STUDIES IN ACUTE NEPHRITIS IN INFANCY AND CHILDHOOD.

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VOLUME I.

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INTRODUCTION.

The work on which this thesis is based was carried out over the past three years in the University department of Paediatrics and the Biochemical laboratory of the Royal Hospital for Sick Children during the tenure of a Carnegie Research Scholarship. A small section, which is included in the following pages, has already been published in the Quarterly Journal of Medicine, 1933, XXVI, 521, under the title "Oedema in Nephritis" and another will shortly appear in the Archives of Disease in Childhood under the title "Nephritis in Infancy". Otherwise the work has not yet appeared in print.

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PART I.

THEORIES OF OEDEMA.

Since Bright's[1] classical description of nephritis the pathogenesis of dropsy has given rise to much discussion. The views which have been put forward may be divided into two main groups, one which ascribes oedema entirely to renal damage and the other which attributes it to some abnormality in the tissues generally, or as it has been called, a pre-renal factor. The basis for this latter view, which on the whole is the more widely favoured by modern workers, was anticipated by Bright himself when he recognized that a diminution of blood protein was of common occurrence in nephritis. While this finding has been repeatedly confirmed and is now commonplace, the deductions drawn therefrom are varied. The bulk of the published work deals with the oedema associated with chronic Bright's disease which includes the conditions known as chronic parenchymatous nephritis and nephrosis. The oedema of acute nephritis however appears to present special difficulties from the point of view of causation and no entirely satisfactory hypothesis has as yet been put forward. In this chapter, therefore, is given a brief summary of the more important views which have been mooted in connection with the causation of nephritis oedema and it is convenient for the sake of clarity to consider in the first place the oedema of chronic Bright's

disease (nephrotic syndrome) and thereafter that which occurs in acute nephritis.

NEPHROTIC SYNDROME.

HYDRAEMIC PLETHORA. A simple explanation of an increase in tissue fluid would appear to be provided by the presence of an excessive amount of water in the blood stream. Such a view was propounded by Solon[2] in 1838 when he suggested that "the blood was thinner than normal." This hypothesis is particularly attractive in that an easy explanation is forthcoming as to the increased fluid content of the blood, which is naturally attributed to the inability of the kidney to excrete water. The evidence for dilution is mainly the observation that the total percentage volume of red cells is reduced. This reduction, however, is not necessarily the result of an increase in the water content of the blood since a fall in the number of red cells, as occurs in anaemia, would clearly lead to an increase in plasma volume. Bock,[3] indeed, considers that any reduction in corpuscular volume which does occur is attributable to anaemia. The force of this objection is strengthened by the findings of Bock[3] and of Brown[4] and Rowntree that the total blood volume was unchanged. Linder[5] and his co-workers estimated the total blood and plasma volumes by means of vital red injections and concluded that there was no evidence of blood dilution. Darrow[6] indeed stated that the plasma volume was usually

diminished in the nephrotic syndrome in childhood. Peters[7] and van Slyke surveyed the literature and found that in the majority of cases reported there was no alteration in plasma volume. Against the dilution theory they urge the fact that the serum albumin and globulin are not proportionately reduced. Furthermore to attribute water retention to an inability of the kidney to excrete water seems somewhat strange in view of the fact that in chronic interstitial nephritis, where fibrosis affects all the renal elements, a very large urinary output is invariable and oedema is absent. From the evidence it would appear therefore that the oedema in chronic Bright's disease cannot be attributed to hydraemic plethora.

SALT RETENTION. Any alteration in the concentration of NaCl will lead to disturbances of osmotic equilibrium. Both in health and disease the body is generally able to regulate the osmolar concentration despite great variations of intake of the various salts. It is obvious that if for any reason excretion of NaCl is impaired, water must be retained in order to maintain the normal salt concentration and osmotic equilibrium. Widal[8] and Javal were the first to suggest that the primary cause of oedema in chronic renal disease was an inability of the kidney to excrete salt. According to their view the retention of water was a secondary phenomenon which occurred in order to keep the salt content of the tissue fluids within normal limits. They showed that by withholding

NaCl from the diet, oedema could be diminished or even made to disappear. Addition of NaCl to the diet, on the other hand, caused oedema to increase. It appears definitely established - and numerous workers have confirmed this - that NaCl is an important factor in the development of oedema. The part played by the kidney in causing retention of NaCl is open to question. If the kidneys are unable, either relatively or absolutely, to excrete NaCl it would naturally be expected that chloride would accumulate in the blood. Examination of the clinical and biochemical reports available in the literature shows quite clearly that there is no apparent relationship between the level of the plasma chloride and the degree of oedema. In anuria, on the other hand, produced by bilateral ureteral obstruction, the blood chloride is high but oedema is absent. Furthermore absence of chlorides from the urine is not confined to Bright's disease since it may occur in lobar pneumonia without nephritis. Again the effect of NaCl on degree of oedema without renal lesion has been observed clinically in dropsy of nutritional origin and experimentally in the oedema following plasmapheresis. These findings go to show that while NaCl plays a part in the production of oedema, its effect cannot be ascribed to renal impairment.

INTRACELLULAR OEDEMA. While most workers are agreed that the oedema fluid in Bright's disease lies in the tissue spaces, there is a view promulgated by Fischer[9] that the increased

water content of the body is situated largely within the cells. The increase in intracellular water is attributed to an excessive production of acids. Aldrich,[10] although in argument as to the site of the oedema, believes that the increased affinity of the tissue cells for water is due to the action of toxins. He maintains that in the early stages of oedema no fluid escapes from the needle following acupuncture and it is only when the toxic process is diminishing that fluid passes from cells to tissue spaces. Kumpf[11] also believes that some of the oedema fluid is intracellular. On the basis of these views it is difficult to explain the shifting of oedema under the influence of gravity, while the fact that no oedema fluid may be obtained on acupuncture seems more easily accounted for by there being insufficient to form a head of pressure. Lastly if a patient in whom no effusion is demonstrable subsequently shows the presence of free fluid, a gain in weight follows which should not occur if fluid is merely changing ground from cells to tissue spaces. Peters,[12] discussing the intracellular oedema theory, points out that there is no oedema of the red corpuscles since the haemoglobin : red corpuscle ratio remains constant. Furthermore during diuresis, potassium, the chief constituent of intracellular fluid, does not appear in increased amount in the urine.

ELWYN'S THEORY.[13] This view is unique and at present incapable of proof or disproof. In chronic renal oedema Elwyn argues that serum albumin is lost in the urine and an attempt is made to replace this by increase in serum globulin. When this compensatory mechanism fails, oliguria is produced to conserve serum albumin by the action of a "centre" in the brain, oedema following to keep the blood volume within normal limits. Little support in the literature has been accorded to this supposition.

INCREASED CAPILLARY PERMEABILITY. By Volhard[14] and Fahr and Aschoff,[15] oedema has been attributed to a generalized capillary damage. Since normally the capillaries are permeable to water and electrolytes, increase of permeability per se should not affect the passage of water to the tissue spaces but would allow leakage of protein from blood stream to tissues. Peters[12] however in a summary of the literature finds that oedema fluid in nephrosis and the nephrotic syndrome contains only 0.5 gm. per cent. or less and claims that if the capillary wall were abnormally permeable in these conditions, protein could almost certainly be in greater concentration in the effused fluid.

STARLING-EPSTEIN HYPOTHESIS. In 1895 Starling[16] demonstrated the cardinal importance of the serum proteins in the maintenance of fluid balance between the blood and the tissues, emphasizing the fact that the inorganic constituents of the serum could not exert osmotic pressure in virtue of their

ability to pass freely through the normal capillary wall into the tissues. According to his view the osmotic pressure exerted by the serum protein, or as it is more commonly termed, oncotic pressure of the serum, is antithetic to hydrostatic pressure in the capillaries, the effect being that decrease in serum protein or increase in hydrostatic pressure both conduce to oedema formation.

These findings constitute the basis of one of the chief conceptions of the extra-renal origin of oedema and were applied by Epstein[17] to explain dropsy in chronic parenchymatous nephritis and later to the syndrome termed lipoid nephrosis. He found that serum protein was much diminished at the expense of the albumin fraction, globulin being either normal, or greatly increased.

Some years later the oncotic pressure exerted by the serum protein was measured by several investigators, Govaerts,[18] Schade[19] and Claussen, and Rusznyák[20] who showed that in nephrotic oedema it was much reduced. It was Govaerts[18] however who indicated that since serum albumin has a smaller molecule than serum globulin it exerts more oncotic pressure and he proposed the following formula for the calculation of oncotic pressure of the serum proteins:-

(5.5 x albumin in gm. per cent.) + (1.4 x globulin in gm. per cent.) = oncotic pressure in mm. Hg.

It therefore follows that fall in serum albumin may be masked by rise in serum globulin if serum total protein is

alone estimated and a false impression of the osmotic capacity of the serum gained.

It is thus clear that so-called inversion of the albumin: globulin ratio of the serum can result from rise in globulin as well as fall in albumin but with very different results as far as the oncotic pressure of the serum is concerned. Mayrs[21] and Cope[22] also found low oncotic pressure in hydraemic nephritis. Mayrs[21] found oedema absent with oncotic pressure above a certain level and recently Muntwyler[23] and his co-workers reported similar findings. The results of these investigations would indicate that fall in oncotic pressure of the serum is directly responsible for chronic renal oedema.

Starling's[16] hypothesis throws light on the part played by NaCl in the production of oedema. This problem is rendered easier of comprehension if the reaction of the normal subject to administration of salt and water is considered. Cohnheim[24] et alii found that if either salt or water were given alone, rapid excretion followed. If however they were given together some temporary retention occurred with rise in body weight. In the subject with low serum oncotic pressure however a very much more marked retention occurs, as was demonstrated in the nephrotic patient by Loeb[25] et alii. A reasonable explanation is thus afforded of so-called chloride retention by the diminished power of the serum to hold salt and water through the fall in serum protein level.

In support of this Starling-Epstein hypothesis some mention of experimental work indicating a relationship between serum proteins and oedema is now made and following this the literature on oedema of nutritional and of cardiac origin is briefly discussed from the point of view of the serum proteins.

Plasmapheresis. This term is applied to the operation of bleeding and replacement of red corpuscles suspended in saline instead of serum. In this way Leiter[26] and Barker[27] and Kirk produced in dogs a reduction of serum protein which was accompanied by oedema. Leiter found that oedema appeared when serum total protein fell below 3.0 gm. per cent. and observed that the amount of protein in the effusions was very low. Usually 1,500 c.c. of 0.85 per cent. saline were given daily by stomach tube and he found that this was not followed by oedema when serum total protein had risen above about 4.0 gm. per cent.. Shelburne[28] and Egloff found in dogs subjected to plasmapheresis that oedema was slight or even absent with a serum albumin level of 1.2 gm. per cent. until sodium chloride or sodium bicarbonate was given. Although a large amount of NaCl was retained during the formation of oedema, more was recovered in the urine than was found in the urine of a normal dog on ordinary diet. From this finding these workers concluded that the kidney could not be held responsible for salt retention. Darrow[29] et alii found that a level of serum

albumin of 2.0 gm. per cent. and below in both arterial and venous blood was associated with oedema. Moreover when serum albumin was over 2.0 gm. per cent. they were unable to produce dropsy by administration of NaCl. The experiments of these workers offer a rational explanation of the secondary rôle played by salt in the production of oedema in the nephrotic syndrome, and also show why it is possible for oedema to be absent while the serum protein is below oedema level.

The results of plasmapheresis on dogs afford strong support for the application of Starling's[16] hypothesis in the explanation of nephrotic oedema. In view of the small amounts of protein present in the effusions, it is hardly likely that there is an increase of capillary permeability. The slight fall in the haematocrit reading observed by Shelburne[28] and Egloff was out of proportion to the diminution of serum proteins and was ascribed to anaemia. There is thus no evidence of dilution of the blood. Lastly since tissue fluid was obtained by acupuncture and effusions were a prominent feature, it is very improbable that there was any imbibition by the tissue cells leading to intracellular oedema.

By the majority of workers on this subject negative urinary findings were reported and any kidney lesions present were not ascribed to the effects of plasmapheresis. Barker[27] and Kirk however considered that hypoprotinaemia was responsible for the changes in the kidneys which were discovered at autopsy.

The main point for consideration however seems to be that oedema of this type is entirely extra-renal and due to reduction of oncotic pressure of the serum.

Nutritional Oedema: Further support was gained for Starling's[16] hypothesis when it was discovered that oedema in an ill-defined group of cases, neither cardiac nor renal in origin, was associated with reduction of serum proteins. For many years the occurrence of dropsy without albuminuria was recognised and during the war it was very prevalent in Central Europe. Jansen[30] in 1918 clearly showed that serum proteins were reduced in so-called war oedema. Maver,[31] reviewing the subject, concluded that protein deficiency was the basic causal factor with fluid and possibly salt intake playing a secondary rôle.

In patients suffering from diseases such as tuberculosis and diabetes Bruckman[32] and his co-workers reported a reduction in the albumin fraction of the serum proteins when clinical evidence of malnutrition was present. That this was due to a low protein intake they considered proved by the rise in serum albumin which followed administration of a diet rich in protein. Oedema was always present when serum albumin was under 3.0 gm. per cent. Weech[33] and Ling observed that dropsy was invariably present when serum albumin fell below 2.5 gm. per cent. and always absent with albumin over 2.9 gm. per cent. After administration of sodium chloride combined

with sodium bicarbonate their patients showed a marked increase in weight and "retention" of chloride occurred, i.e., depression of the amount excreted in the urine. In one patient these effects could not be reproduced when serum proteins had returned to normal. Weech,[34] Snelling and Goettsch observed that oedema occurred at a higher level of the serum protein in nutritional oedema than in that due to plasmapheresis. They concluded that this was due to the better physical condition and therefore greater elasticity of the tissues in the subjects of the latter group. Peters[35] and Eisenman emphasized the importance of this point in a recent article where they noted reduction of serum albumin in many pathological states such as diabetes, anaemia, liver diseases, certain neoplasms and severe infections. The fall in serum albumin they associated with malnutrition and wasting of body protein. When serum albumin was below 3.0 gm. per cent. oedema was present unless (1) globulin was sufficiently above the normal level to compensate for reduction of oncotic pressure from fall in serum albumin, or (2) dehydration was present as a result of vomiting, diarrhoea or abstention from fluids.

