observations were made on children over ten years of age, and the three highest figures obtained were 289, 227 and 171 mg.% respectively.

The highest values occurred, therefore, between six and ten years of age. It is interesting to compare these results with those found in normal children, where the highest values were noted to occur within the same age group.

Duration of the disease.

In about one third of the cases the disease had been present for a period of six to ten years, and the highest cholesterol values were usually found in children who had suffered from the disease for some considerable time. In every case, however, the cholesterol fell eventually to within normal limits, during the course of insulin and dietetic treatment.

Mantoux test.

It is interesting to note that this test was positive in three children with a blood cholesterol of over 200 mg.%, while the test was negative in all but one of the subjects with

Cholesterol values of less than 200 mg.%. The cholesterol fell, eventually, in every case, to a normal figure.

Summary.

1. There was a tendency for children with high cholesterol values to be more difficult to stabilise in respect of diet and insulin, than those with low values. No case observed during the past two years has exhibited a persistent hypercholesterolemia, and all the children are alive and in good health at the time of writing.

2. Low cholesterol values with the present insulin dietetic regimen did not predict a fatal termination.

3. Hypoglycaemic coma was always accompanied by hypocholesterolemia, and it is suggested that high cholesterol values inhibit the action of insulin.

TABLE 76.

The blood cholesterol in 30 diabetic patients.

Case No.	Name	Age (yrs)	Length of illness (yrs.)	Date	Cholesterol mg.%	Blood Sugar mg.%
		(1) Disease began before 2 years of age.				
1	J.McC.	5	4	10.7.36	117.2	333.3
2	I.G.	4	2	6.8.37	131.0	200.0
3	A.C.	6	2	21.5.37	157.4	69.9
				22.5.37	108.5	113.0
				26.5.37	111.5	48.8
		(2) Disease began between 2 and 5 yrs. of age.				
4	C.D.	3	2/12	28.5.36	134.0	-
				30.6.36	111.5	102.0
				3.7.36	111.5	140.8
				4.7.36	93.1	78.1
				5.7.36	93.1	92.8
				6.7.36	98.9	99.0
				7.7.36	90.2	156.2
				9.7.36	93.1	120.0
				10.7.36	96.0	117.6
				12.7.36	84.9	135.1
				13.7.36	84.9	97.1
				14.7.36	87.3	96.1
				17.7.36	87.3	64.5
5	S.N.	9	4	7.12.34	57.5	34.2
				2.7.36	124.1	219.7
				6.8.37	133.7	176.9
6	L.McB.	2	1/12	2.7.36	127.6	50.5
7	M.G.	13	8	7.12.34	260.9	377.0
				3.12.35	204.0	-
				2.7.36	171.2	45.4
				30.12.36	108.5	96.1
				3.9.37	102.3	151.5
8	H.K.	2	2/12	12.5.37	98.9	952.4
				13.5.37 9 a.m.	111.5	166.7
				13.5.37 3 p.m.	111.5	44.6
				15.5.37 9 a.m.	111.5	49.5
				15.5.37 3 p.m.	124.1	148.2

Table 76 (Contd.)

Case No.	Name	Age (yrs)	Length of illness (yrs)	Date	Cholesterol mg.%	Blood Sugar mg.%
8				22.5.37	96.0	55.6
				26.5.37	96.0	89.0
				6.8.37	157.4	232.4
9	R.K.	6	1	21.11.35	157.4	-
				27.8.37	150.8	224.7
10	A.McC.	10	10	14.12.34	143.6	107.5
				1.11.35	219.0	-
				10.7.36	98.9	370.3
				1.11.36	124.1	312.5
				4.11.36	105.7	344.8
				20.8.37	124.1	347.6
11	H.McI.	4	$\frac{2}{12}$	30.9.36	150.6	196.1
				1.10.36	154.0	281.7
				10.10.36	108.5	100.0
				13.10.36	136.9	120.5
				15.10.36	111.5	75.2
				19.10.36	150.6	138.8
				21.10.36	136.9	232.5
				26.10.36	131.0	243.1
				1.11.36	98.9	86.2
				5.11.36	98.9	131.6
				12.11.36	102.3	69.9
				17.11.36	111.5	67.1
				18.11.36	98.9	41.6
				27.8.37	117.2	285.7
12	A.G.	16	12	2.7.36	124.1	206.2
				6.1.37	102.3	246.9
				27.8.37	131.0	285.7
	(3) Disease began between 6 and 10 years.					
13	J.L.	11	6	2.7.36	127.6	98.0
				6.1.37	108.5	94.3
14	J.P.	14	5	27.11.34	263.2	121.9
				18.10.35	404.6	-
				20.8.37	102.3	38.0
15	W.D.	10	4	16.11.34	243.1	74.6
				25.10.35	410.3	-
				10.2.36	326.4	689.6
				2.7.36	134.0	81.9
				13.8.37	131.0	33.0
16	E.McC.	6	$\frac{3}{52}$	6.3.37	105.7	82.6
				8.3.37	93.1	71.4
				13.8.37	124.1	82.0

Table 76 (Contd.)

Case No.	Name	Age (yrs)	Length of illness (yrs)	Date	Cholesterol mg.%	Blood Sugar mg.%
17	T.D.	11	1	2.7.36	117.2	222.2
				6.1.37	98.9	62.5
				3.9.37	124.1	327.8
18	A.McL.	9	1	10.7.36	102.3	204.1
				4.9.36	117.2	115.1
				9.7.37	87.3	-
				13.8.37	124.1	83.0
19	P.D.	9	2	14.12.34	147.1	101.0
				15.11.35	133.0	136.9
				2.7.36	131.0	67.7
				3.9.37	117.2	400.0
	(4) Disease began between 10 and 12 years of age.					
20	V.G.	12	1	16.11.34	227.1	172.4
				15.11.35	167.4	370.3
				3.1.36	131.0	263.1
21	B.S.	11	$\frac{5}{12}$	13.8.37	181.5	250.0
22	R.F.	10	$\frac{3}{52}$	6.11.36	114.3	1081.1
				7.11.36	81.6	24.4
				18.11.36	111.5	80.6
				20.11.36	114.3	93.4
				23.11.36	114.3	56.2
				20.8.37	93.1	76.0
23	J.H.	10	$\frac{8}{365}$	26.2.37	117.2	317.4
				27.2.37	111.5	76.9
				1.3.37	102.3	166.6
				20.8.37	98.9	76.0
24	J.McN.	10	$\frac{6}{52}$	25.2.37	126.5	645.1
				27.2.37	98.9	243.9
				1.3.37	96.0	-
				6.8.37	111.5	138.8
25	M.G.	10	$\frac{6}{12}$	2.7.36	143.7	54.3
26	H.M.	12	1	23.11.34	289.6	82.6
				1.11.35	223.0	-
				3.1.36	143.7	175.4
				10.7.36	131.0	200.0
				30.12.36	117.2	250.0
				3.9.37	143.7	97.5

Table 76 (Contd.)

Case No.	Name	Age (yrs)	Length of illness (yrs)	Date	Cholesterol mg.%	Blood Sugar mg.%
27	T.H.	12	6/52	5.3.37	131.0	401.2
				6.3.37	111.5	200.0
				8.3.37	114.3	150.3
				6.8.37	140.3	102.6
28	W.D.	12	3/12	2.7.36	131.0	108.1
				4.9.36	102.3	140.8
				6.1.37	120.6	338.9
				6.8.37	133.7	80.6
29	M.G.	9	1	1.4.36	157.4	-
				21.8.37	87.3	57.0
				24.8.37	111.5	70.4
				31.8.37	98.9	-
30	M.D.	13	2	14.12.34	136.9	119.04
				3.1.36	160.9	208.3

B. The effect of the administration of cholesterol and olive oil and some endocrine preparations on the blood cholesterol.

Adrenalin.

There has been considerable controversy among investigators respecting the rôle of the supra-renal glands in cholesterol metabolism, and it is, therefore, of some interest to observe the effect of the administration of adrenalin on the blood cholesterol.