In conclusion two points emerge from the reports on nutritional oedema. Firstly the oedema appears to be due to reduction of oncotic pressure; tissue elasticity and NaCl intake are important but secondary factors. Secondly the reduction of serum oncotic pressure is seemingly ascribed to deficiency of protein in the diet. In this connection it may

be noted that Frisch,[36] Mendel and Peters induced oedema in rats on a protein poor diet and caused it to disappear when the protein deficiency was made good.

Cardiac Oedema. While great stress is laid on fall of oncotic pressure in the production of oedema, it must not be forgotten that an equally important factor in Starling's[16] hypothesis is change in hydrostatic pressure. In cardiac oedema it is apparently the great increase in hydrostatic pressure resulting from back pressure due to cardiac failure which is of major importance. But in addition, the fall of oncotic pressure may play an important part since many investigators have reported changes in the serum proteins.

Govaerts[18] observed that the A/G ratio was much reduced in a case of cardiac oedema and Fahr[37] and Swanson reported a similar case. In the cardiac cases of Starlinger[38] and Winands no constant relation was detected between oedema and the serum protein level but serum albumin was not infrequently low and globulin high: haematocrit readings showed a normal proportion of cells to plasma. Kumpf[11] reported similar findings in six cases with oedema, in only one of which was there more than a trace of albumin in the urine. Mayrs,[21] who measured oncotic pressure, found that cardiac oedema occurred at a higher level than in hydraemic nephritis

increased venous pressure and possibly also to "ill-

capill endothelium. Kylin[39] reported that oncotic

pressure was often normal, while Iversen[40] and Nakazawa found both high and low values for oncotic pressure and concluded that stasis played the chief rôle. Payne[41] and Peters found cardiac oedema with normal serum proteins but more frequently some reduction in serum albumin was present but never below the oedema level of the nephrotic syndrome. Dilution as an explanation of this they think untenable as the serum protein fractions were not equally reduced. Nor did loss of protein by the urine adequately account for the fall in oncotic pressure since albuminuria only occurred, and then but slightly, in 5 out of 25 cases. Payne[41] and Peters believed that the main factor in the diminution of serum albumin was malnutrition due to anorexia. Whatever be the reason for diminution of oncotic pressure the important contribution in their paper was the conclusion that a combination of increase of hydrostatic with fall in oncotic pressure is obviously more active in the production of oedema than an increase of hydrostatic pressure alone.

Nephrotic Syndrome. Further support has been given to Starling's[16] hypothesis in the work of numerous investigators who have estimated the serum proteins in chronic renal oedema. Moore[42] and van Slyke found that oedema existed in nephritis when total protein was below 5.5 $\pm$ 0.3 gm. per cent. or albumin below 2.5 $\pm$ 0.2 gm. per cent.. With serum proteins above these levels oedema was absent save when car-

diac failure was present or when the nephritis was acute. They stressed the importance of the absence of sodium chloride in the diet and pointed out that if under such treatment diuresis should occur the tendency for oedema to return on salt-containing diet would remain until proteins rose above oedema level. Wiener[43] and Wiener also reported a marked decrease in serum albumin in nephrotic oedema which they attributed to fall in serum oncotic pressure. Van Slyke[44] and his collaborators found that oedema in nephritis was related to the plasma albumin level but that this relationship did not hold good in the majority of cases of acute nephritis, although oedema was always present when serum albumin was below 2.5 gm. per cent.. They pointed out that when plasma proteins were close to oedema level, dropsy was often observed to disappear with the onset of fever or much vomiting or after surgical procedure. Peters[45] et alii held that nephrotic oedema was associated with low plasma proteins. With total protein between 4 and 5 gm. per cent. oedema could be eliminated by the vigorous use of diuretics and salt restriction, but with serum proteins below that level these measures failed. They indicated that such treatment was merely palliative, the tendency to oedema remaining till serum proteins rose above the critical level. Leiter[46] in his very extensive review of the literature on nephrosis makes the significant remark that no case of nephrosis has been reported with normal serum proteins.

While perhaps the majority of reports in the literature

agree that absolute reduction of serum proteins is responsible for chronic renal oedema, not a few workers deny the relationship. Such disagreement based on cases where serum total protein alone has been determined, for reasons already given (p.7) need not be considered since a true picture of the oncotic pressure cannot be formed without estimation of the serum albumin and globulin. Fahr[37] and Swanson found that oedema could be marked with normal serum proteins. These cases however were of acute nephritis and it is generally held that other factors are at work in that form of the disease. They quoted a case without oedema and a serum albumin level of 2.7 gm. per cent. but this is not incompatible with absence of dropsy if the diet is salt-free. Calvin[47] and Goldberg, while they found serum albumin very much reduced, even as low as 0.12 gm. per cent., could determine no relation between the albumin of the serum and the degree of oedema. Because of this, and the fact that the serum albumin level appeared to lag behind the fluctuations in oedema, these workers concluded that nephrotic oedema was not entirely explained by fall in oncotic pressure. In their series the highest serum albumin found in the presence of oedema was about 3.0 gm. per cent.; moreover they state that with increase of oedema albumin usually fell and certainly never rose. Some exception might be taken to their results on the ground that a serum albumin of 0.12 gm. per cent.

would be approximately in equilibrium with the albumin content of the oedema fluid as reported by other workers. Frankly it is difficult to conceive of such an occurrence. Cowie[48] et alii were unable to believe that oedema was caused by diminution of serum osmotic pressure because blood chloride and cholesterol were invariably (one case!) high and more than offset the diminution due to the loss of serum protein. They ignored the fact that the capillary wall being normally permeable to salt, the effective oncotic pressure of that substance is nil. Elwyn[13] objected to Starling's[16] hypothesis being applied to chronic renal oedema on the ground that exudation of fluid from the vessels would continue till blood volume was reduced. Peters[12] however pointed out that tissue elasticity must play a part in producing equilibrium.

Kylin,[39, 49, 50] one of the most inveterate antagonists of Starling's[16] hypothesis measured the oncotic pressure and estimated total protein by refractometer and stated that they are not related to oedema. Frequently after the disappearance of oedema he found that total protein remained low. In estimating total protein Kylin used the refractometric method which gives readings which in lipaemic sera found in chronic renal oedema are too high, and his results generally were above oedema level whether oedema was present or not. As regards oncotic pressure Kylin reported actual fall during

diuresis but gave little indication of salt intake or treatment. Meyer[51] also found the oncotic pressure falling during diuresis and like Kylin attributed it to movement of water from tissues. These workers along with McLure[52] et alii believe that active water retention by the tissues is the cause of oedema. It is of interest however to note that Kylin[50] in his latest paper on the subject in 1933 admitted that the serum protein level and salt intake are important factors in the pathogenesis of oedema. In this connection he quoted the work of Leiter[26] who by plasmapheresis induced low serum proteins in dogs and then caused oedema to appear or to increase greatly by administration of sodium chloride. In such experiments it is improbable that an oedema-producing toxic effect on the tissues is present. Kumpf[11] found in nephritis generally, with the exception of the hypertensive type, a lowering of serum albumin and an increase of serum globulin. Since such changes were also found in pneumonia, malnutrition, infections generally, and in liver disease, without oedema necessarily occurring, he concluded that oedema was not caused by reduction of serum proteins. With the exception of nutritional cases and some examples of pneumonia, however, as Kumpf[11] admits, serum albumin was not below the oedema level and the figures obtained by him for pneumonia are considerably lower than those reported elsewhere in the literature. Furthermore the tendency to chloride retention does exist in that disease, dropsy indeed hav-

ing been induced by administration of NaCl,[53] and the cases quoted by Kumpf[11] were probably on a diet containing minimal amounts of NaCl. With regard to malnutrition Kumpf[11] stated that the same protein levels were observed whether oedema was present or absent but as in the latter case the subjects took neither food nor water, the absence of dropsy is not inexplicable.

Shaw Dunn[54,55] found difficulty in explaining the apparently unimpaired absorption of water from the intestine and why the separation of fluid from the blood by the kidney was not more effective if the oncotic pressure was reduced. It seems reasonable to believe that oncotic pressure, although much reduced, is still great enough to allow absorption of water from the bowel. As Mayrs[21] suggested it is possible that fluid does not reach the kidney owing to pre-renal deviation to the tissues. Shaw Dunn[55] recently put forward a view which although perhaps incapable of direct proof yet offers a reasoned argument in favour of the kidney being directly responsible for oedema of the nephrotic type. Owing to slight glomerular damage all the nephrons are constantly at work, instead of as normally, in relays. It follows that the amount of glomerular filtrate remains unchanged, because the blood supply to the glomeruli is unimpaired; reabsorption however must be much greater since many more tubules are in

action. Shaw Dunn[55] points out that the blood flowing through the glomeruli loses water and salts and thereafter passes to the tubules where reabsorption is aided by the raised oncotic pressure.

ACUTE NEPHRITIS.

While the evidence is strongly in favour of the application of Starling's[16] hypothesis to explain the problem of the pathogenesis of renal oedema, it would appear from the literature that the dropsy of acute nephritis cannot be explained on that basis. Many investigators have found that the serum proteins in acute nephritis, if reduced, are above the level at which oedema occurs in so-called nephrotic cases. Fahr[37] and Swanson could find no relation between oedema and serum protein level and actually quoted a case with normal proteins and marked oedema. Starlinger[38] and Winands found that serum proteins were essentially normal in the acute stages of nephritis, while Blackfan,[56] and Harrison[57] and Wyllie, working with children, stated that in acute nephritis serum proteins generally fell within normal limits. From the figures reported by the last-named investigators (Table 11) it is apparent however that considerable reduction in serum albumin did occur. Wiener[43] and Wiener, Kumpf,[11] and Moore[42] and van Slyke also found albumin below and globulin above normal. None of these workers was able to establish a relation

between serum protein level and oedema.

Actual measurement of oncotic pressure by Kylin,[39, 49] and Schade[19] and Claussen showed normal levels with slight oedema. Cope[22] found little alteration in acute nephritis. These workers attributed oedema in acute nephritis to other factors.

While in the main concurring with these findings, van Slyke[44] and his collaborators and Peters[58] et alii made the important observation that in a certain number of cases of acute nephritis serum proteins quite early in the disease were below oedema level. On the analogy of cases of the nephrotic type it was therefore unnecessary to postulate other factors in the causation of the oedema when such biochemical findings were obtained. Mayrs[21] also, while he found in acute nephritis oedema irrespective of oncotic pressure level, in one case reported a very low figure comparable with the state of affairs in the nephrotic syndrome.

It would appear therefore that except in a comparatively small group of cases little relation has been found in acute nephritis between oedema and oncotic pressure so that some other factor must be adduced.

HYDRAEMIA. In his report to the Medical Research Council on war nephritis Maclean[59] held that with the acute circulatory disturbances in the kidney occurring in acute nephritis oliguria and retention of water occurred leading to hydraemia

and rise in blood pressure. Since oncotic pressure was diminished through dilution it was unable to counteract rise in blood pressure and oedema occurred. Maclean's[59] evidence of hydraemia was drawn mainly from haemoglobin estimations. The 28 patients on whom the investigation was carried out fell into three groups:-

(1) Slight oedema, hydraemia marked.

(2) Cases in which the degrees of hydraemia and of oedema were in proportion.

(3) Marked oedema with but slight or absent hydraemia.

Boyd[60] in acute nephritis in children reported low haematocrit readings but a normal total serum protein and concluded that anaemia, not dilution, was present, a conclusion which was supported by the findings of Brown[4] and Rowntree. Peters[7] and van Slyke found no evidence in the literature that changes occurred in blood or plasma volume in acute nephritis. They also pointed out that changes of blood or plasma volume should be accompanied by alteration in both fractions of the serum protein to the same extent whereas diminution of serum albumin and increase of globulin are almost invariably reported. Among their own cases a few were observed however in which the plasma proteins, haemoglobin and red cell volume rose together during diuresis. No explanation other than blood dilution was forthcoming to explain such a sequence of events. There would seem therefore to be

some evidence of the existence of blood dilution in certain cases of acute nephritis although in the majority neither the oedema nor fall in serum albumin is explained by the presence of hydraemia.

INCREASED HYDROSTATIC PRESSURE. Blackfan[56] stated that in acute nephritis of children serum proteins were normal and that oedema was directly related to the blood pressure level. Maclean[59] and Kylin[61] also observed a fair degree of relationship in their patients, but from the case reports of van Slyke[44] and his co-workers a close relationship is not apparent. It would appear therefore that the association of oedema with rise of blood pressure cannot be considered to be definitely established. Bennett[62] indeed states that hypertension is not by any means invariably present in acute nephritis.

INTRACELLULAR OEDEMA. Kylin[61] considers that the oedema of acute nephritis arises primarily in the tissues and quotes cases of scarlatinal nephritis in which oedema and rise of blood pressure appeared before albuminuria. Fischer,[9] Aldrich,[10] and McLure[52] et alii believe that in the early stages at least oedema is intracellular. The arguments which have already been used against this view in the nephrotic syndrome hold good here also.

INCREASED CAPILLARY PERMEABILITY. Peters,[12] unable to apply Starling's[16] hypothesis to the pathogenesis of oedema in acute nephritis, held that increased capillary permeability was present. In oedema fluids protein was in greater concentration in the acute form of nephritis than in the nephrotic type, while evidence of capillary damage was shown clinically by haemorrhages in the fundi and elsewhere. Kylin[61] also stated that haemorrhage into the retina was common and was evidence of increased capillary permeability. On this hypothesis Peters[12] argued that the effective oncotic pressure would be lower than the actual owing to the protein lost into the tissues exerting oncotic pressure against that remaining in the blood stream.