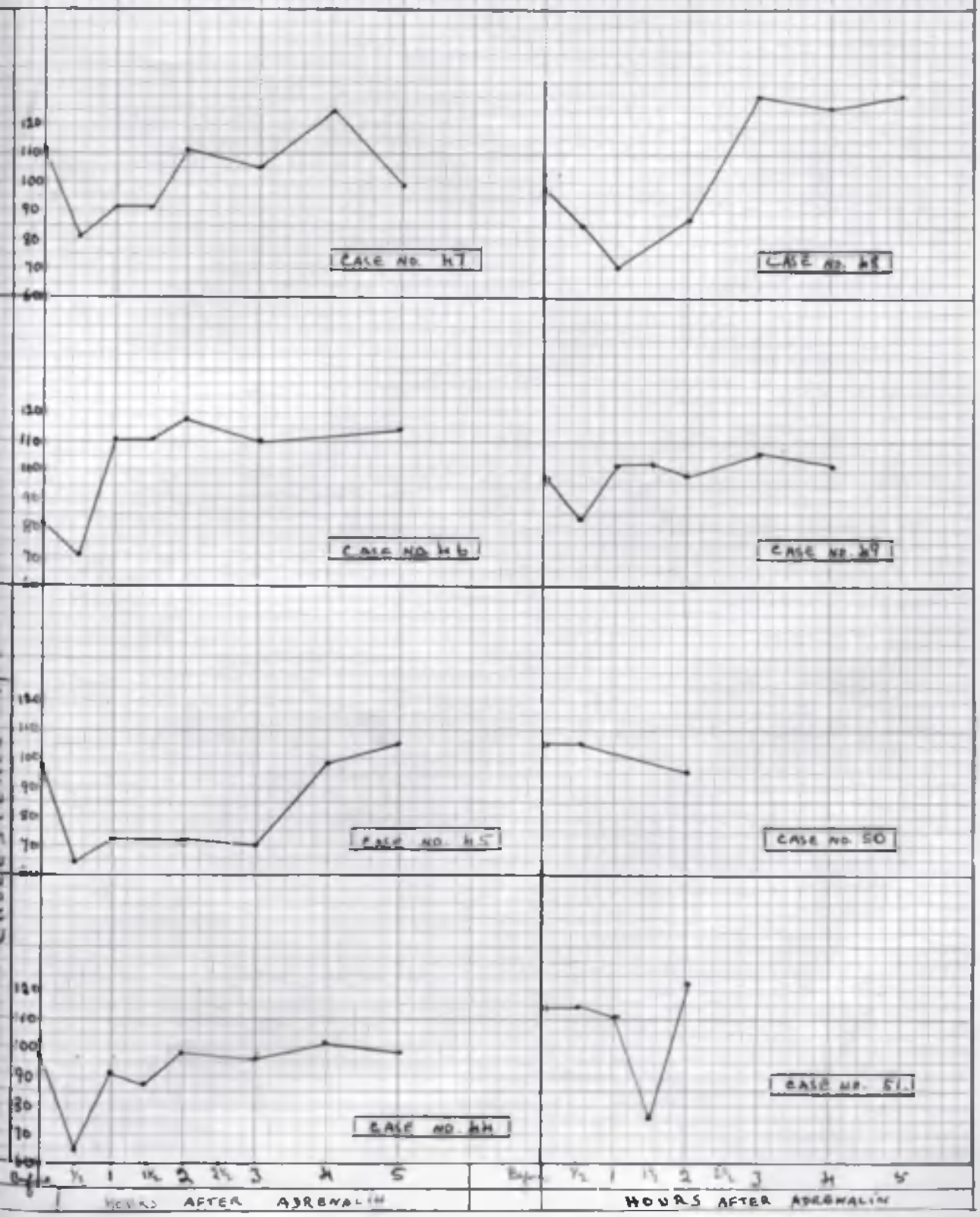
Bruger and Mosenthal[8] in quoting the literature on the subject show the lack of uniformity in the results of different authors regarding the effect of epinephrine on the blood cholesterol. Their own cases did not exhibit any change in the cholesterol after epinephrine, in five out of six subjects. Essinger and Györy,[9] working with children, observed that the subcutaneous injection of adrenalin lowered the cholesterol in practically all their cases.

In the present investigation, the blood cholesterol was estimated in eight children, after injecting 1 c.c. of 1/1000 adrenalin subcutaneously (vide Table 77). A fall in the blood cholesterol occurred in seven subjects. The patient (No. 46) who exhibited an increase after adrenalin, was acutely ill with tuberculous meningitis. The other children in this group were afebrile and in good general condition.

The uniformity of the above results is noteworthy and one may conclude from them that adrenalin lowers the cholesterol in children who are not acutely ill.

Chart No. 17.

CHOLESTEROL CHANGES AFTER ADRENALIN 1 c.c. 1/1000 SOLUTION



Pituitary extract (anterior and posterior).

There appear to be few, if any, references in the literature to the action of pituitary extract on the blood cholesterol in children.

Wartin[10] found cholesterol infiltration and retention at the autopsy in two cases of pituitary tumour. Moehlig and Ainslee[11] noted an increase of 35% in the cholesterol in 85% of rabbits, after injecting 1 c.c. posterior pituitary extract.

In the present investigation 1 c.c. posterior pituitary extract was given to ten children. It was followed by an increase of the blood cholesterol in five subjects, a fall in two, and in the remaining three cases the cholesterol values did not show any significant change (vide Table 78a).

Eleven children received 1 c.c. of anterior pituitary extract. This was followed by an increased cholesterol in four subjects, a decrease followed by an increase in two and an increase followed by a fall in one. Of the remaining four cases a slight fall was noted in three and the cholesterol values remained practically stationary in the remaining case (vide Table 78b).

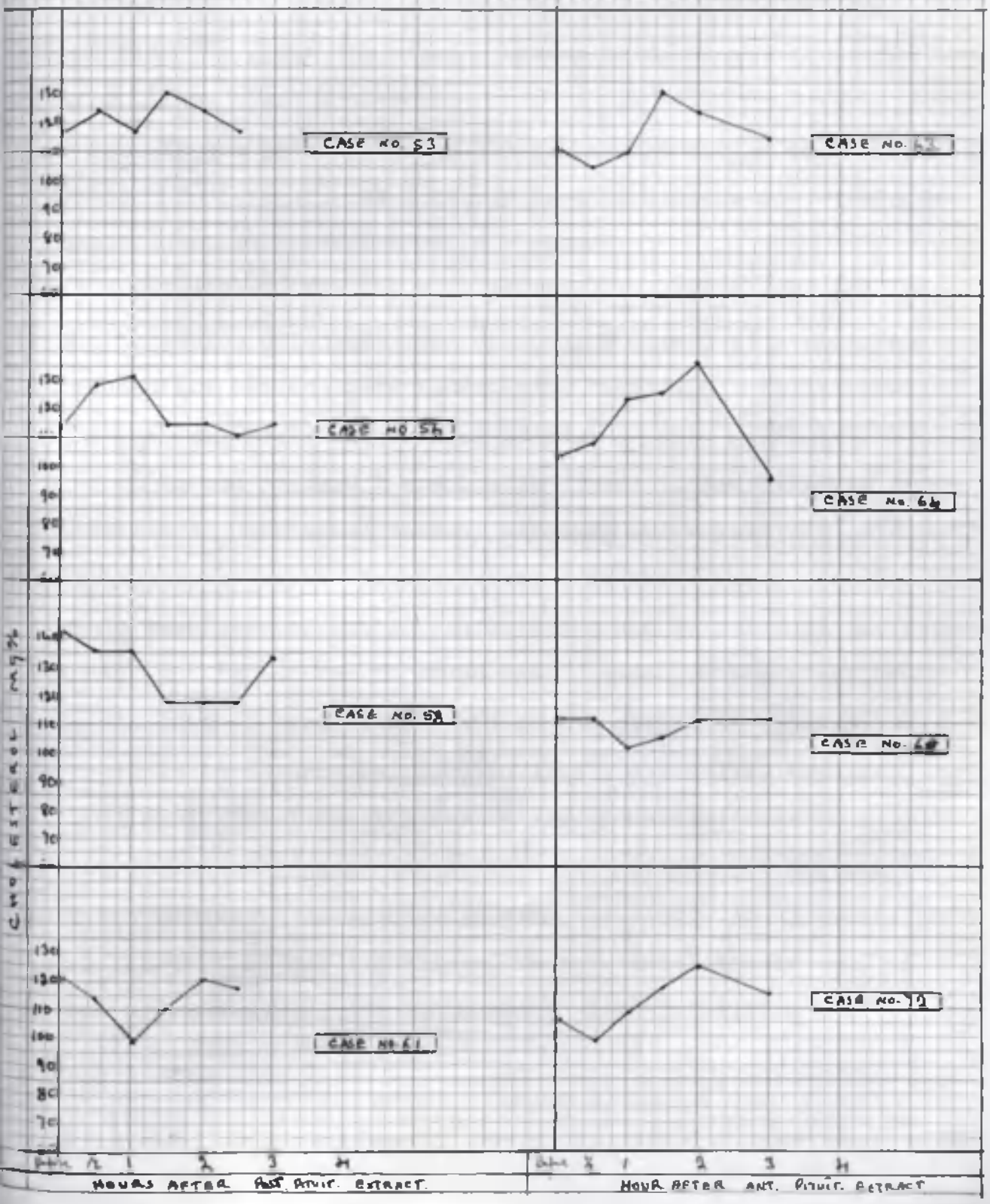
The results, after pituitary injection, are therefore somewhat inconclusive, but on the whole there is a tendency for the blood cholesterol to increase after both anterior and posterior pituitary extracts.