This hypothesis is attractive but it must be pointed out that there is little evidence that capillary damage does occur. In children at all events retinal haemorrhages or indeed haemorrhage in any situation is rare in acute nephritis while the difference between protein content of effusions in acute and chronic oedema is very slight. (See table 7). Furthermore the actual increase in serum globulin is difficult to explain if permeability be increased. Although the globulin molecule might escape less easily than the smaller albumin molecule, thus accounting for the maintenance of the normal level, the actual increase so frequently noted in the globulin fraction is difficult of explanation on this assumption.

MALNUTRITION. According to Peters (58) and his co-workers, malnutrition, through its influence in lowering the serum proteins, is a potent factor even in acute nephritis. In their cases reduction of serum albumin below oedema level was associated with anorexia and vomiting, and to these factors in conjunction with proteinuria was ascribed the decrease of serum albumin. This view has not yet received any criticism but opportunity will be taken later in this work to bring forward evidence to show that it is untenable.

By none of the aforementioned theories is a satisfactory explanation of oedema of acute nephritis afforded. The following facts emerge:-

(1) Occasionally hydraemia is present.

(2) In some cases a relationship can be made out between hyperpiesis and oedema.

(3) In a proportion of cases oedema can be explained entirely by reduction of oncotic pressure.

(4) By no single factor can oedema be explained in the majority of cases.

PART II.

THE SERUM PROTEINS IN HEALTH.

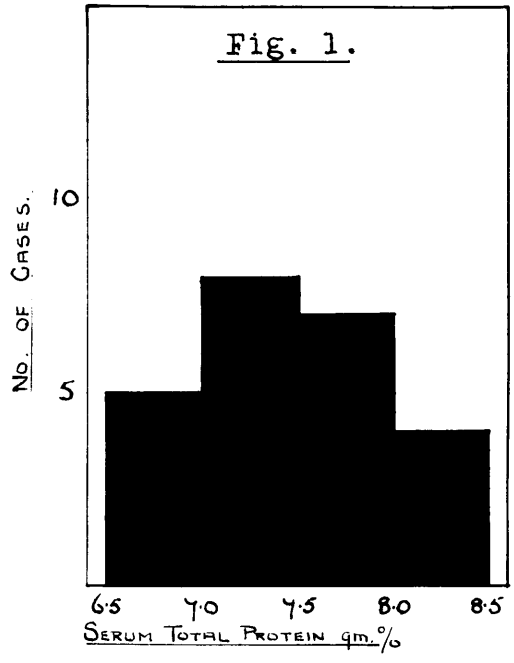
Since most of the work in this investigation is concerned with the serum proteins it is necessary to have a clear idea of the variations that take place in the individual fractions of serum protein in infants and children who are not suffering from any disorder of nitrogen metabolism. A survey of the literature has shown that few results have been published dealing with albumin and globulin levels in the serum where the estimations have been made by the Kjeldhal method. As it is now recognized that this is the most reliable method, it was necessary to obtain a series of observations in which it was used. In this chapter therefore are recorded 24 observations on apparently normal children between the ages of 3 and 11 years and on 22 infants. The former subjects were all well nourished and afebrile and consisted of patients convalescent from rheumatism or suffering from enuresis and epilepsy. The method used was that of Howe[1] as modified by Hawk [2] and Bergeim. Table 1 and figures 1-4 show the results in detail, together with calculated oncotic pressure obtained by Govaert's[3] formula. Total protein ranged from 6.83 to 8.24, albumin from 4.45 to 5.94 and globulin from 1.52 to 2.94 gm. per cent. Calculated serum oncotic pressure ranged from 27.8 to 35.5 mm. Hg. These results are very similar to those published in a recent article

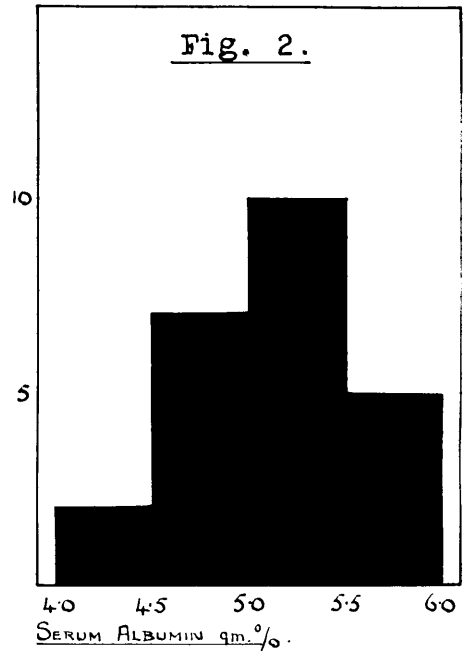
TABLE I.

The serum proteins between 2 and 11 years in normal subjects.

Case No.	Sex.	Age in years.	Total Protein. Gm.%	Albumin. Gm.%	Globulin. Gm.%	Calculated oncotic pressure. mm.Hg.
135	F.	4	6.84	5.32	1.52	31.4
136	F.	3	6.87	4.49	2.38	28.0
137	M.	5	7.75	4.81	2.94	30.6
138	M.	5	6.84	4.74	2.10	28.9
139	M.	5	8.01	5.22	2.79	32.6
140	M.	5	8.24	5.43	2.81	33.9
141	F.	5	7.25	4.97	2.28	30.5
142	M.	7	7.38	5.10	2.28	31.2
143	M.	7	7.54	5.18	2.36	31.8
144	M.	8	7.22	4.72	2.50	29.4
145	F.	8	6.84	4.45	2.39	27.8
146	F.	9	7.58	5.94	1.64	34.9
147	F.	9	7.43	4.70	2.73	29.6
148	M.	10	7.10	4.72	2.38	28.4
149	F.	10	7.64	5.28	2.36	32.3
150	F.	11	7.78	5.27	2.51	32.9
151	F.	11	7.27	5.52	1.75	32.8
152	F.	11	7.34	5.12	2.22	31.2
153	F.	11	6.83	4.99	1.84	30.0
154	M.	10	8.02	5.92	2.10	35.5
155	M.	8	7.78	5.62	2.16	34.0
156	F.	9	8.04	5.25	2.79	32.8
157	M.	8	7.03	5.42	1.61	32.5
158	M.	10	7.62	5.59	2.03	33.6
Average:-			7.42	5.15	2.27	31.5

Serum Protein Levels Between 2 and 11 years in Normal Children.





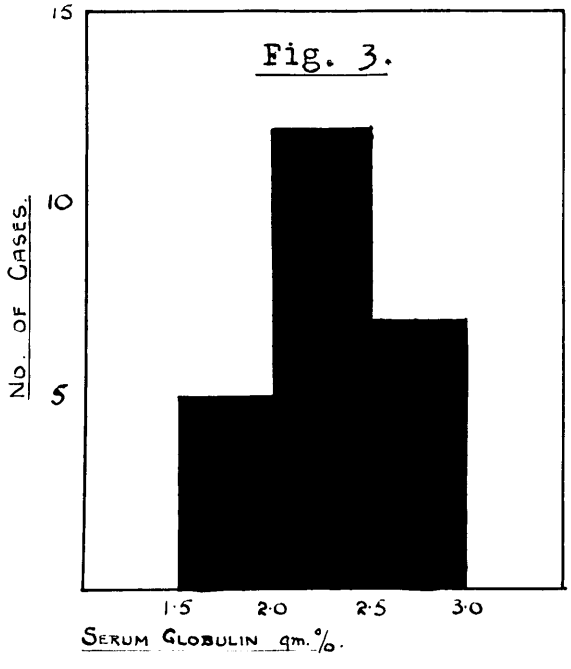
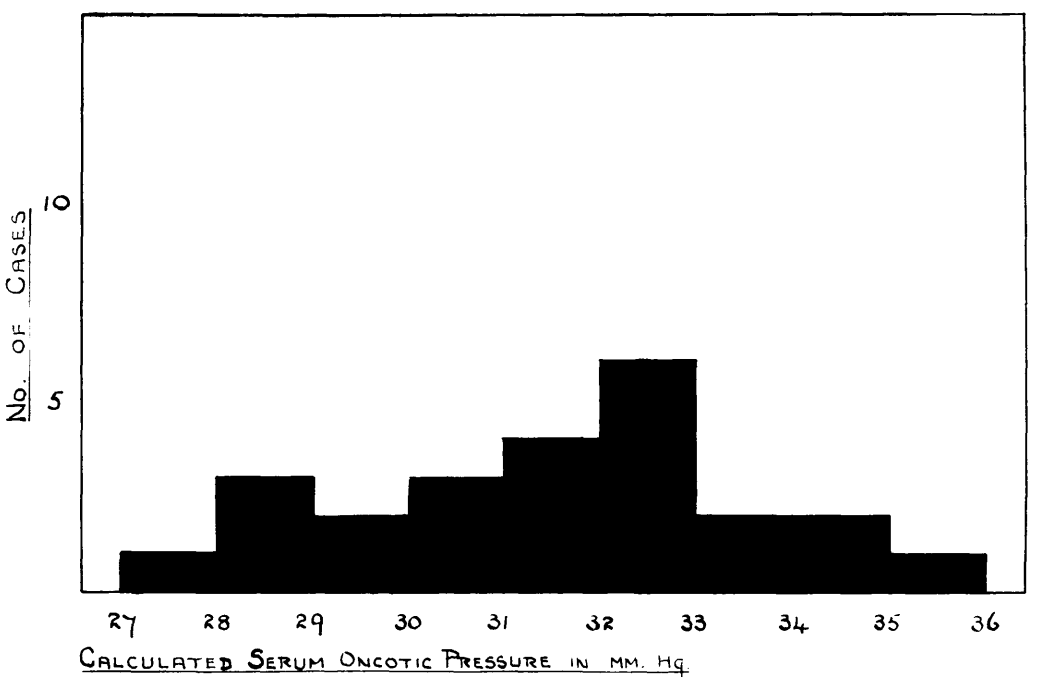


Fig. 4.

Calculated Oncotic Pressure of the Serum Between 2 and 11 years in Normal Children.



by Peters[4] and Eisenman who estimated total serum protein by a modification of Howe's method in 52 adults on 109 occasions. They found that it lay between 6.3 and 7.7 gm. per cent. in 90 per cent. of instances. Fifty estimations of serum albumin in 34 subjects lay between 4.1 and 6.1 gm. per cent. but in only one case was the level above 5.5 gm. per cent.. Serum globulin ranged from 0.9 to 3 gm. per cent.. In only one instance did it fall below 1.4 gm. per cent.. They conclude that the normal limits of variation are:- Serum total protein 6.0-8.0 gm. per cent., serum albumin 4.0-5.5 gm. per cent. and serum globulin 1.4 to 3.0 gm. per cent..

The results of other workers who have employed Howe's[1] method are given in table 2 together with those obtained in the present series and little difference is apparent.

Earlier reports have indicated that globulin is slightly higher in females than in males. In the large series of Peters[4] and Eisenman no difference was observed, a finding in keeping with the results obtained in this work.

TABLE 2.

The Normal Serum Proteins.

Author.	Serum* or Plasma	No. of Patients	Age.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated oncotic pressure. mm.Hg.	Sex.
Present series.	S.	12	Children.	7.54	5.20	2.34	31.9	M.
"		12	"	7.32	5.11	2.21	31.2	F.
McLure (5) et alii	P.	3	"	7.01	4.90	2.10	30.3	
Salvesen (6)	P.	16	Adults	7.00	4.44	2.58	28.9	M.
"		16	"	7.02	4.35	2.68	27.7	F.
Linder (7) et alii.	P.	8	"	6.73	4.11	2.61	26.2	
Bruckman (8) et alii	S.	13	"	6.93	5.06	1.89	30.5	M.
"		8	"	7.61	4.98	2.62	31.0	F.
Kumpf (9)	S.	8	"	7.17	4.82	2.34	29.8	
Moore (10) & van Slyke	P.	9	"	7.10	4.30	2.80	27.7	

* According to Peters (11) and van Slyke serum total protein may be 0.3 to 0.4 gm. per cent. less in plasma than in serum if potassium oxalate be used as an anti-coagulant owing to abstraction of water from the red blood corpuscles.

Age.

Several authors have reported that the serum proteins in the first months of life are lower than the adult level. Mello-Leitao[12] and Bakwin[13] and Rivkin reported that adult level for serum total protein was not attained until eighteen months. Kylin[14] found that under 2 years serum total protein ranged from 4.6 to 6.5 gm. per cent. as compared with 6.4 to 8.6 gm. per cent. in subjects over two years. He also measured serum oncotic pressure and found that it ranged from 17.0 to 26.0 mm. Hg. under two years to 29.0 to 37.0 mm. Hg. over that age. Darrow,[15] quoted by Peters and Eisenman,[4] lends support to the results of previous investigators with the following figures.

Age.	No.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.
"Premature"	26	4.94 ± 0.6	3.58 ± 0.5	1.18 ± 0.7	20.4
Two weeks	20	5.52 ± 0.6	3.73 ± 0.3	1.78 ± 0.4	23.0
5-8 months	14	6.29 ± 0.3	4.28 ± 0.4	2.01 ± 0.3	26.3

All these workers, save Darrow, whose method is not stated, used the refractometer.

Ray[16] and Phatak on the other hand employing Greenberg's[17] modification of Howe's[1] method found in twenty new-born infants the following averages:- Total protein 7.0 gm. per cent., albumin 5.1 gm. per cent. and globulin 1.9 gm. per cent.. Govaert's[3] formula applied to these figures

gives a calculated oncotic pressure of 30.7 mm. Hg.

In this work the serum proteins have been estimated in twenty-two apparently normal infants whose ages ranged from three to twenty-three months. The majority of the cases suffered from rickets or some disease of the nervous system. None were acutely ill or had fever. Table 3 shows the results. Serum total protein ranged from 6.04 to 8.00 gm. per cent., albumin from 4.12 to 5.91 gm. per cent. and globulin from 1.13 to 2.82 gm. per cent.. Calculated oncotic pressure ranged from 26.5 to 34.4 mm. Hg.. The average figures were total protein 7.08, albumin 4.95 and globulin 2.13 gm. per cent., and the average calculated oncotic pressure was 30.1 mm. Hg.. The results are shown graphically in figures 5-8.

Comparison of the figures for infants and for older children shows little difference either in range or in average. If the infants are grouped in age periods (table 4) a slight rise is seen in serum albumin and a slight decrease in serum globulin with advancing age. The slight rise in oncotic pressure which also occurs reflects the increase in albumin.

TABLE 3.

Normal Serum Proteins under 2 years of age.

Case No.	Age.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.
159	15 weeks	6.87	4.49	2.38	27.8
160	16 "	7.19	5.10	2.09	30.9
161	17 "	7.22	4.96	2.26	30.4
162	19 "	7.10	4.48	2.62	28.3
163	27 "	6.56	5.43	1.13	31.5
164	9 months	7.63	5.38	2.25	32.7
165	9 "	6.94	4.12	2.82	26.7
166	9 "	7.33	4.77	2.56	29.8
167	10 "	6.79	4.92	1.87	27.1
168	11 "	7.72	4.95	2.77	31.1
169	11 "	6.82	4.14	2.68	26.5
170	1 year	6.04	4.83	1.21	28.5
171	1 "	6.41	4.92	1.49	29.1
172	13 months	6.31	5.05	1.26	29.5
173	14 "	7.69	5.21	2.48	32.1
174	16 "	7.64	4.95	2.69	31.0
175	17 "	7.91	5.39	2.52	33.2
176	17 "	6.38	5.04	1.34	29.6
177	18 "	8.00	5.22	2.78	32.6
178	18 "	6.55	4.84	1.71	29.0
179	20 "	7.33	4.82	2.51	30.0
180	23 "	7.31	5.91	1.40	34.4
	Average:-	7.08	4.95	2.13	30.1

Serum Proteins in Infants - Under 2 years.

Fig. 5.

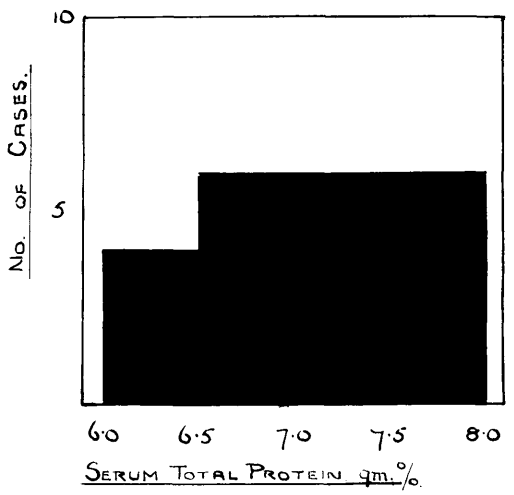


Fig. 6.

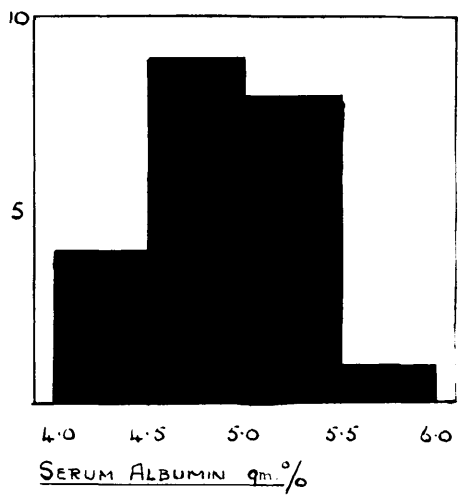


Fig. 7.

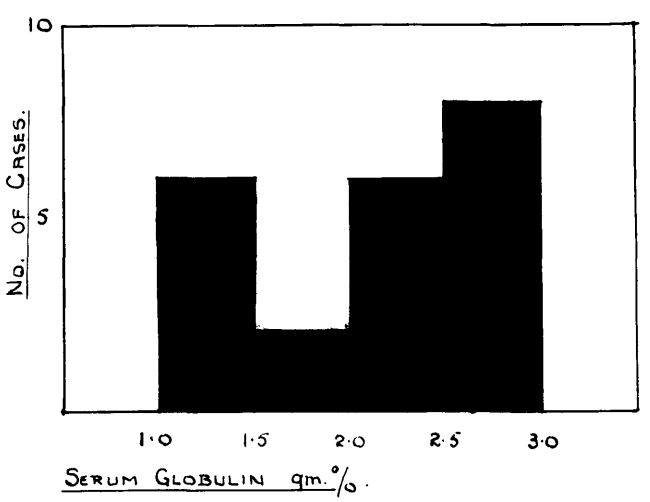


Fig. 8.

Calculated Oncotic Pressure of the Serum of Infants Under 2 years in mm, Hg.

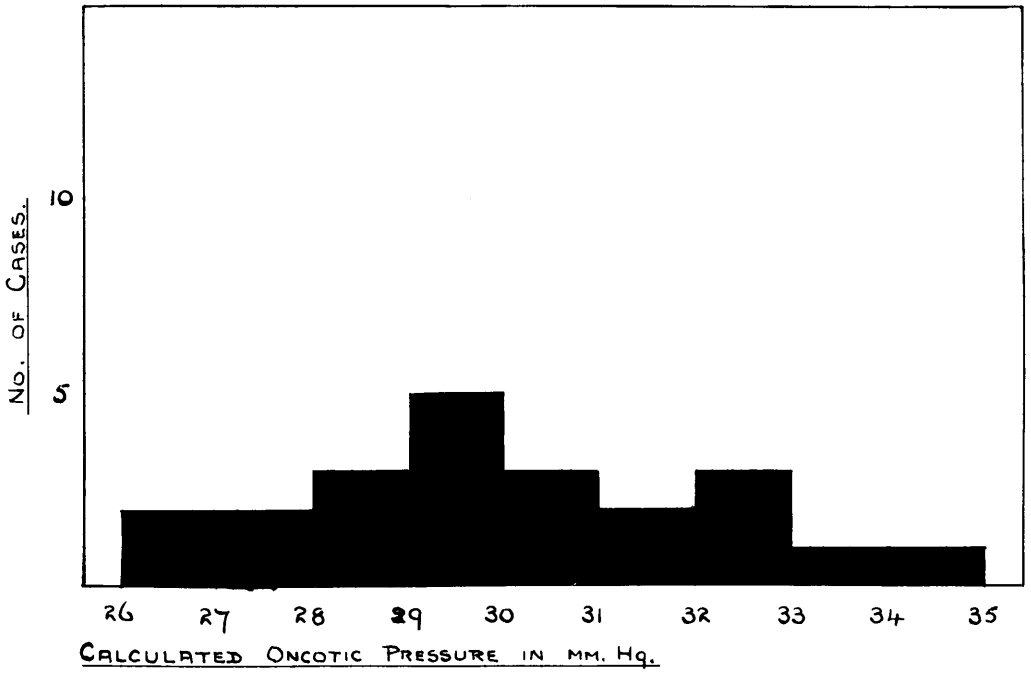


TABLE 4.

The serum proteins in infants according to age.

Age.	No. of cases.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.
3-6 months	4	7.09	4.75	2.34	29.4
6-12 "	7	7.11	4.81	2.30	29.8
12-18 "	6	7.00	5.06	1.94	30.5
18-23 "	5	7.11	5.16	1.95	31.1

PART III.

OEDEMA OF ACUTE NEPHRITIS IN INFANCY AND CHILDHOOD.

In this section of the thesis it is hoped to adduce evidence showing the important rôle of serum protein reduction in the pathogenesis of oedema in acute Bright's disease. It will facilitate a discussion of this problem if prior to dealing with the results of serum protein determinations some consideration is given to findings which throw light on the various other hypotheses of renal oedema. Accordingly the first chapter is devoted to this purpose. This is followed by a consideration of other clinical and biochemical data with special reference to their relationship to oedema. Then follows a critical discussion of the relationship between serum protein and oedema together with the part played by NaCl retention and elevation of blood pressure. This work is based on data obtained from 100 cases of acute nephritis between the ages of 20 months and 12 years. The final chapters deal with the peculiar characteristics of acute Bright's disease in infancy, as observed in 10 cases under 18 months of age and with the clinical and biochemical findings in the disease when complicated by acute cerebral manifestations.

Chapter 1.

Observations on factors having a possible bearing on the pathogenesis of oedema in acute nephritis.

CARDIAC DECOMPENSATION.

Maclean[1] in his report to the Medical Research Council on war nephritis found a temporary enlargement of the heart to the left in 23 per cent. of cases. He ascribed this to the fact that so many patients had to continue heavy manual labour while actually suffering from nephritis. Numerous authors[2,3,4] have observed some cardiac dilatation in acute nephritis and Still[5] has found that an apical V.S. murmur with some cardiac enlargement is common in children. In only 2 cases of the present series of 100 cases of acute nephritis (age 20 months to 13 years) was enlargement of the area of cardiac dulness observed. In 12 others a V.S. murmur was detected at the base; of these one child aged 20 months (case 75) had a loud pulmonic murmur probably indicative of congenital pulmonic stenosis, two had pneumonia and one scarlet fever.

The following brief summaries give the essential clinical and biochemical findings in the two cases with cardiac enlargement.

*Case 37 was a boy of 10 years who developed oedema ten days before admission. When admitted he was in coma with frequent convulsive seizures. The systolic blood pressure was 150 mm.

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* In volume 2 the case reports are given in greater detail.

Hg. and the heart was dilated both to the right and the left of the middle line. Oedema was general. Blood chemistry:-

Total protein.....	6.38	gm.%
albumin.....	4.17	"
globulin.....	2.21	"
Calculated oncotic pressure.	26.0	mm.Hg.

As will be demonstrated later (Chapter 5) the association of hyperpiesis with even slight diminution of oncotic pressure is sufficient to account for the oedema.

Case 45 was a boy of 11 years who developed oedema 10 days before admission. In hospital oedema was general, but there was no ascites. Blood pressure was 156 mm. Hg. systolic. Cardiac dulness was considerably increased to the right of the middle line and slightly to the left. Blood chemistry:-

Total protein.....	5.93	gm.%
albumin.....	4.31	"
globulin.....	1.62	"
Calculated oncotic pressure.	25.9	mm.Hg.

In this series it was rare to find cardiac dilatation in association with acute nephritis possibly because the factors mentioned by Maclean did not operate. 72 per cent. of the cases were admitted to hospital within eight days of the start of the illness and nearly all were confined to bed from the onset. It is of interest to note that the two patients in this series with cardiac dilatation were not confined to bed, one till admission to hospital, the other till the onset of convulsions the day before. In children therefore there is no evidence that a cardiac element plays any significant part in the pathogenesis of oedema of acute nephritis.

INCREASED CAPILLARY PERMEABILITY.

Since the capillaries are normally permeable to electrolytes and water, increase of permeability must mean at least functional damage to the capillary wall with consequent escape of serum protein into the tissues. Peters[6,7,8] and his associates have invoked this to explain oedema in acute nephritis where serum proteins are usually maintained well above oedema level. Presumably any protein which has left the blood stream will exert oncotic pressure against the protein remaining in the vessels thus further reducing the oncotic pressure of the serum. As evidence in favour of this view Peters and his collaborators state that the amount of protein in the oedema fluid of acute nephritis is greater than that found in the oedema fluid of the nephrotic syndrome. They further claim that evidence of capillary damage is denoted by the presence of haemorrhages into the retina and elsewhere.

During the course of this work an ophthalmoscopic examination of the fundi was made in 58 cases of acute nephritis. In only one of these, a patient (case 55) showing cerebral manifestations (uraemia) with a systolic blood pressure of 180 mm. Hg., was a haemorrhage into the retina observed. In this child the blood chemistry was:-

Total protein.....	6.37 gm.%
albumin.....	4.16 "
globulin.....	2.21 "
Calculated oncotic pressure....	26.0 mm. Hg.

A slight reduction was thus present but much less than in many cases without evidence of capillary damage.

That gross changes in the capillaries are rare in acute nephritis in childhood may also be inferred from the rarity of purpura in association with nephritis in this series. According to Osman[9] purpura is practically never found in acute nephritis although he states that in the condition of Henochs' purpura acute nephritis is a frequent and dangerous complication. In 112 cases of acute nephritis of all ages from 4 months to 13 years only once was purpura observed to accompany the disease. The following is a brief summary of the clinical and biochemical findings.

Case 53. A child of 5 years. Five weeks before admission she had a purpuric rash lasting 2 weeks. A week later, purpura, haematuria and joint pains appeared together. On admission oedema was present and a purpuric rash was well marked. The spleen was not palpable and the platelet count, bleeding time and clotting time were normal. Ophthalmoscopic examination was negative. The systolic blood pressure was 108 mm. Hg. The urine contained much blood and a large quantity of albumin, 3-12 parts per litre, much more than could be accounted for by the blood present. Granular casts and blood casts were numerous. The urea concentration test was poor:-

Before urea.....	1.6 gm. %.
One hour after.....	1.7 " "
Two hours after.....	1.9 " "

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure mm.Hg.	N.P.N. mgm.%
12.2.34	5.02	3.06	1.96	19.6	21.8
23.2.34	6.56	3.88	2.68	25.1	29.0
16.3.34	5.06	3.04	2.02	19.5	24.0
4.4.34	6.22	3.81	2.41	24.3	31.2

These observations show that a considerable reduction in serum albumin took place and that there was no nitrogen retention.