Olive oil and cholesterol.

There is some disagreement among investigators regarding the effect of the administration of olive oil alone, and of

CHOLESTEROL CURVES AFTER POSTERIOR PITUITARY EXTRACT 1cc.

CHOLESTEROL CURVES AFTER ANTERIOR PITUITARY EXTRACT 1cc.



cholesterol in oil, on the blood cholesterol. It had already been noted (page 5) that the existence of alimentary hypercholesterolemia is denied by the majority of authors. Blotner and Fitz[12] found the blood cholesterol unchanged after 500 c.c. of 20% fat.

In the present series the administration of one to two ounces of olive oil was followed by a diminution of the blood cholesterol in three out of four cases.

Kreis[13] found a fall of the cholesterol one hour after the ingestion of cholesterol and fat, followed by a rise, which reached its maximum four hours after ingestion. He attributed the preliminary fall to reflex action.

In the present investigation three to four grammes of cholesterol were given to four subjects and a fall of the blood cholesterol occurred in every case. In three cases serial estimations were carried out for three hours and in one case for four hours, and in each child there was a return of the blood cholesterol to the initial level at the end of the period of observation.

It is interesting that in this small series of cases the blood cholesterol usually fell after the administration of olive oil, or cholesterol in olive oil. An increase was not observed in any subject. These results are, therefore, in agreement with the findings of the majority of recent investigators that alimentary hypercholesterolemia does not occur.

Chart No. 19.

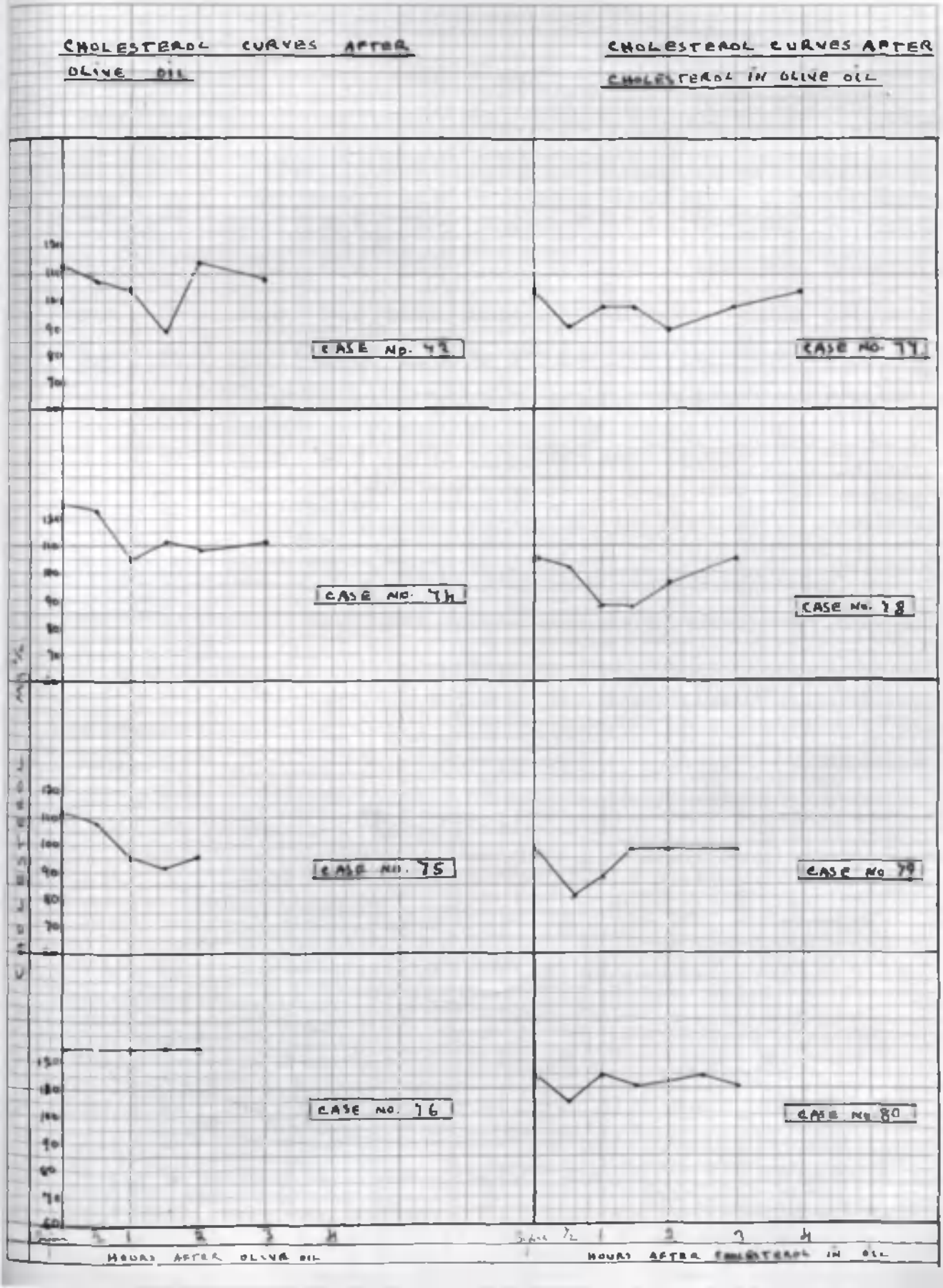

CHOLESTEROL CURVES AFTER OLIVE OIL
CHOLESTEROL CURVES AFTER CHOLESTEROL IN OLIVE OIL
CASE No. 73
CASE No. 77
CASE No. 74
CASE No. 78
CASE No. 75
CASE No. 79
CASE No. 76
CASE No. 80
HOURS AFTER OLIVE OIL
HOURS AFTER CHOLESTEROL IN OIL

TABLE 77.

Cholesterol curves after adrenalin 1 c.c.

Case No.	Name	Age (yrs)	Cholesterol mg.% Hours after adrenalin								Diagnosis
			Before	½	1	1½	2	3	4	5	
44	T.B.	9	98.9	64.3	90.2	87.3	108.6	96.0	102.3	98.9	Hydronephrosis.
	"	"	102.3	98.9	98.9	96.0	102.3	98.9	98.9	102.3	"
45	T.L.	9	98.9	64.3	73.0	-	73.0	70.0	98.9	105.7	Normal child.
46	F.D.	10	81.6	70.0	111.5	111.5	117.2	111.5	-	114.1	Tb. meningitis.
47	J.M.	10	111.5	81.5	93.1	93.1	111.5	105.7	124.1	98.9	Pulm. Tb.
48	R.R.	10	98.9	85.6	70.0	-	87.3	131.0	128.1	131.0	(Unresolved (pneumonia.
49	J.T.	11	98.9	84.5	102.3	102.3	98.9	105.7	102.3	-	(Erythema (nodosum.
50	E.W.	11	105.7	105.7	-	-	96.0	-	-	-	(Cerebral (Diplegia.
51	E.G.	2	114.8	114.8	111.5	75.9	117.2	-	-	-	Convulsions.

TABLE 78.

(a) Cholesterol curves after Posterior Pituitary Extract 1 c.c.

Case No.	Name	Age (yrs)	Cholesterol mg.% Hours after pituitrin.							Diagnosis
			Before	½	1	1½	2	2½	3	
52	B.McC.	6	134.0	131.0	131.0	136.9	131.0	134.0	-	Bronchiectasis.
53	M.W.	7	117.2	124.1	117.2	131.0	124.1	117.2	-	Hemiplegia.
54	P.H.	9	117.2	120.7	127.6	185.6	127.6	114.3	120.7	Rheumatism.
55	W.B.	10	134.0	131.0	131.0	134.0	-	-	134.0	Pleural effusion.
56	E.P.	10	114.3	127.1	131.0	114.3	114.3	111.5	114.3	Rheumatism.
57	S.C.	10	117.2	114.2	111.5	117.2	114.3	117.2	114.3	Rheumatism.
58	E.V.	11	143.7	136.9	136.9	117.2	117.2	117.2	134.0	Pyuria.
59	I.B.	12	108.3	117.2	111.5	108.3	120.7	120.7	117.2	Pleurisy.
60	J.G.	11	120.6	131.0	127.5	124.1	117.2	117.2	-	Arthritis of knee.
61	J.A.	8	120.6	114.3	98.9	111.5	120.6	117.2	-	Convulsions.