Case 49. In this series another case, a boy aged 8 years, was observed in which the association of purpura and acute nephritis is doubtful. Four weeks before admission with acute nephritis he attended the out-patient department with an attack of purpura simplex lasting about a week. The urine at that time contained neither blood nor albumin. On subsequent admission to hospital, there was marked oedema, haematuria and very heavy albuminuria. Azotaemia was present and the systolic blood pressure was 118 mm. Hg.. No evidence of purpura was observed. The blood chemistry was:-

Total protein.....	6.25	gm.%
albumin.....	2.50	"
globulin	3.75	"
Calculated oncotic pressure..	19.0	mm. Hg.
Non-protein nitrogen.....	50.0	mgm. %

It is clear from these observations that the capillaries in acute nephritis do not permit the passage of blood into tissues any more than in health. It may be urged, however, that the serum proteins escape more readily from the blood stream although no evidence of gross leakage is apparent. If this is the case diminution of serum albumin and globulin should be equal. This, however, is not in accordance with the facts as is evident from the average figures obtained in the present series (100 cases): these show a reduction of serum albumin and a slight increase in globulin:-

Total protein.....	6.73	gm.%.
albumin.....	3.96	"
globulin....	2.77	"

It may, however, be argued that albumin escapes more

readily than globulin from the vessels since its molecule is smaller and that the increase of globulin, which is often found, is to be explained by the presence of infection. It will be shown later that infection is not invariable and if it is present a rise in globulin is not always found (p.207). Further a high globulin may occur when no demonstrable infection is present as in long-standing cases of the nephrotic type. Perhaps the most convincing evidence against capillary permeability in acute nephritis is shown by the serum proteins in idiopathic purpura where, if in any condition, they ought to pass easily from the blood stream.

TABLE 5.

The serum proteins in idiopathic purpura.

Case	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Remarks
101	9.11	6.17	2.94	No urinary changes.
102	9.56	5.35	4.21	" " "
103	8.22	5.20	3.02	" " "
104	9.56	5.36	4.20	" " "

In the foregoing table (table 5) are given the biochemical findings in 4 cases of idiopathic purpura with extensive capillary leakage. In all these patients with gross capillary damage serum albumin remained at high normal level and serum globulin was increased. On the other hand,

if capillary permeability be the cause of reduction of serum proteins in acute nephritis, it is remarkable that as many as 12 per cent. of the present series of patients with acute nephritis should have oedema, sometimes very marked, without alteration in either serum albumin or serum globulin (table 6).

TABLE 6.

Cases of acute nephritis showing oedema with normal serum proteins.

Case	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	Degree of oedema.	Duration of oedema in days.
83	7.33	4.69	2.64	29.4	±	6
5	7.38	5.00	2.38	30.9	++	8
77	7.65	5.19	2.46	31.9	++	3
65	6.98	4.45	2.53	28.0	++	4
35	7.94	5.48	2.46	33.6	±	3
97	8.64	6.12	2.52	37.2	+	6 ?
47	7.32	4.56	2.76	28.9	±	15
80	7.02	5.31	1.71	31.8	±	4
31	7.40	4.93	2.47	30.6	+	7
79	8.63	6.12	2.51	37.1	±	7
3	7.70	6.15	1.55	35.9	±	4
92	6.58	4.77	1.80	28.7	±	5

Peters and his associates state that the concentration of protein in oedema fluid is higher in acute

nephritis than in the nephrotic syndrome and offer this in support of the capillary damage theory. Peters[6] himself however admits that the difference between the two conditions is but slight. The following table (table 7), adapted from Peters and van Slyke[8] shows this.

TABLE 7.

Protein in oedema fluids.

Diagnosis.	Source.	Total Protein gm.%	Albumin gm.%	Globulin gm.%
Nephrotic syndrome. Nephrosis.	Subcutaneous oedema.	0.1	-	-
" " "	Pleural effusion.	0.3-0.6	-	-
" " "	Ascites.	0.1-0.9	0.1-0.5	tr.-0.4
Acute nephritis.	Subcutaneous oedema.	0.1	0.1	-
" "	Pleural effusion.	0.6	0.5	0.1
" "	Ascites.	0.6-1.0	0.4-0.6	0.3-0.4

The only specimen of oedema fluid examined in this investigation was obtained from the abdominal cavity at operation on a case of acute nephritis (case 49). The results of analysis show that the protein concentration was only slightly higher than that given by Peters and van Slyke[8] for nephrosis.

Source.....	Ascitic fluid.	
Total Protein.....	0.98	gm.%
Albumin.....	0.61	"
Globulin....	0.37	"

In brief it may be said that a consideration of the clinical and biochemical evidence gives no support to the view that damage to capillary endothelium is a cause of serum protein reduction and oedema.

INCREASED ACID PRODUCTION.

The general objections to Fischer's[10] view that oedema results from the imhibition of fluid caused by an increased acid production have already been stated in Part I. This hypothesis has not received much special consideration but it is of interest to record the relationship of blood carbon dioxide to acute nephritis. If Fischer's view were correct one might logically expect reduction in the carbon dioxide of the blood in that condition. From the results of the investigation of 30 cases (table 8) it is evident that unless acute nephritis is complicated by cerebral manifesta-

TABLE 8.

The CO_2 in Acute Nephritis.

Class of case.	Number of Cases.	Range of CO_2. vols.%	Average. vols.%
Acute nephritis.	24	42.5-68.2	52.9
Acute nephritis with uraemia.	6	27.5-54.0	40.4

tions (uraemia), the carbon dioxide of the blood falls within normal limits. No relationship was observed between the carbon dioxide level and the degree of oedema in either group. Furthermore in the nephrotic type of case when oedema is a marked feature, Graham[11] and Morris find that no abnormality of the alkaline reserve of the blood occurs. The reaction of the oedema fluid itself was noted by Maclean to be alkaline. These findings seem to provide an additional argument against the acceptance of Fischer's[10] hypothesis.

Summary.

(1) Cardiac dilatation is infrequent in acute nephritis in childhood, being detected in only 2.0 per cent. of cases.

(2) No clinical or biochemical support is given to the view that increased permeability of the capillaries is a factor in the production of oedema in acute nephritis.

(3) No reduction of the CO_2 of the blood was noted in acute nephritis except in uraemic cases where it was slight and inconstant. This militates against the acceptance of Fischer's hypothesis of increased acid production.

Chapter 2.

Some biochemical and clinical findings in acute nephritis with special reference to oedema.

AZOTAEMIA.

Incidence.

The incidence of azotaemia in 100 cases of acute nephritis between 20 months and 13 years is shown in figure 9. In 57 per cent. of patients non-protein nitrogen was above the upper limit of normal. One case, not shown in the figure, had the high value of 280.0 mgm. per cent..

Relation to oedema.

For the purposes of this paper oedema has been classified by clinical estimation as follows:-

0	=	No oedema.
$\bar{+}$	=	Puffiness of the face.
+	=	Pitting.
++	=	Anasarca. Effusions.

In 12 cases which were observed at times varying from one to nineteen days after the onset of the nephritis no oedema was detected clinically. Table 9 shows that there was little relationship between oedema and the non-protein nitrogen level of the blood.

Fig. 9.

Incidence of Azotaemia in Acute Nephritis - Initial Observations.

(One case, not shown in the figure, had a level of 280 mgm.%)

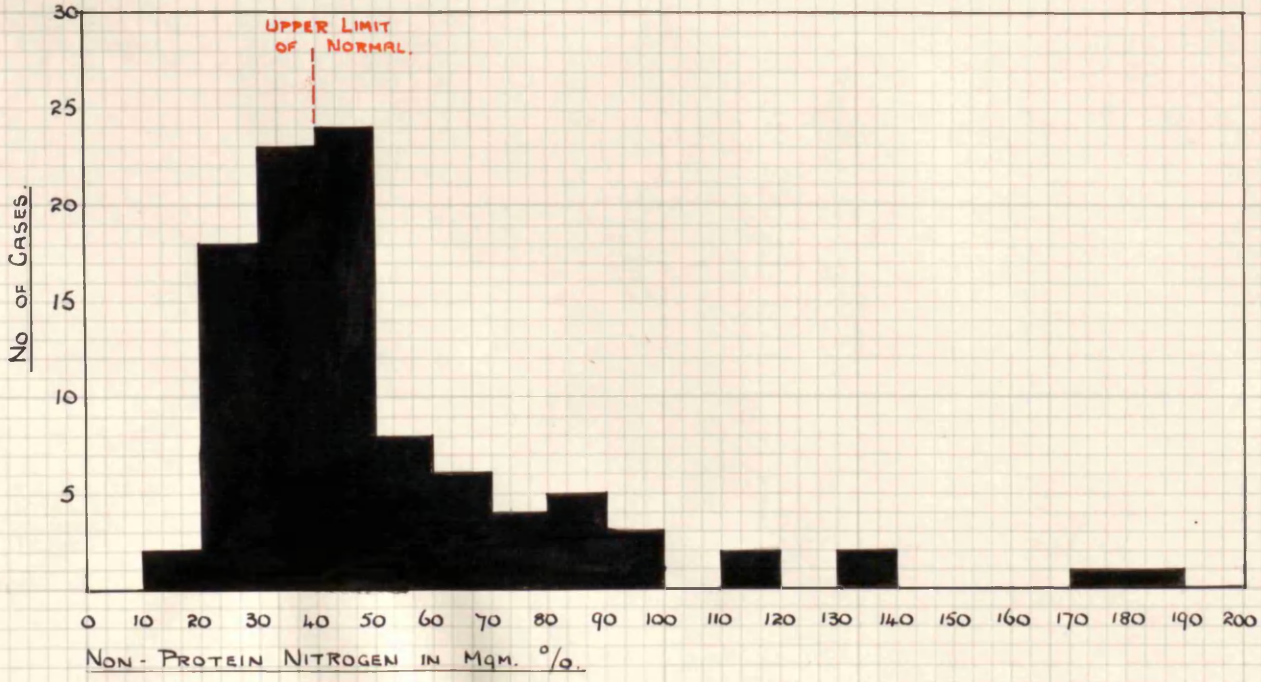


TABLE 9.

The relation of azotaemia to oedema.

Oedema.	No. of cases.	N.P.N.Ave. mgm.%	N.P.N.range mgm.%	Per cent. of cases with normal N.P.N.
0	12	60.0	20.6-190.0	42
±	31	48.8	19.1-113.0	39
+	27	55.4	22.4-176.5	48
++	30	55.7	17.0-280.0	43

Relation to blood pressure.

If rise of blood pressure in acute nephritis is a reaction to the blockage of the renal circulation one would expect some relationship between the height of the blood pressure and the level of the non-protein nitrogen of the blood. Figure 10 however shows the complete absence of such a relationship in 75 cases who were examined immediately after admission to hospital early in the illness. Furthermore very high levels of blood pressure were found with little or no rise in non-protein nitrogen while with slight or moderate hyperpiesis marked azotaemia was not infrequent.

Value in Prognosis.

The following figures confirm the general belief that the initial level of non-protein nitrogen of the blood in the early stage of the disease is of little prognostic value. In this series very high or normal levels occurred with no apparent relation to the course or duration of the disease. (table 10).

Fig. 10.

The Relation of Blood Pressure to the Non-Protein Nitrogen of the Blood in Acute Nephritis.

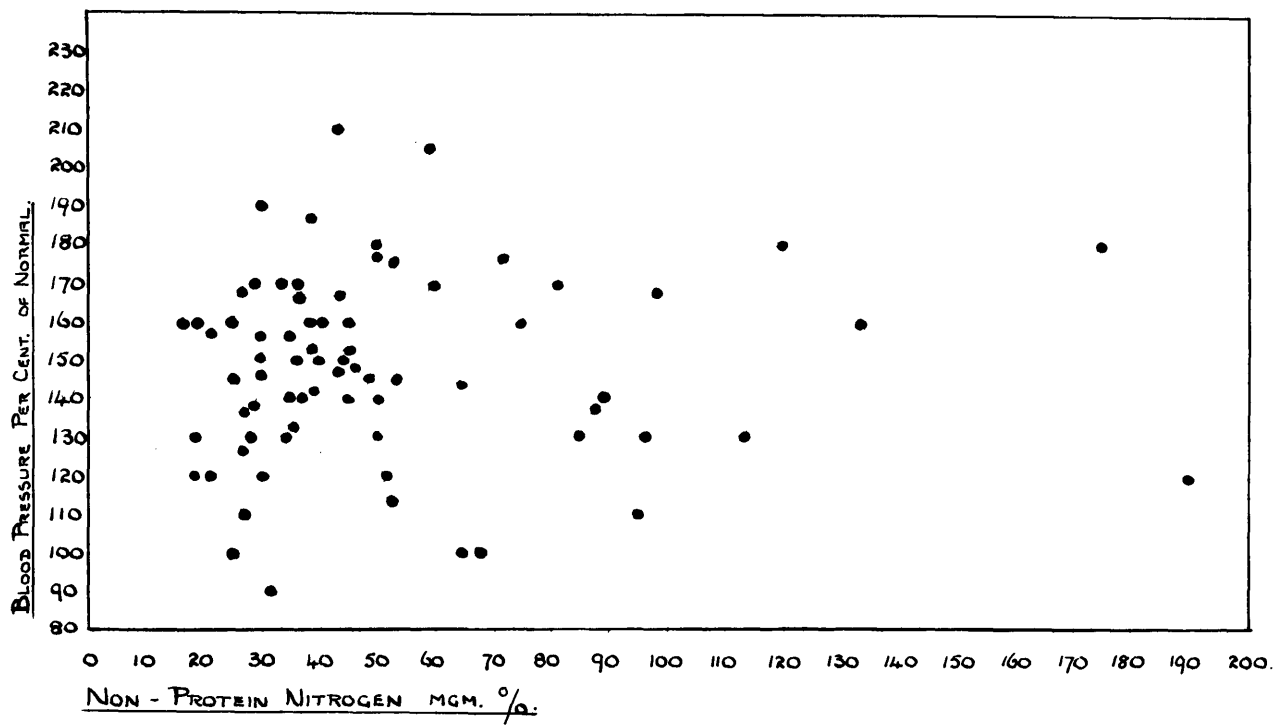


TABLE 10.

Case No.	N.P.N. mgm.%	Result.
82	96.3	Well
41	88.2	Well. Uraemic.
97	42.2	Died. Pneumococcal meningitis.
12	40.6	Well. Uraemic.
87	90.9	Well.
70	133.0	Well.
49	50.0	Died.
58	31.3	Much improved.
29	280.0	Much improved. Uraemic.
38	33.3	Well.
4	18.0	I.S.Q.
48	74.6	Died.
37	29.8	Well. Uraemic.

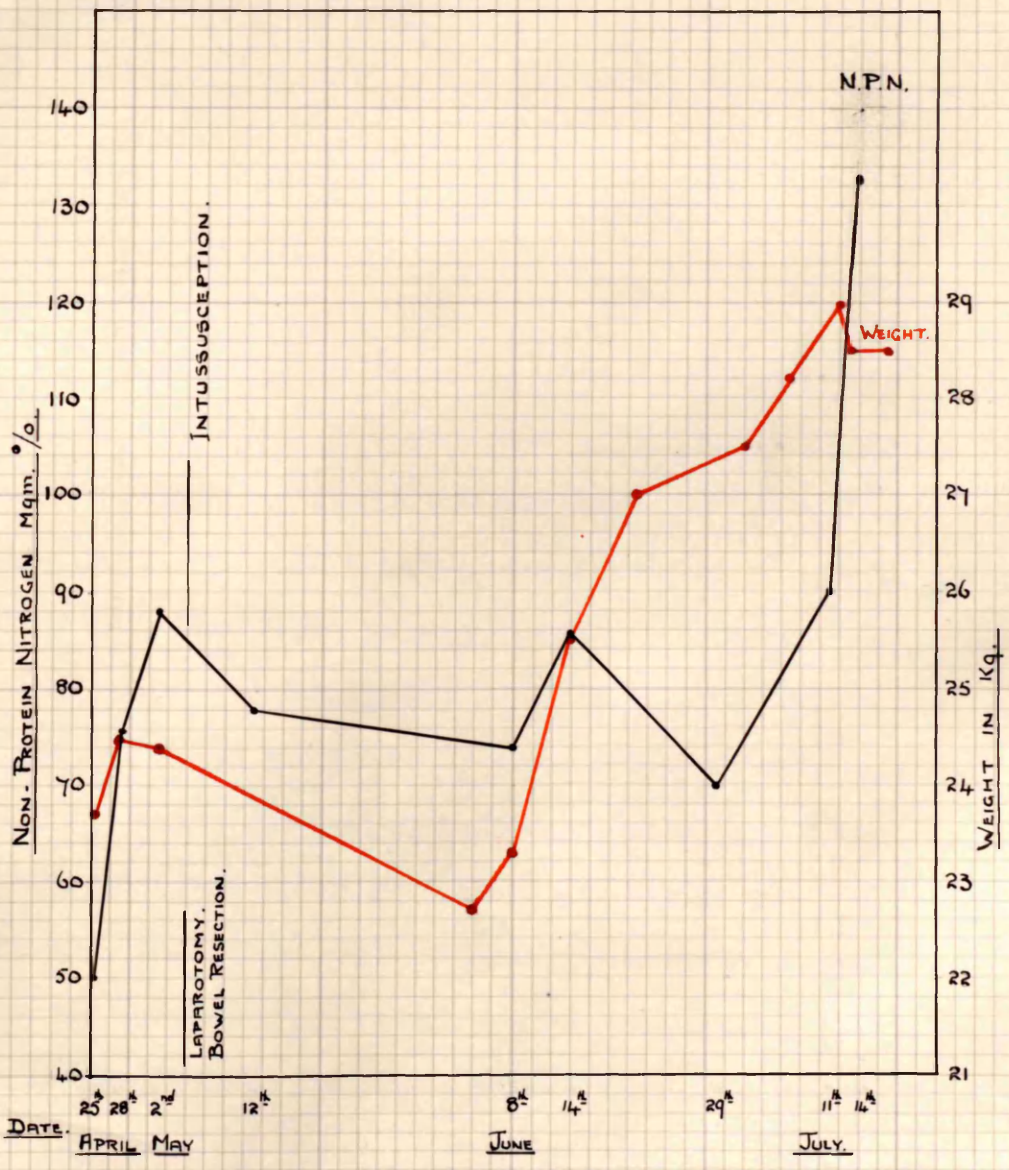
But in accordance with the finding of other investigators the persistence of a high non-protein nitrogen level in the blood was noted to be of grave prognostic import. Figure 11 illustrates this point.

Four of the patients (cases 48, 49, 29, 62) in this series showed prolonged azotaemia. Two of these (cases 48 and 49) died with symptoms suggestive of uraemia after several months in hospital. A third patient (case 29) showed per-

Fig. 11.

Persistent Elevation of Non-Protein Nitrogen of the Blood in a Fatal Case of Acute Nephritis.

Case 49.



Oedema present throughout.

sistent elevation of non-protein nitrogen for some eight weeks, after which return to the normal level was observed. This child still shows impaired renal function, and a trace of albumin in the urine is apparent nine months after the onset of the illness. The fourth case (62) when removed from hospital by his parents, still had a moderate degree of azotaemia four months after the onset of the illness.

BLOOD PRESSURE.

Incidence.

According to Bennett[1] the incidence of hyperpiesis in acute nephritis has not been efficiently studied. He comes to the conclusion however that in acute focal nephritis there is no rise of blood pressure while in the acute diffuse type a moderate rise is only occasionally present. An attempt to determine the incidence of hyperpiesis in the nephritis of childhood is complicated by the fact that the normal level of blood pressure gradually increases with age. The adult figure is not attained until at least the tenth year is passed. Allowance for this must be made in estimating degrees of hyperpiesis. Accordingly blood pressure is estimated as a percentage of the normal for the age. The standard used is that given by Findlay.[2]

Age in years.	Systolic blood pressure in mm. Hg..
2-5	70
5-10	90
10-13	100

Fig.12.

The Incidence of Hyperpiesis in Acute Nephritis.

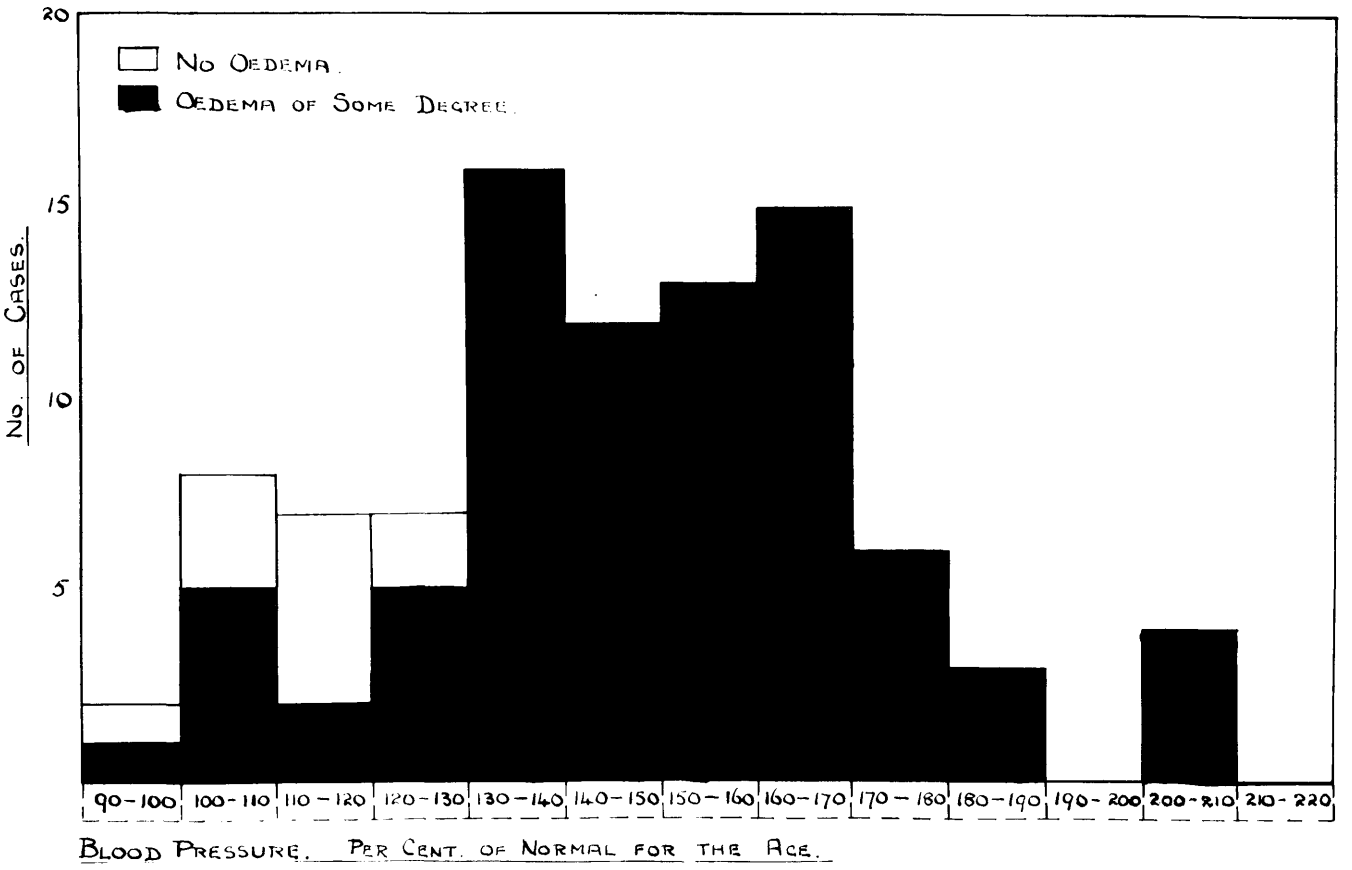


Fig.13 .

To Show Relation Between Fall in Blood Pressure and Loss of Oedema.

Case 34.

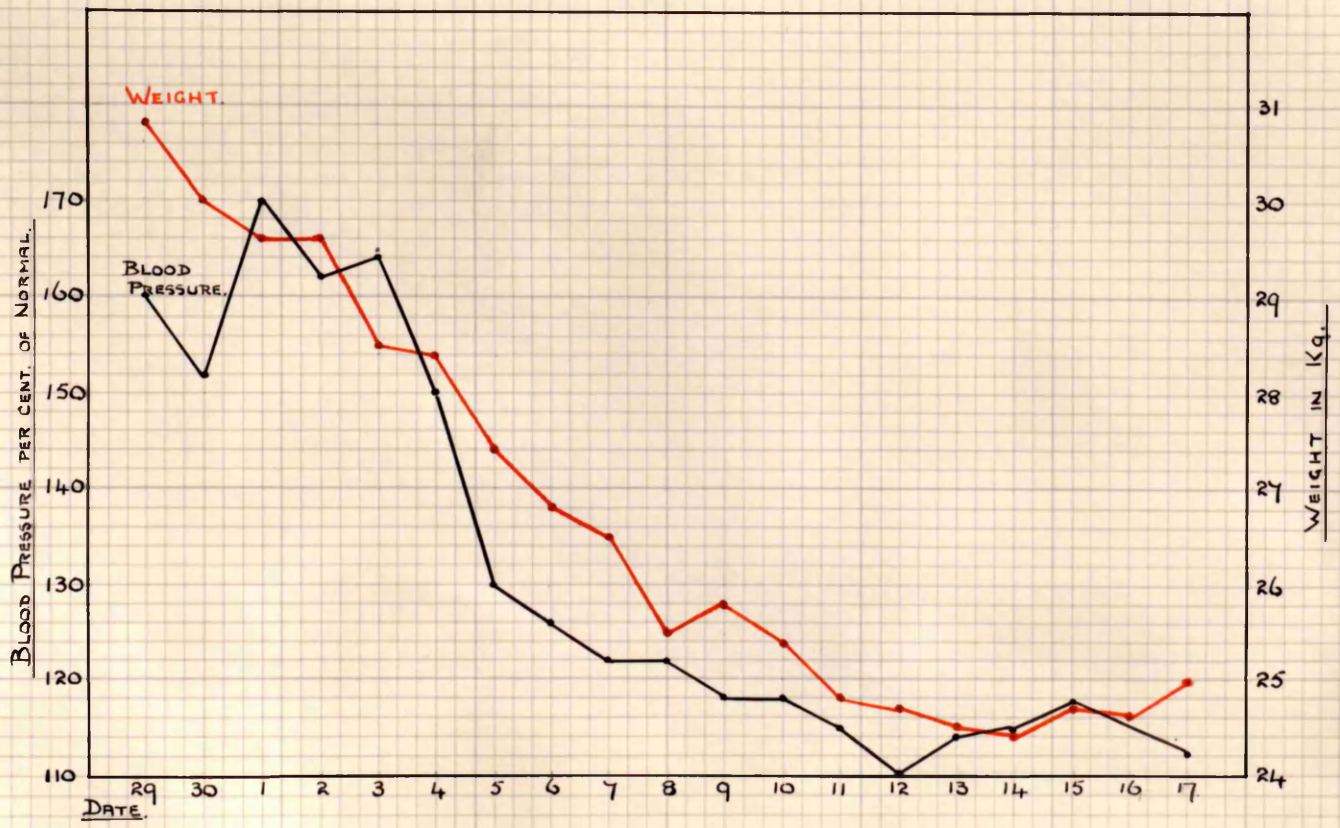


Fig. 14

To Show Relation of Blood Pressure to Oedema.

Case 79.