TABLE 78.

(b) Cholesterol curves after anterior pituitary extract 1 c.c.

Case No.	Name	Age (yrs)	Cholesterol mg.% Hours after antuitrin							Diagnosis
			Before	½	1	1½	2	2½	3	
62	N.McC.	2	111.5	98.9	102.3	105.7	102.3	-	102.3	Poliomyelitis.
63	W.B.	4	111.5	105.7	111.5	131.0	124.1	-	114.3	Fibrosis of right lung.
64	J.L.	6	114.2	117.2	124.1	126.5	136.9	-	105.7	Bronchiectasis.
65	L.D.	6	117.2	117.2	120.6	117.2	117.2	-	117.2	Abdominal Tb.
66	R.McD.	7	126.5	131.0	131.0	131.0	157.4	-	167.7	Resolving pneumonia.
67	A.G.	7	147.1	155.1	150.6	143.7	143.7	-	147.1	Tonsillitis.
68	M.B.	7	111.5	111.5	102.3	105.7	111.5	-	111.5	Chorea.
69	J.D.	8	131.0	120.6	124.1	131.0	131.0	-	131.0	Rheumatism.
70	E.W.	9	120.6	120.6	131.0	120.6	131.0	-	124.1	Rheumatism.
71	E.D.	11	178.0	200.0	255.0	131.0	120.7	131.0	-	Chorea.
72	R.C.	11	105.7	98.9	108.5	117.2	124.1	-	114.3	Polyneuritis.

TABLE 79.

(a) Cholesterol curves after olive oil.

Case No.	Name	Age (yrs)	Cholesterol mg.% Hours after olive oil.								Diagnosis and quantity of oil.
			Before	½	1	1½	2	2½	3	4	
73	M.D.	10	111.5	108.5	105.7	89.2	114.3	-	108.5	-	Rheumatism. Oil ℥ ii.
74	M.B.	7	124.1	117.2	105.7	111.5	108.5	-	111.5	-	Chorea. Oil ℥ ii.
75	J.A.	9	111.5	108.5	98.0	93.1	96.0	-	-	-	Talipes. Oil ℥ i.
76	C.M.	8	124.1	124.1	124.1	124.1	-	-	114.3	-	Pulm. Tb. Oil ℥ i.
			(b) Cholesterol curves after cholesterol in oil.								
77	O.P.	5	105.7	93.1	98.9	98.9	90.1	-	98.9	105.7	Cerebral diplegia. Cholesterol gm. iv.
78	J.R.	7	105.7	102.3	87.3	87.3	96.0	-	105.7	-	Asthma. Cholesterol gm. iv.
79	H.B.	10	98.9	81.6	87.3	98.9	98.9	-	98.9	-	Pulm. Tb. Cholesterol gm. iii.
80	J.H.	7	114.3	105.7	114.3	111.5	-	114.3	111.5	-	Fröhlich's Syndrome. Cholesterol gm. iv.

C. Hypothyroidism.

It is well known that hypercholesterolemia occurs in cretinism, and that thyroid therapy reduces the blood cholesterol to a normal or subnormal level. Bronstein[14] has shown that the determination of the blood cholesterol is the most simple and accurate method of controlling thyroid therapy in hypothyroidism. He draws attention to the fact that both in the very young and in older children, the performance of the basal metabolism test is beset with difficulties. Hurxthal[15] has demonstrated that hypometabolism associated with supra-renal or pituitary insufficiency is not accompanied by hypercholesterolemia. Boyd and Connel[16] find the blood cholesterol values of considerable assistance in the diagnosis of mild hypothyroidism.

The blood cholesterol value has also been used for controlling the X-ray dosage in the treatment of hyperthyroidism[17].

One may conclude that the determination of the blood cholesterol is a valuable aid in the diagnosis and treatment of disorders of the thyroid gland.

In the present investigation there were three cases of hypothyroidism and they all displayed an initial hypercholesterolemia. The diminution of the blood cholesterol in these three subjects during the course of thyroid therapy is indicated in Table 80.

TABLE 80.

The blood cholesterol values during the course of thyroid treatment in 3 cases of hypothyroidism.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	
81	M.McM.	18/12	7.10.36	193.1	History - Developed normally during early period of infancy, but is now somewhat backward. Cut first tooth one month ago. Cannot stand or talk.
			14.10.36	227.0	
			17.10.36	189.0	
			20.10.36	171.2	Exam.- Typical cretin. Backward mentally. X-ray of wrist shows delayed ossification. R.B.C. = 3,200,000; W.B.C. = 11,000; Hb. = 50%.
			24.10.36	150.6	
			28.10.36	131.0	
			29.10.36	117.2	15.10.36 - Ext. thyroid gr.½ b.d. started.
			2.11.36	117.2	21.10.36 - Child much brighter.
			5.11.36	52.9	22.10.36 - Thyroid increased to gr. i b.d.
			18.11.36	96.0	29.10.36 - Thyroid stopped.
			24.11.36	111.5	24.11.36 - Thyroid gr. i b.d. resumed.
			30.11.36	108.5	14.11.36 - Child very well and learning to walk. Plays with toys.
			14.12.36	64.3	
			8.1.37	75.9	22.1.37 - Says a few words. Progress in walking not very good.
			22.1.37	81.6	
			5.2.37	85.0	5.2.37 - General condition still improving.
82	M.W.	4	24.8.37	168.3	History - Was late in cutting first tooth. Is not growing.
			25.8.37	168.3	Exam. - Though not a typical cretin, child shows signs of hypothyroidism. X-ray of wrist shows ossification equivalent to 2 years of age.
			28.8.37	164.0	
			11.10.37	133.9	14.9.37 - Thyroid gr. i b.d. started.
					1.10.37 - Thyroid gr. i t.i.d.
					11.10.37 - Child much brighter & general condition is improving.

Table 80 (Ctd.)

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	
83	A.McL.	8	22.10.35	160.8	History - said to be normal and healthy until 3 months ago, began to complain of abdominal pain.
			10.11.35	93.1	
			30.11.36	84.8	Exam. - Child is not a typical cretin but there is definite evidence of hypothyroidism. X-ray shows ossification to be considerably delayed. 29.10.35 - Thyroid gr.iii b.d. started. 16.11.35 - Child much brighter. 30.11.36 - Condition greatly improved.

D. Coeliac Disease

Most authorities agree that the blood cholesterol is low in coeliac disease. Goldbloom and Gottlieb[18] found very low values and Schally[19] observed a marked hypocholesterolemia in a case of coeliac disease.

Personal observations.

Eight cases of coeliac disease are included in this series, and with three exceptions, all the values were below 100 mg.%. The highest figure noted was 102.3 mg.% and the lowest 75.9 mg.%. In one case (No. 84) determinations were made from time to time over a period of two months. This child was very small, emaciated and ill, and she had severe diarrhoea and vomiting on admission to hospital. The initial cholesterol value was 98.9 mg.%, and a relapse six weeks later was accompanied by a fall to 75.9 mg.%. When the child's condition improved the cholesterol rose to 102.3 mg.%.

TABLE 81.

Coeliac disease.

Case No.	Name	Age (yrs)	Date	Cholesterol mg.%	Remarks.
84	M.McN.	8	12.8.36	98.9	Moderately severe diarrhoea
			13.8.36	98.9	and vomiting.
			22.8.36	93.1	Condition improved.
			22.9.36	75.9	General condition much worse. Severe diarrhoea.
			15.10.36	102.3	Child much better.
85	C.C.	2	31.8.37	96.0	Diarrhoea.
			6.9.37	102.3	Much improved.
86	M.S.	3	6.9.37	96.0	Diarrhoea.
			13.9.37	96.0	Improved.
87	E.P.	1	6.9.37	87.3	Diarrhoea.
88	E.C.	2	13.2.36	98.9	Diarrhoea.
89	A.S.		6.9.37	102.3	Diarrhoea.
90	L.B.	12	6.9.37	98.9	Diarrhoea.
91	B.S.	7	13.3.37	98.9	Diarrhoea.
			16.9.37	81.6	Motions normal. General condition improved.

PART V.

SUMMARY AND DISCUSSION OF PERSONAL OBSERVATIONS.

Low cholesterol values have been found in many cases of pneumonia, acute rheumatism and other infections. Hypocholesterolemia, however, usually occurred in a prolonged or recurrent infection, rather than in a short acute illness, e.g. children suffering from a second attack of pneumonia exhibited lower values than children suffering from a first attack. There does not appear to be any correlation between hypocholesterolaemia and diminished resistance to infection, for it has been shown that a substantial increase of the blood cholesterol during the convalescent period was not necessarily associated with a rapid and uneventful convalescence. It is also apparent in the sections on pneumonia and rheumatism that a fatal termination was not always preceded by hypocholesterolemia. In the section dealing with pneumonia, attention has been drawn to the fact that in nephrosis, where extremely high cholesterol values are found, there is an increased susceptibility to pneumococcal and other infections.

In acute nephritis fever was accompanied by diminished cholesterol values in the majority of cases. All the children made a good recovery, and it was therefore impossible to come to any conclusion respecting the prognostic value of the blood cholesterol in this condition.

Hypercholesterolemia was observed in catarrhal jaundice and in congenital atresia of the bile ducts. Increased cholesterol

values are apparently associated with biliary stasis or obstruction. Ottenberg (page 176) has suggested that the determination of the blood cholesterol might be a useful aid in differentiating between catarrhal jaundice and acute yellow atrophy of the liver.

Diabetic patients in hypoglycaemic coma exhibited low cholesterol values. Although one cannot draw any conclusions from the small number of cases in this group, the results suggest that patients with hypocholesterolemia may be more susceptible to hypoglycaemic coma than patients displaying normal or increased cholesterol values.

Hypercholesterolemia was found in hypothyroidism and the blood cholesterol gradually diminished during the course of thyroid therapy. Investigators have been quoted who believe that determination of the blood cholesterol is the most simple and accurate method of controlling thyroid therapy in cretinism and hypothyroidism.

GENERAL SUMMARY.

In Part I a brief account is given of the history, chemistry and physiology of cholesterol. It has been indicated that cholesterol is chemically related to vitamin D and some of the hormone preparations.

Part II contains a résumé of the divers theories which have been suggested to explain the pathological variations of the blood cholesterol.

In Part III the variations of the blood cholesterol in normal children are discussed.

Personal observations are recorded in Part IV.

BIBLIOGRAPHY.

PART I.

History - Chemistry - Physiology.

(1) POULLETIER DE LA SALLE, 1758, quoted by G. L. Muller, Medicine, Balt., 1930, ix, 119.

(2) CHEVREUL, 1815, quoted by Muller, ibid.

(3) DENIS, 1830, quoted by Muller, ibid.

(4) DORÉE, ELLIS, FRASER, GARDNER, etc., various contributions to the Proc. Royal Soc., Ser. B., London, between 1908 and 1912.

(5) MOORE, F.C., Medical Chronicle, Manchester, 1907, xiv, 204.

(6) GAINSBOROUGH, H., Proc. Royal Soc.,Med., London, 1935, xxviii, 989.

(7) CALLOW, R.K. and A.S. PARKES, Brit. Med. Journ., London, 1937, 27th Feb., 456.

(8) VOLLMER, H., Amer. Journ. Dis. Childr., Chicago, 1928,xxxvi, 583, Ext. current lit.

(9) WADDELL, J., Journ. Biolog. Chem., Balt., 1934, cv, 711.

(10) HATHAWAY, M. and F.C. KOCH, ibid., Balt., 1935, cviii, 773.

(11) FLINT, A. Jr., Amer. Journ. of the Med. Sciences, Philadelphia, 1862, xliv, 20.

(12) DORÉE, C., and J.A. GARDNER, Proc. Royal Soc. Ser. B., London, 1909, lxxxi, 109.

(13) GARDNER, J.A., Brit. Med. Journ. London, 1932, 27th August, 392.

(14) FOX, F.W., and J.A. GARDNER, Proc. Royal Soc. Ser. B. London, 1925, xcviii, 76.

(15) SCHÖNHEIMER, R., and F. BREUSCH, Journ. Biolog. Chem., Balt., 1933, ciii, 439.

(16) HURXTHAL, L.M. and H.M. HUNT, Ann. Inter. Med., Lancaster, 1935, ix, 717.

(17) MUELLER, J.H., Journ. Biolog. Chem., Balt., 1916, xxvii, 463.

(18) DENIS, W., Journ. Biolog. Chem., Balt., 1917, xxix, 93.

(19) CHAIKOFF, I.L., T. H. McGAVACK and A. KAPLAN, Journ. Clin. Invest., N. York, 1934, xiii, 1.

(20) BLOTNER, H., and R. FITZ, ibid., N. York, 1934, xiii, 707.

(21) BLOTNER, H., Archiv. Int. Med., Chicago, 1935, lv, 121.

(22) WILSON, W.R., and J.P. HANNER, Journ. Biolog. Chem., Balt., 1934, cvi, 323.

(23) GARDNER, J.H., and H. GAINSBOROUGH, Biochem. Journ., London, 1928, xxii, 1048.

(24) BLOOR, W.R., Journ. Biolog. Chem., Balt., 1916, xxiv, 447.

(25) BLOOR, W.R., ibid., Balt., 1933, ciii, 699.

(26) BARKER, M.H., Proc. Soc. Exp. Biolog. and Med., N. York, 1931, xxviii, 1081.

(27) TOLSTOI, E., Journ. Biolog. Chem., Balt., 1929, lxxxiii, 753.

(28) ROTHSCHILD, M.A., and N. ROSENTHALL, Amer. Journ. of the Med. Sc., Philadelphia, 1916, cliii, 394.

(29) BLOOR, W.R., Journ. Biolog. Chem., Balt., 1932, xcv, 633.

(30) BRUGER, M., and I. SOMACH, ibid., Balt., 1932, xcvii, 23.

(31) GLUSKER, D., ibid., Balt., 1930, lxxxviii, 381.

(32) WRIGHT, A., and G. H. WHIPPLE, Journ. Exper. Med., N. York, 1934, lix, 407.

(33) BLOOR, W.R., and A. KNUDSON, Journ. Biolog. Chem., Balt., 1917, xxix, 7.

(34) BOYD, E.M., ibid., Balt., 1935, cx, 61.

(35) BOYD, E.M., ibid., Balt., 1933, ci, 623.

(36) BLOOR, W.R., R. OKEY and G. W. CORNER, ibid., Balt., 1930, lxxxvi, 291.

(37) PANZER and ASCHOFF, both quoted by J. W. McNee, Quart. Journ. Med., Oxford, 1914, vii, 221.

(38) GRIGAUT, A., Le Cycle de la Cholesterinémie - Thèse de Paris, 1913, No. 412.

(39) WESTON, P., Journ. Med. Res., Boston, 1915, xxxiii, 119.

(40) MACKEY, W.A., Brit. Journ. Surgery, Bristol, 1937, xxiv, 570.

(41) CHAUFFARD, A., C.RICHET, fils, and A. GRIGAUT, Compt. rend. de la soc. de biol., Paris, 1911, lxx, 317.

(42) GARDNER, J.A., Proc. Royal Soc. Med., London, 1932, xxv, 505.

(43) SCHUBE, P.G., Journ. Lab. and Clin. Med., St. Louis, 1936, xxii, 280.

(44) BRUGER, M., Amer. Journ. Clin. Path., Balt., 1935, v, 504.

(45) BRUGER, M., ibid., Balt., 1935, v, 384.

(46) SALISBURY, J.H., Amer. Journ. of the Med. Sciences, Philadelphia, 1863, xlv, 289.

PART II.

PATHOLOGY

Some interpretation of the pathological oscillations of the blood cholesterol.

(1) GRIGAUT, A., Thèse de Paris, 1913, No. 412.

(2) McNEE, J.W., Quart. Journ. Med., Oxford, 1914, vii, 221.

(3) CAMPBELL, J.M.H., Ibid, 1925, xviii, 393.

(4) SCHALLY, A.O., Erg. Inn. Med., Berlin, 1936, 1, 480.

(5) ROTHSCHILD, M.A., and N. ROSENTHAL, Amer. Journ. of the Med. Sc., Philadelphia, 1916, clii, 394.

(6) GAINSBOROUGH, H., Proc. Royal Soc. Med., London, 1935, xxviii, 989.