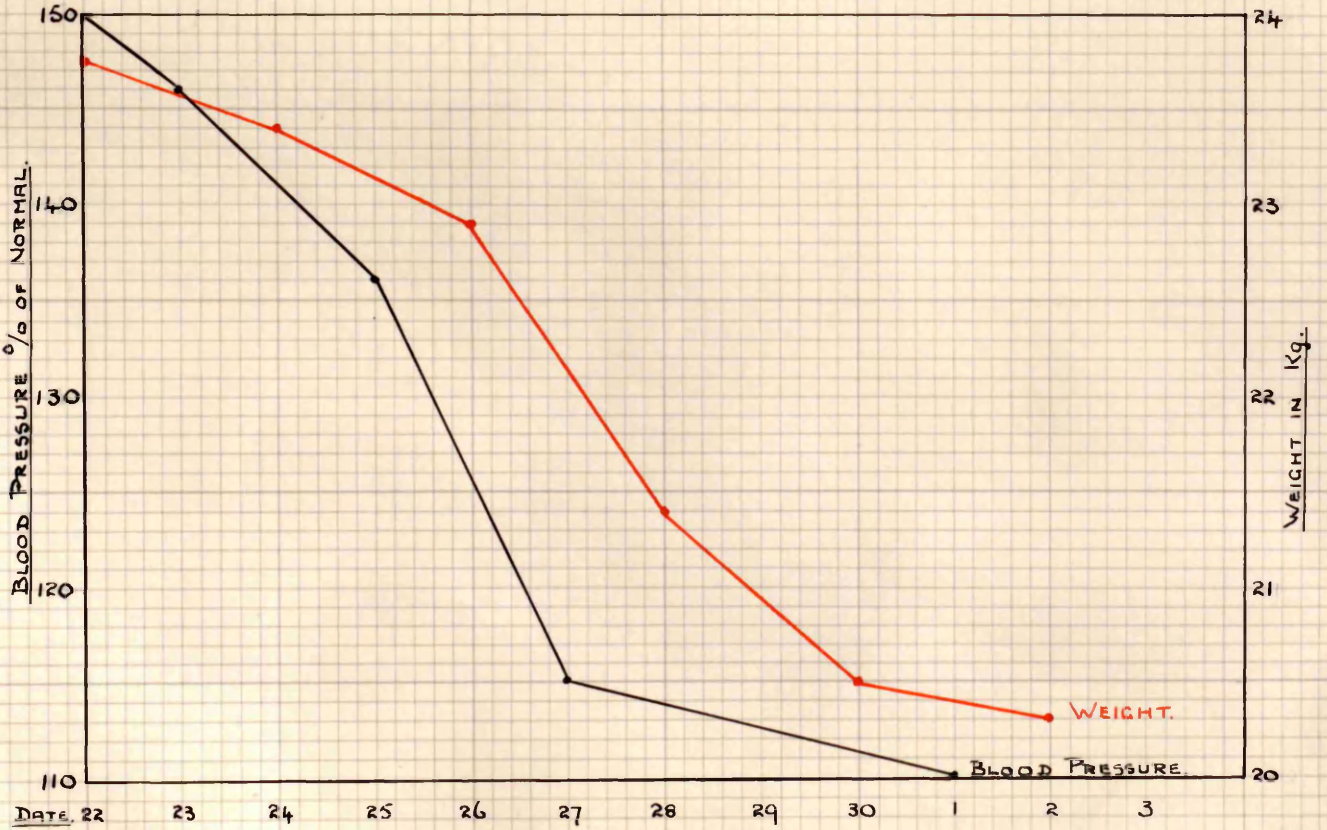
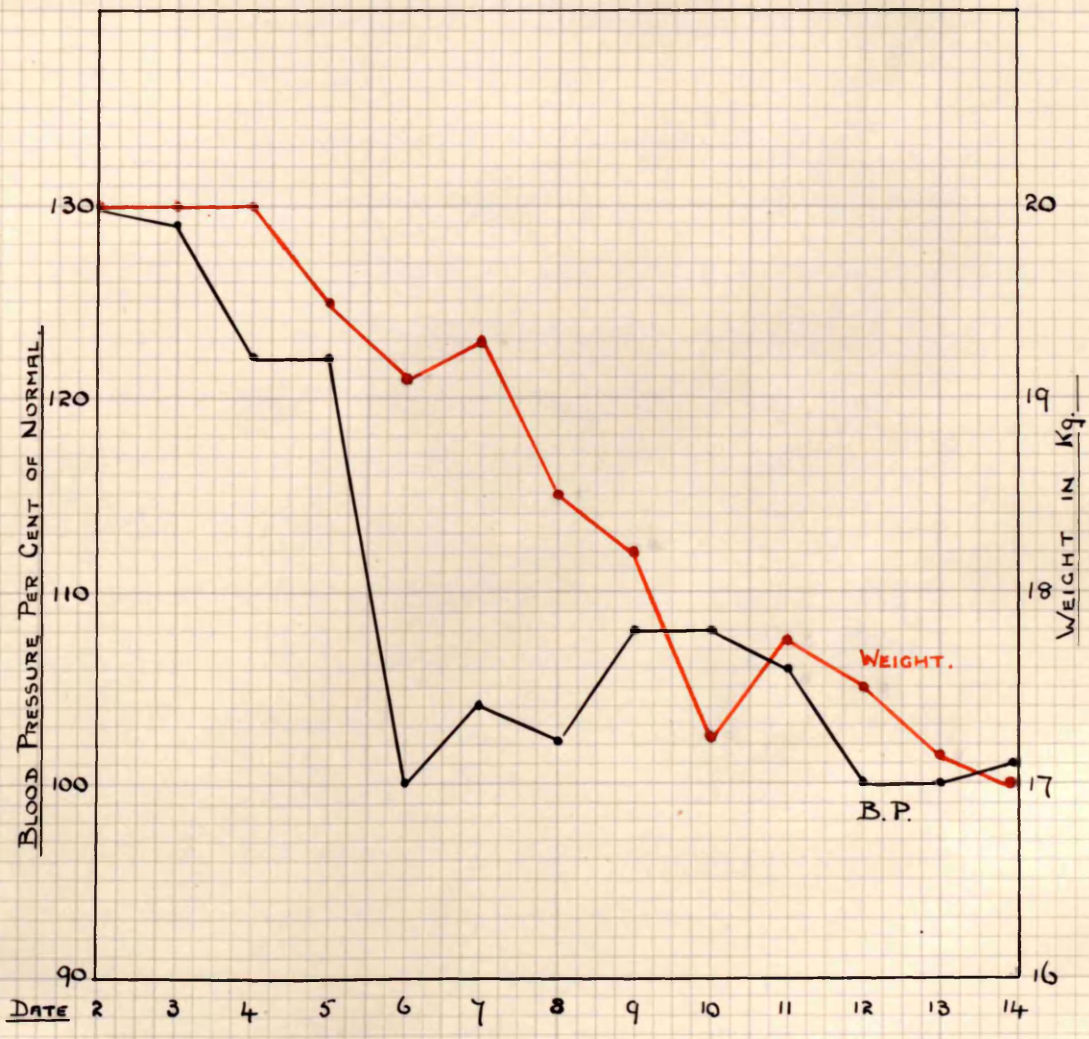


Fig. 15.

Absence of Relation Between Fall in Blood Pressure and Loss of Oedema.

Case 27.



Chapter 3.

The serum proteins in acute nephritis.

THE SERUM PROTEIN LEVEL.

Numerous investigators have reported normal findings in many cases of acute nephritis. (Blackfan,[1] Starlinger[2] and Winands, Fahr[3] and Swanson). Some of their cases, however, did show some reduction but not below the oedema level associated with the nephrotic syndrome. Kumpf,[4] Moore[5] and van Slyke, Wiener[6] and Wiener, Peters[7] et alii and van Slyke[8] et alii found that not infrequently a reduction occurred at the expense of the albumin fraction, globulin being usually higher than normal. Van Slyke[8] and his collaborators indeed reported that in 30 per cent. of their cases of acute nephritis the serum albumin actually fell below 2.5 gm. per cent..

From the literature the position may be summed up as follows. In a certain number of cases the serum proteins remain at a normal level, in some marked reduction occurs and in the majority a moderate reduction is found. Harrison[9] and Wyllie, however, state that in "acute and acute haemorrhagic nephritis the plasma proteins generally fall within normal limits." A glance at their own figures (table 11) shows that even they obtained a reduction of serum albumin at least in some of their cases.

TABLE 11.

Adapted from Harrison and Wyllie.

Type of nephritis.		In gm. per 100 c.c. of plasma.		
		Total Protein.	Albumin.	Globulin
"Acute"	(max.	8.27	5.04	3.15
	(min.	5.02	2.84	1.76
	(ave.	6.93	4.16	2.41
"Acute haemorrhagic."	(max.	8.66	5.47	2.97
	(min.	6.99	3.91	2.02
	(ave.	7.72	4.80	2.47

In the following tables (12, 13) are given the results of estimation of the serum proteins in 100 cases of acute nephritis between $1^{8}/12$ year and 13 years of age. The observations were made as soon after admission to hospital as was practicable.

TABLE 12.

The serum proteins in 100 cases of acute nephritis: initial observations on admission.

Case.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure mm.Hg.
1	6.64	3.54	3.10	23.8
2	5.27	3.78	1.49	22.9
3	7.70	6.15	1.55	35.9
4	4.36	1.92	2.44	13.9
5	7.38	5.00	2.38	30.9
6	6.23	3.73	2.50	24.0

TABLE 12 (contd).

Case.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
7	6.84	4.41	2.43	27.6
8	5.79	3.18	2.61	21.4
9	4.44	3.01	1.43	18.5
10	6.25	3.75	2.50	24.1
11	6.91	3.94	2.97	25.8
12	5.60	3.60	2.00	22.6
13	6.71	3.54	3.17	23.9
14	7.36	3.92	3.44	26.4
15	6.02	3.71	2.31	23.5
16	9.00	5.30	3.70	33.8
17	8.46	3.34	5.12	26.6
18	6.32	4.12	2.20	25.7
19	5.84	2.96	2.88	20.3
20	8.12	3.02	5.10	23.7
21	6.67	4.37	2.30	27.2
22	8.70	5.79	2.91	35.9
23	6.34	4.62	1.72	27.9
24	8.52	3.79	4.73	27.6
25	6.17	4.19	1.98	25.8
26	6.14	3.48	2.66	22.9
27	4.61	2.81	1.80	18.2
28	6.72	3.75	2.97	24.9
29	7.62	2.39	5.23	20.5
30	6.90	4.27	2.63	27.1

TABLE 12 (contd).

Case.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
31	7.40	4.93	2.47	30.5
32	8.19	4.17	4.02	28.5
33	6.03	3.36	2.67	22.2
34	6.04	3.57	2.47	22.5
35	7.94	5.48	2.46	33.6
36	5.97	4.67	1.30	28.2
37	6.38	4.17	2.21	26.0
38	5.08	1.71	3.37	14.1
39	7.35	5.93	1.42	34.6
40	8.86	3.67	5.19	27.4
41	8.36	3.51	4.85	26.1
42	7.11	4.54	2.57	28.6
43	7.25	3.92	3.33	26.2
44	6.77	3.81	2.96	25.1
45	5.93	4.31	1.62	25.9
46	5.95	3.48	2.47	22.5
47	7.32	4.56	2.76	28.9
48	4.27	1.66	2.61	12.8
49	6.25	2.50	3.75	19.0
50	8.02	4.22	3.80	28.5
51	7.66	4.27	3.39	28.2
52	5.86	4.06	1.80	24.8
53	5.02	3.06	1.96	19.6
54	8.19	4.17	4.02	28.7

TABLE 12 (contd).

Case.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
55	6.37	4.16	2.21	26.1
56	6.31	2.91	3.40	20.9
57	6.57	3.29	3.28	23.7
58	4.92	2.06	2.86	15.3
59	6.75	4.36	2.39	27.3
60	6.34	3.87	2.47	24.7
61	8.27	3.55	4.72	25.5
62	3.96	2.03	1.93	13.8
63	7.26	3.44	3.82	24.0
64	8.90	4.25	4.65	29.9
65	6.98	4.45	2.53	28.0
66	6.46	3.11	3.35	21.8
67	4.82	3.74	1.08	22.0
68	6.72	3.76	2.96	24.8
69	5.40	2.78	2.62	18.9
70	6.69	2.82	3.87	20.9
71	6.34	2.45	3.89	18.9
72	7.84	5.14	2.70	32.0
73	6.05	3.32	2.73	22.9
74	5.72	3.30	2.42	21.7
75	6.84	4.07	2.77	26.2
76	6.58	2.72	3.86	20.4
77	7.65	5.19	2.46	31.9
78	6.62	4.11	2.51	26.1

TABLE 12 (contd).

Case.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure mm.Hg.
79	8.63	6.12	2.51	37.1
80	7.02	5.31	1.71	31.8
81	8.30	4.04	4.26	28.1
82	5.02	3.75	1.27	22.4
83	7.33	4.69	2.64	29.4
84	7.09	5.13	1.96	30.9
85	5.87	3.44	2.43	22.3
86	5.18	3.72	1.46	22.4
87	5.06	2.63	2.43	17.6
88	6.71	5.32	1.39	31.2
89	6.76	4.01	2.75	25.8
90	6.99	4.90	2.09	29.8
91	6.32	4.44	1.88	27.0
92	6.58	4.77	1.81	28.7
93	5.86	3.07	2.79	20.8
94	7.25	3.91	3.34	26.2
95	7.89	4.50	3.39	29.5
96	8.66	4.92	3.74	32.9
97	8.64	6.12	2.52	37.2
98	5.36	2.12	3.24	16.1
99	6.86	2.47	4.39	19.7
100	10.06	3.98	6.08	30.3

TABLE 13.

Initial observations on the present series of 100 cases of acute nephritis.

	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.	No. of cases.
Maximum	10.06	6.15	6.08	37.1	100
Minimum	3.97	1.66	1.08	12.8	100
Average	6.73	3.96	2.77	25.6	100
Normal	7.42	5.15	2.27	31.5	24

These figures show that gross reduction in serum albumin and total protein occurred in several instances. On the other hand while serum globulin on occasion was much increased, the average figure was at the upper limit of normal. The very high maximal figures for serum total protein and globulin were obtained in case 100, a boy with terminal bronchopneumonia complicating acute nephritis with uraemic manifestations. The high levels were to be attributed to excessive vomiting.

Figures 16-19 show graphically the range of the results which may be summarized as follows.

(1) Serum total protein was below normal limits in 56 per cent. of cases.

(2) Serum albumin was below normal limits in no less than 76 per cent. of cases. This indicates how frequently a reduction of serum albumin may occur.