(7) HORVATH, A.A., Journ. Biolog. Chem., Balt., 1926, lxviii, 343.

(8) SMITH, M.E., and B. SURE, Proc. Soc. Exp. Biol. and Med., N. York, 1931, xxix, 158.

(9) MAN, E., and J.P. PETERS, Journ. Clin. Invest., N. York, 1934, xiii, 237.

(10) HURXTHAL, L.M., and H.M. HUNT, Ann. Inter. Med., Lancaster, 1935, ix, 717.

(11) FISHBERG, E.H., Journ. Biolog. Chem., Balt., 1929, lxxxi, 205.

(12) FLINT, A. Jr., Amer. Journ. of the Med. Sc., Philadelphia, 1862, xliv, 20.

(13) INGLESSI, E., La Clin. Pediat., Modena, 1932, xiv, 1003. December.

(14) MOUKHINE, S.A., Journ. de physiol. et de path.général, 1935, xxxiii, 1120.

(15) CASTEX, M.R., L.E. ONTANEDA and M. SCHTEINGART, Compt. rend. de la soc. de biol., Paris, 1931, cvi, 147.

(16) JOELSON, J.J., and E. SHORR, Archiv. Inter. Med., Chicago, 1924, xxxiv, 841.

(17) BAUMANN, E.J., and O.M. HOLLY, Journ. Biolog. Chem., Balt., 1923, lv, 457.

(18) BRUGER, M., and H. O. MOSENTHAL, Journ. Clin. Invest., N. York, 1934, xiii, 399.

(19) MARAÑÓN, G., An. de med. int., Madrid, 1932, I, 305.

(20) ECK, M., and J. DESBORDES, Compt. rend. de la soc. de biol., Paris, 1935, cxviii, 498.

(21) SPERRY, W. M., Journ. Biolog. Chem., Balt., 1932, xcvi, 759.

(22) SPERRY, W. M., Ibid., Balt., 1929, lxxxi, 299.

(23) SCHÖNHEIMER, R., quoted by Gainsborough, H., Proc. Royal Soc. Med., London, 1935, xxviii, 989.

(24) SCHÖNHEIMER, R., Kl. Med., Moskva, 1933, cxxiii, 719.

(25) OFFENKRANTZ, F. M., and F. FERARU, Journ. Lab. and clin. Med., St. Louis, 1937, xxii, 780.

(26) SCHALLY, A. O., Erg. Inn. Med., Berlin, 1936, 480.

(27) GALDÓ, A., Archiv. Espan. de pediat., Madrid, 1933, xvii, 97.

(28) PETERSILIE, H., Journ. Lab. and Clin. Med., St. Louis, 1934, xx, 144.

(29) BLOOR, W. R., Journ. Biolog. Chem., Balt., 1921, xlix, 201.

(30) CALVIN, J. K., and A. H. GOLDBERG, Amer. Journ. Dis. Children, Chicago, 1931, xli, 1066.

(31) SIMONDS, J. P., and O. E. HELPLER, Journ. Amer. Med. Assoc., Chicago, 1932, xcviii, 283.

(32) KAUFMANN, G., and D. MÜHLBOCK, Journ. de phys. et de path. gén., Paris, 1932, xxx, 541. Ext.

(33) PARHON, C. J., and V. MARZA, Compt. rend. de la soc. de biol., Paris, 1925, xcii, 727.

(34) MOEHLIG, R. C., and H. B. AINSLEE, Amer. Journ. Phys., Balt., 1927, lxxx, 649.

(35) LONG, M. L., E. HILL and F. BISCHOFF, ibid., 1932, cii, 402

(36) WARTIN, A. S., Proc. Soc. Exp. Biol. and Med., N. York, 1917, xiv, 42.

(37) BRONSTEIN, I. P., Journ. Amer. Med. Assoc., Chicago, 1933, c, 1661.

(38) HESS, J. H., Ann. Int. Med., Lancaster, 1934, viii, 607.

(39) GILLIGAN, D. R., M. VOLK, D. DAVIS and H. L. BLUMGART, Archiv. Inter. Med., Chicago, 1934, liv, 746.

(40) HURXTHAL, M., ibid., Chicago, 1934, liii, 762.

(41) EPSTEIN, A. A., and L. LANDE, ibid., Chicago, 1922, xxx, 563.

(42) BOYD, E., and W. F. CONNELL, Quart. Journ. Med., Oxford, 1937, vi, 467.

(43) LÉVY, M. and L. GALLY, Presse Med., Paris, 1936, No. 57, 15th July, 1147.

(44) HURXTHAL, L., Archiv. Inter. Med., Chicago, 1933, li, 22.

(45) LESNÉ, E., BRISKAS, and LARDE, rev. franç. de pediat., Paris, 1935, xi, 104.

(46) HINTON, W., Amer. J. of the Med. Sc., Philadelphia, 1930, clxxx, 681.

(47) GAINSBOROUGH, H., Proc. Royal Soc. Med., London, 1935, xxviii, 989.

(48) LOEPER, M., A. LEMAIRE and A. LESURE, Compt. rend. de la soc. de biol., Paris, 1928, xcviii, 101.

(49) ECK, M., and J. DESBORDES, ibid., Paris, 1934, cxvii, 428.

(50) GARDNER, J.A., Proc. Royal Soc. Med., London, 1932, xxv, 505.

(51) MULLER, G. L., Medicine, Balt., 1930, ix, 119.

(52) ASCHOFF, quoted by Baumann and Holly(17).

PART III.

The blood cholesterol in normal children.

(1) GAMBLE, J. L., and K. BLACKFAN, Journ. Biolog. Chem., Balt., 1920, xlii, 401.

(2) ACUÑA, M., and P. WINOCUR, Archiv. de méd. des enfants, Paris, 1931, xxxiv, 409.

(3) WARD, K. M., Archiv. Dis. Childh., London, 1931, vi, 329.

(4) SYLVESTRE, R., "Contribution a l'étude de la cholestérinémie chez l'enfant." Thèse de Paris, 1929.

(5) VARONE, L., Amer. Journ. Dis. Children, Chicago, 1929, xxxviii, 1285, Ext. current lit.

(6) BINGENHEIMER, E., Ztschr. f. d. ges. exp. Med., Berlin, 1933, lxxxvii, 592.

(7) GORDON, M. B. and D. J. COHN, Amer. Journ. Dis. Child., Chicago, 1928, xxxv, 193.

(8) HINGLAIS and GOVAERTS, Amer. J. of the Med. Sciences, Philadelphia, 1931, clxxxi, 283. Ext. current lit.

(9) SPERRY, W. M., Amer. J. Dis. Child., Chicago, 1936, li, 84.

(10) HIRSCH, quoted by Lin & Eastman, Amer. Journ. Obstet., St. Louis, 1937, xxxiii, 317.

(11) GALDÓ, A., Archiv. Espan. de Pediat., Madrid, 1933, xvii, 100.

(12) SIMONINI, A., La Clin. Pediat, Modena, 1933, xv, 411.

(13) BARANSKI, R., Archiv. de Méd. des enfants, Paris, 1926, xxix, 139.

(14) GOLDBLOOM, A., and R. GOTTLIEB, Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 1333.

(15) FOX, F. W., and J. A. GARDNER, Proc. Royal Soc., Ser. B., London, 1925, xcviii, 76.

(16) DORLENCOURT, H., and E. PALFY, Compt. rend. de la soc. de biol., Paris, 1925, xcii, 239.

(17) STRATHMANN-HERWEG, quoted by Muller, Medicine, Balt., 1930, ix, 119.

(18) SHOPE, R. E., and J. W. GOWEN, Journ. Exp. Med., N. York, 1928, xlviii, 21.

(19) MANICATIDE M., A. BRATESCO and R. RUSESCO, Compt. rend. de la soc. de biol., Paris, 1927, xcvi, 1240.

(20) SLEMONS, J. M., and H. J. STANDER, Johns Hopkins Hosp. Bull., Balt., 1923, xxxiv, 7.

(21) GRIGAUT, A., Thèse de Paris, 1913.

(22) PALACIOS COSTA, N. and M. V. FALSIA, Endocrinology, Los Angeles, 1930, xiv, 270. Ext. current lit.

(23) GOVAERTS, J., Brux. Med., Brussels, 1930, No. 35, 29th June, 954

(24) BAYLAC, J., and M. SENDRAIL, Archiv. de Méd. des enfants, Paris, 1928, xxxi, 662.

(25) FOX, F. W. and J. A. GARDNER, Proc. Royal Soc., Ser. B., London, 1925, xcviii, 76.

(26) MULLER, quoted by Fox and Gardner, ibid.

(27) GARDNER, J. A., and M. WILLIAMS, Biochem. Journ., London, 1921, xv, 363.

(28) WEIDMAN, F. D. and F. W. SUNDERMAN, Archiv. Derm. and Syph., Chicago, 1925, xii, 678.

(29) LEIBOFF, S. L., Journ. Biolog. Chem., Balt., 1924, lxi, 177.

(30) DUTTON, R. L., Lancet, London, 1932, ccxxiii, 787, 8th Oct.

(31) BLOOR, W. R., Journ. Biolog. Chem., Balt., 1917, xxix, 437.

(32) OFFENKRANTZ, F. M., and M. KARSHAN, Amer. Journ. Dis. Childr., Chicago, 1936, lii, 784.

(33) KAISER, A. D., and M. S. GRAY, ibid., Chicago, 1934, xlvii, 9.

(34) MOLITCH, M., and S. POLIAKOFF, Archiv. Paed., N. York, 1936, liii 613.

(35) GØRTZ, S., Acta Paed., Uppsala, 1937, xix, 553.

(36) TEILUM, G., Acta Med. Scand., Stockholm, 1935, lxxxv, 316.

(37) DENIS, W., Journ. Biolog. Chem., Balt., 1917, xxix, 93.

(38) CAMPBELL, J. M. H., Quart. Journ. Med., Oxford, 1924, xviii, 123.

(39) GARDNER, J. A., Proc. Royal Soc. Med., London, 1932, xxv, 505.

(40) SCHUBE, P. G., Journ. of Lab. and Clin. Med., St. Louis, 1936, xxii, 280.

(41) SPERRY, W. M., Journ. Biolog. Chem., Balt., 1936, cxiv, 125.

(42) ROTHBART, H. B., Amer. Journ. Dis. Childr., Chicago, 1935, xlix, 672.

(43) CURRIE, A. N., Brit. Journ. of Exp. Path., London, 1924, v, 293.

PART IV.

Pneumonia.

(1) KIPP, H.A., Journ. Biolog. Chem., Balt., 1920, xliv, 215.

(2) CHAUFFARD, A., G. LAROCHE and A. GRIGAUT, Ann. de méd., Paris, 1920, viii, 69.

(3) GOLDBLOOM, A., and R. GOTTLIEB, Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 1333.

(4) SIMONINI, A., La Clin. Pediat. Modena, 1933, xv, 411.

(5) MENELAS, V., Thèse de Paris, 1934, No. 630.

(6) STROESSER, A.V., Proc. Soc. Exper. Biol. and Med., N. York, 1936, xxxiv, 10, and 1935, xxxii, 1324.

(7) NOBECOURT, P., A. COMMINOS and P. DUCAS, Archiv. de méd. des enfants, Paris 1932, xxxv, 250.

(8) SYLVESTRE, R., "Contribution a l'etude de la cholestérinémie chez l'enfant," These de Paris, 1929.

(9) LESNÉ, E., P. ZIZINE and R. SYLVESTRE, Rev. franç. de pediat., Paris, 1929, v, 423.

(10) RASPI, M., Scritti Medici, dedicati a carlo comba, 1929, 758.

(11) LAVERGNE V. de, and P. KISSEL, La Presse Med., Paris, 1934 10th March, 393.

(12) STROESSER, A.V., and MCQUARRIE, Amer. Journ. Dis. Childr., Chicago, 1935, xlix, 658.

(13) MAN, E.B., and E.F. GILDEA, Journ. Clin. Invest., N. York, 1936, xv, 203.

(14) GRIGAUT, A., Thèse de Paris, 1913.

(15) BOYD, E.M., Journ. Biolog. Chem. Balt., 1933, ci, 623.

(16) OFFENKRANTZ, F.M., and M. KARSHAN, Amer. Journ. Dis. Childr., Chicago, 1936, lii, 784.

(17) CANNATA, quoted by Lesné et alii(9).

(18) BARANSKI, R., Archiv. de méd. des enfants, Paris, 1926, xxix, 139.

(19) RICH, A.R., Bull. Johns Hopkins Hosp., Balt., 1930, xlvii, 338.

Tuberculosis, gastro-enteritis, etc.

(1) EICHELBERGER and McCLUSKY, Archiv. Inter. Med., 1927, xl, 831.

(2) SPOUJITCH, V. and D. BORITCH, Compt. rend. de la Soc. de biolog., Paris, 1936, cxxii, 340.

(3) KING, E., and M. BRUGER, Ann. Int. Med., 1934, viii, 1427.

(4) VARONE, L., Amer. Journ. Dis. Childr., Chicago, 1929, xxxviii, 1285. Ext. current lit.

(5) GOLDBLOOM, A., and R. GOTTLIEB, Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 1333.

(6) BAYLAC, J., and M. SENDRAIL, Archiv. de méd. des enfants, Paris, 1928, xxxi, 662.

(7) SCHALLY, A.O., Erg. Inn. Med., Berlin, 1936, 480.

(8) GALDÓ, A., Arch. Espan. de Pediat., Madrid, 1933, No. 3, 97.

Rheumatism.

(1) GOLDBLOOM, A., and R. GOTTLIEB, Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 1333.

(2) RASPI, M., Scritti Medici, dedicati a Carlo Comba. 1929, 758.

(3) WARD, K.M., Archiv. Dis. Childh., London, 1931, vi, 329.

(4) KAISER, A.D., and M.S. GRAY, Amer. Journ. Dis. Child., Chicago, 1934, xlvii, 9.

(5) OFFENKRANTZ, F.M., and M. KARSHAN, ibid, Chicago, 1936, lii, 784.

(6) LESNÉ, E., P.ZIZINE and R. SYLVESTRE, Rev. franç. de pediat., Paris, 1929, v, 423.

(7) HARTUNG, E.F., and BRUGER, Journ. Lab. and Clin. Med., St.Louis, 1935, xx, 675.

(8) PEMBERTON, R., Arch. Inter. Med., Chicago, 1920, xxv, 351.

(9) ABEL and FAUST, quoted by K. M. Ward, Thesis for the degree of M.D., Liverpool, 1930.

(10) GARROD, BATTEN, THURSFIELD and PATERSON, Diseases of children, London, 1934, 1033.

(11) GRIGAUT, A., Thèse de Paris, 1913.

(12) MAXWELL, J., Quart. Journ. Med., Oxford, 1928, xxi, 297.

(13) HURXTHAL, L., Arch. Int. Med., Chicago, 1933, li, 23.

(14) STROESSER, A.V., and McQUARRIE, Amer. Journ. Dis. Childr., Chicago, 1935, xlix, 658.

(15) LYONS, C., Amer. Journ. Phys., Balt., 1931, xcviii, 156.

(16) DOBREFF, M., L.PENEF, and E. WITTKOWER, Ztschr. ges. exp. Med., Berlin, 1934, xcviii, 428.

(17) DUNCAN, A.G., Journ. Ment. Science, London, 1930, lxxvi, 294.

(18) LOCKWOOD, M.R., ibid, 1932, lxxviii, 901.

Nephritis.

(1) CAMPBELL, J.M.H., Quart. Journ. Med., Oxford, 1924, xviii, 393.

(2) MAXWELL, J., Quart. Journ. Med., Oxford, 1928, xxi, 297.

(3) GARDNER, J.A., Brit. Med. Journ., London, 1932, 27th Aug., 392.

(4) TRUMPER, M. and A. CANTAROW, Biochemistry in Internal Medicine, London, 1932.

(5) CANTAROW, A. and S.G. McCOOL, Amer. Journ. Clin. Path., Balt., 1935, v, 516.

(6) GARROD, BATTEN, THURSFIELD and PATERSON, Diseases of Children, London, 1934.

(7) VAN SLYKE, D. D., et alii. Medicine, Balt., 1930, ix, 257.

(8) FLEMING, C.M., Lancet, London, 1931, 27th June, 1390.

(9) SYLVESTRE, R., Thèse de Paris, 1929.

(10) PETERS, J. P., and D. D. VAN SLYKE, Quantitative Clinical Chemistry, London, 1931, 22.

(11) DENIS, W., Journ. Biolog. Chem., Balt., 1917, xxix, 93.

(12) ASHE, B.I. and M. BRUGER, Amer. Journ. of the Med. Sciences, Philadelphia, 1933, clxxxvi, 670.

(13) HENES, E., Archiv. Inter. Med., Chicago, 1920, xxv, 411.

(14) GRIGAUT, A., Thèse de Paris, 1913.

(15) GAINSBOROUGH, H., Proc. Royal Soc. Med., London, 1935, xxviii, 989.

(16) CALVIN, J.K. and A.H. GOLDBERG, Amer. Journ. Dis. Childr., Chicago, 1931, xli, 1066.

(17) SCHWARZ, H. and J. KOHN, ibid, Chicago, 1935, xlix, 579.

(18) COWIE, JARVIS and COOPERSTOCK, ibid., Chicago, 1930, xl, 465.

(19) LEITER, L., Medicine, Balt., 1931, x, 135.

(20) LICHTENSTEIN, L. and E.Z. EPSTEIN, Archiv. Int. Med., Chicago, 1931, xlvii, 122.

(21) PAGE, I.H., E. KIRK and D. VAN SLYKE, Journ. Clin. Invest., N. York, 1936, xv, 101.

(22) LEITER, L., Proc. Soc. Exp. Biol. and Med., N. York, 1930, xxvii, 1002.

(23) PAGE, I.H. and L. E. FARR, Journ. Clin. Invest., N. York, 1936, xv, 181.

(24) EPSTEIN, A.A., and H. LANDE, Archiv. Inter. Med., Chicago, 1922, xxx, 563.

(25) BRUGER, M., Amer. Journ. Clin. Path., Balt., 1935, v, 504.

(26) SCHALLY, A.O., Erg. Inn. Med., Berlin, 1936, 480.

(27) LIU, SHIH-HAO, Arch. Inter. Med., Chicago, 1927, xl, 73.

Jaundice, diseases of the blood, malignant tumours, and histamine liver function test.

(1) NAUNYN, quoted by W. M. Sperry, Journ. Biolog. Chem., Balt., 1926, lxxi, 351.

(2) MACKEY, W.A., Brit. Journ. Surgery, Bristol, 1937, xxiv, 570.

(3) FLINT, A., Jr., Amer. Journ. of the Med. Sciences, Philadelphia, 1862, xliv, 20.

(4) SPERRY, W.M., Journ. Biolog. Chem., Balt., 1926, lxxi, 351.

(5) BORGATTI, G., Policlinico, Rome, 1925, xxxii, 477.

(6) THANNHAUSER, quoted by E. Z. Epstein, Arch. Inter. Med., Chicago, 1931, xlvii, 82.

(7) McNEE, J.W., Quart. Journ. Med., Oxford, 1914, vii, 221.

(8) RICH, R.R., Johns Hopkins Hosp. Bull., Balt., 1930, xlvii, 338.

(9) EPSTEIN, E.Z., and E.B. GREENSPAN, Archiv. Inter. Med., Chicago, 1936, lviii, 860.

(10) OTTENBERG, R., Journ. of the Amer. Med. Assoc., Chicago, 1935, civ, 1681.

(11) COLOMBIÈS, F.H., Thèse, University of Toulouse, 1923-4.

(12) CAMPBELL, J.M.H., Quart. Journ. Med., Oxford, 1924, xviii, 123.

(13) HEINLEIN, H., Ztschr. f. d. ges. exp. Med., 1933, xci, 638.

(14) ROTHSCHILD, M.H. and J. FELSEN, Archiv. Inter. Med., Chicago, 1919, xxiv, 520.

(15) CHAUFFARD, A., G. LAROCHE and A. GRIGAUT, Ann. de Med., Paris, 1920, viii, 69.

(16) CERVERA, L., and FORNELLS-PUIG, Amer. Journ. Physiol., Balt., 1929, xc, 309. Abst.

(17) ORNSTEIN, I., M. SIBI, F. BRANOVER, Compt. rend. de la soc. de biol., Paris, 1934, cxv, 779.

(18) STEPHANUTTI, P., Klin. Woch., Berlin, 1934, 1187.

(19) GOEBEL, F., Journ. de physiol. et de path. général, Paris, 1934, xxxii, 408.

(20) CORNELL, B.S., Journ. of Lab. and Clin. Med., St. Louis, 1929, xiv, 209.

(21) SOFFER, L.J. and M. PAULSON, Archiv. Inter. Med., Chicago, 1934, liii, 809.

(22) MULLER, G.L., Medicine, Balt., 1930, ix, 119.

(23) CSONKA, F.A., Journ. Biolog. Chem., Balt., 1916, xxiv, 431.

(24) BISCONS and ROUZAUD, quoted by Colombiès(11).

(25) GOVAERTS, J., Brux. Med., Brussels, 1930, x, 954.

(26) SPERRY, W.M., Amer. Journ. of Dis. of Childr., Chicago, 1936, li, 84.

(27) McADAM, W., and C. SHISKIN, Quart. Journ. Med., Oxford, 1922, xvi, 193.

(28) DIDRY, J., Compt. rend. de la soc. de biol., Paris, 1934, cxv, 369.

(29) MOUKHINE, S.A., Journ. de physiol. et de path. général, Paris, 1935, xxxiii, 1120.

(30) PAXTON, W.T.W., Thesis for the degree of M.D., Glasgow, 1938.

(31) FEIGL, quoted by Muller(22).

(32) BLOOR, W.R., Journ. Biol. Chem., Balt., 1921, xlix, 201.

Diseases of the nervous system.

(1) DUNCAN, A.G., Journ. of Mental Sc., London, 1930, lxxvi, 284.

(2) LOLLI, N., Amer. Journ. Dis. Childr., Chicago, 1934, xlviii, 1417. Ext. current lit.

(3) McQUARRIE, I., W.R. BLOOR, C. HUSTED and H.A. PATTERSON, Journ. Clin. Invest., N. York, 1933, xii, 247.

(4) RAMPININI M., Riv. di clin. Pediat., Firenze, 1934, xxxiii, 1281.

(5) VARONE, L., Amer. Journ. Dis. Childr., Chicago, 1934, xxxviii, 1285. Ext. current lit.

(6) WADE, P.A., Amer. Journ. of the Med. Sciences, Philadelphia, 1929, clxxvii, 790.

(7) GOEBEL, F., Nutrition Abstracts and Reviews, 1932-1933, ii, No. 345.

(8) INGLESSI, E., La clin. Pediat. Modena, 1932, xiv, 1003.

Diabetes and Hypothyroidism, etc.

(1) MAN, E., and P. PETERS, Journ. Clin. Invest., N. York, 1934, xiii, 237.

(2) JOSLIN, E.J., The Treatment of Diabetes Mellitus, Boston, 1937, 129.

(3) RABINOWITCH, I.M., Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 171.

(4) CHAIKOFF, I.L., F.S. SMYTH and G.E. GIBBS, Journ. Clin. Invest., N. York, 1936, xv, 627.

(5) LANGE, H., and R. SCHOEN, Arch.f.exper. Path. v. Pharmakol, Leipsig, 1926, cxiii, 92.

(6) SHIH-HAO, L., and C.A. MILLS, Proc.Soc. Exp. Biol. and Med., N. York, 1926, xxiv, 191.

(7) LEWIN, A.I., Arch. f. exper. Path. v. Pharmakol, Leipsig, 1935, clxxviii, 308.

(8) BRUGER, M. and H.O. MOSENTHAL, Journ. clin. Invest., N. York, 1934, xiii, 399.

(9) ESSINGER, R. and P. GYÖRGY, Biochem. Zeit., Berlin, 1924, cxlix, 339.

(10) WARTIN, A.S., Proc. Soc. Exp. Biol. and Med., N. York, 1916, xiv, 42.

(11) MOEHLIG, R.C., and H.B. AINSLEE, Amer. Journ. Physiol., Balt., 1926, lxxx, 649.

(12) BLOTNER, H. and R. FITZ, Journ. Clin. Invest., N. York, 1934, xiii, 707.

(13) KREIS, H., Ztschr. f. d. ges. exp. Med., 1933, lxxxviii, 271.

(14) BRONSTEIN, I.P., Journ. of the Amer. Med. Assoc., Chicago, 1933, c, 1661.

(15) HURXTHAL, L.M., Arch. Inter. Med., Chicago, 1934, liii, 825.

(16) BOYD, E., and W. F. CONNEL, Quart. Journ. Med., Oxford, 1937, vi, 467.

(17) LÉVY, M. and L. GALLY, La Presse Med., Paris, 1936, 15th July.

(18) GOLDBLOOM, A., and R. GOTTLIEB, Canad. Med. Assoc. Journ., Montreal, 1927, xvii, 1333.

(19) SCHALLY, A.O., Erg. Inn. Med., Berlin, 1936, 480.