Fig.16 .

Initial Observations on the Serum Total Protein Level in Acute Nephritis.

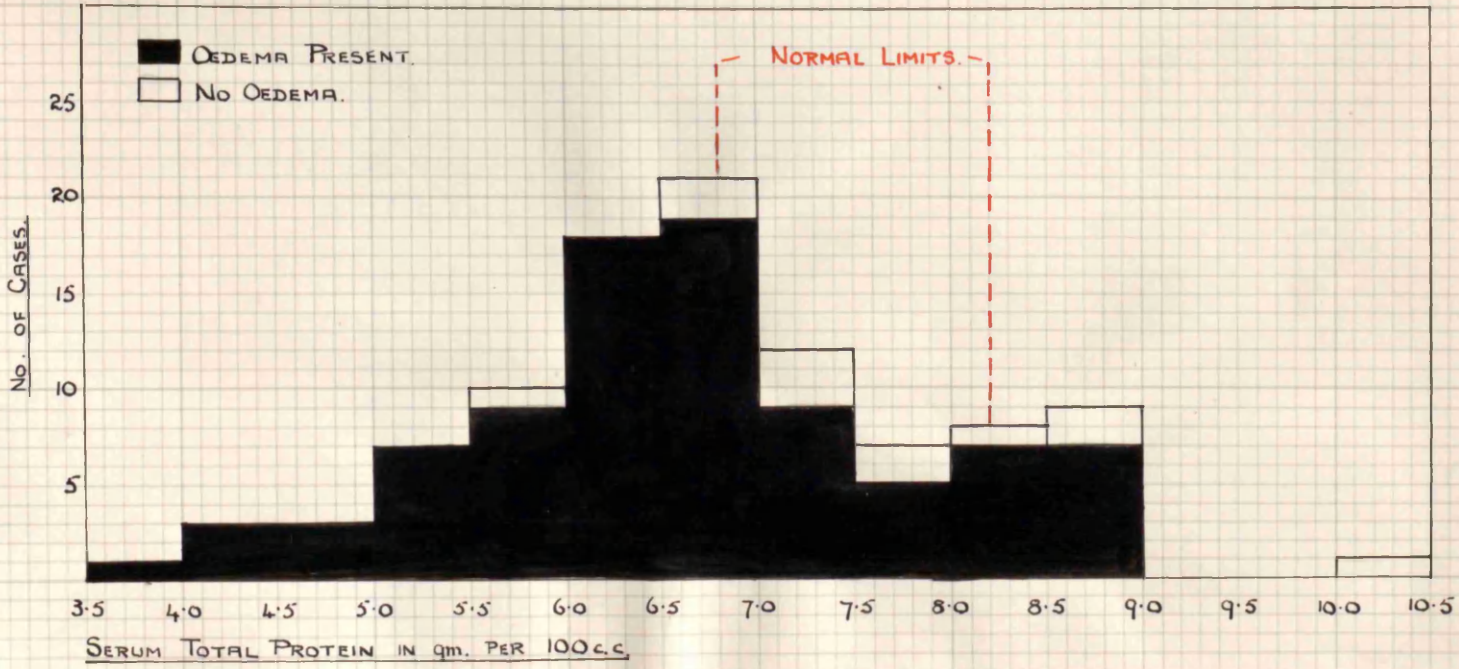


Fig.17 .

Initial Observations on the Serum Albumin Level in Acute Nephritis.

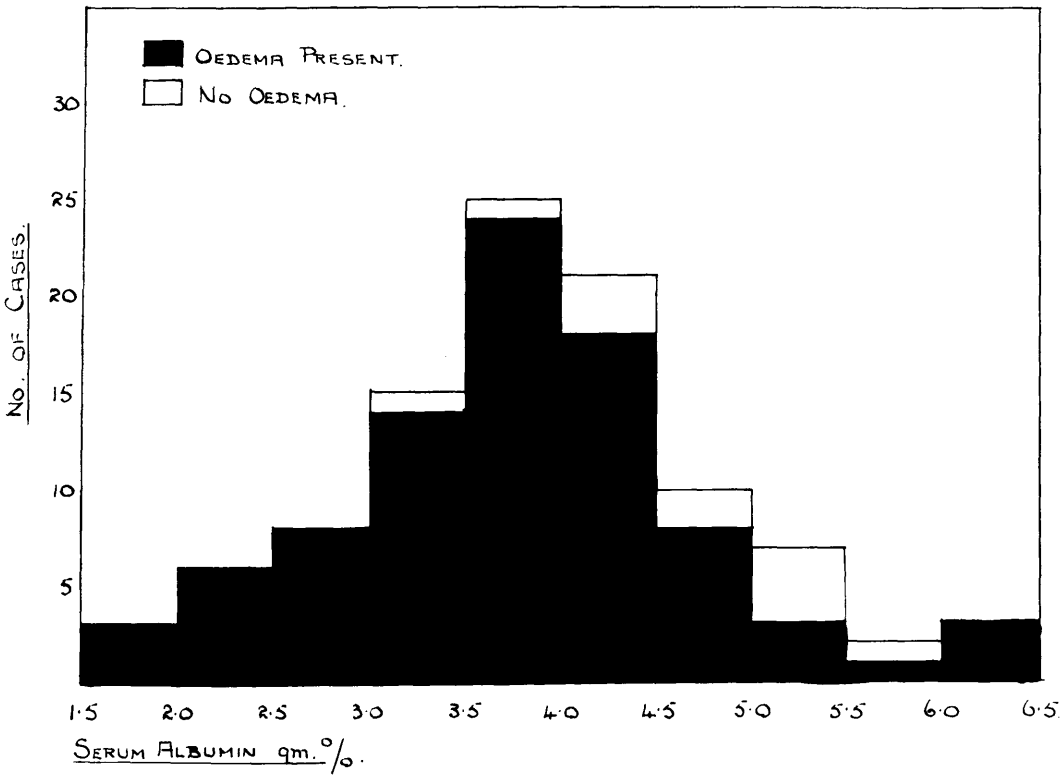


Fig.18.

Initial Observations on the Serum Globulin Level in Acute Nephritis.

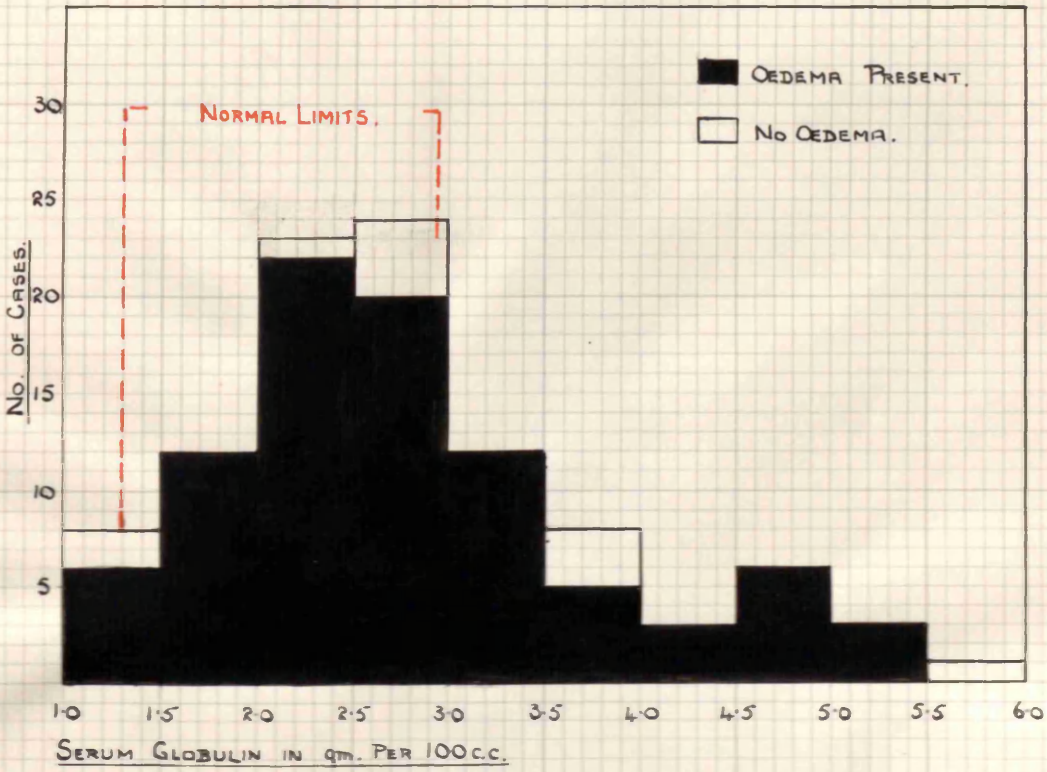
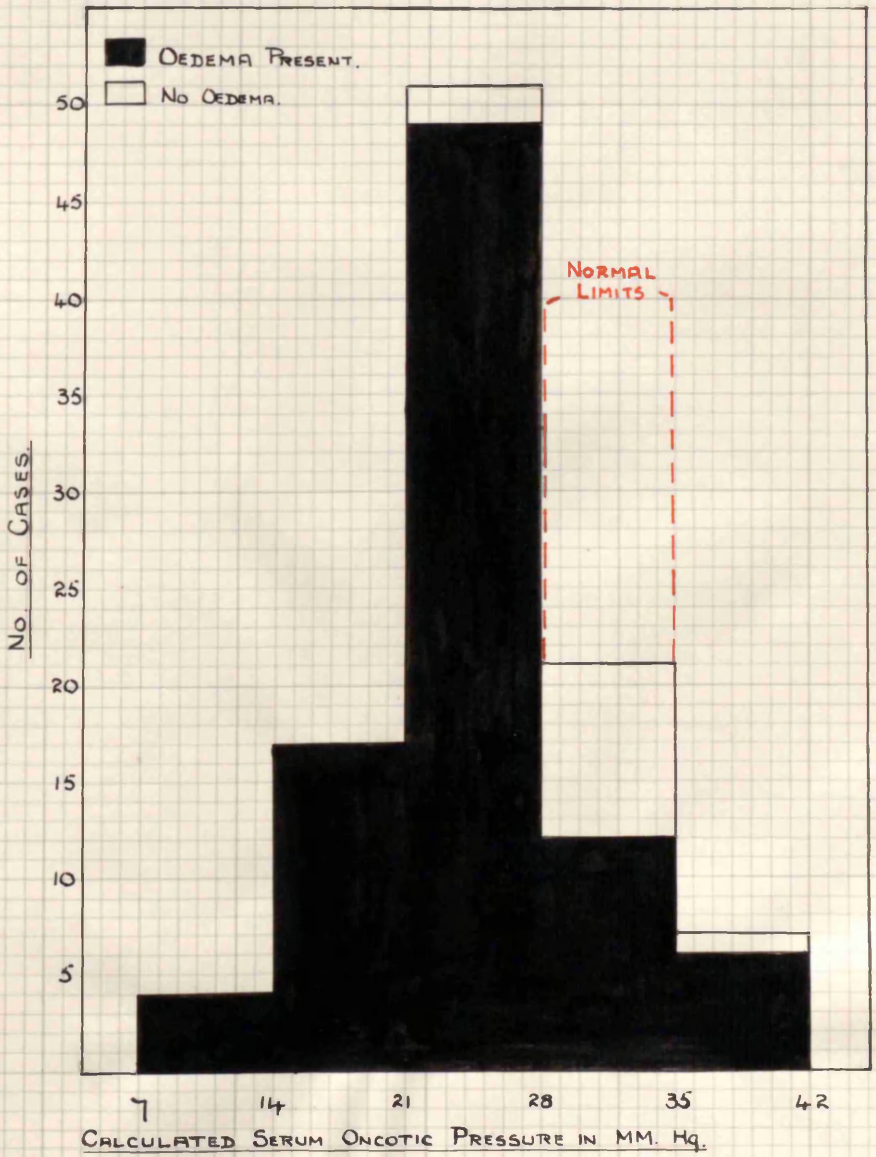


Fig. 19.

Initial Observations on the Calculated Serum Oncotic Pressure Level in Acute Nephritis.



(3) Serum globulin was seldom found below normal limits. A level of over 3.0 gm. per cent., just outwith the upper limit of normal, was observed in 33 per cent. of cases. These high globulin levels afford an explanation for the less frequent reduction in total protein than albumin.

(4) The calculated oncotic pressure was found to be definitely below 28.0 mm. Hg. in 72 per cent. of cases.

RELATION TO OEDEMA.

In the review of the literature it has been shown that all authors, even those who adhere to the hypothesis of Starling[10] in the explanation of chronic renal oedema, are unable to find in the majority of cases of acute nephritis a relation between oedema and the serum protein level. A number of cases have been reported by van Slyke[8] et alii in which serum albumin has been found to be sufficiently reduced to explain on the basis of Starling's theory the presence of oedema without invoking other factors.

The results in the present series would at first sight appear to confirm these views. Figures 16-19 show that oedema was present with total protein values varying from under 4.0 to over 8.5 gm. per cent., albumin from under 2.0 to over 6.0 gm. per cent. and globulin from under 1.5 to over 5.0 gm. per cent. It is clear therefore that oedema is

not an uncommon phenomenon when the levels of total protein and albumin in the serum are normal. Closer consideration of the data however showed that a certain degree of relationship did exist particularly between the serum albumin level and the occurrence of oedema. Dropsy was never absent when the serum albumin fell below 3.44 gm. per cent. or total protein below 5.87 gm. per cent.. In table 14 the 100 cases are grouped according to the degree of oedema and it is obvious when this is done that some relationship can be made out between the fall of serum protein and the degree of oedema. It should be specially noted that the reduction of the protein is at the expense of the albumin fraction which exerts a much greater oncotic pressure than does globulin. Accordingly when the oncotic pressure is calculated it has a greater correlation with oedema than has total protein. Although serum globulin was highest in the group without oedema there was no correlation between the globulin value and the intensity of the oedema. (Figure 18).

TABLE 14.

Relation of degree of oedema to serum protein level.

Group.	No. of cases.	Oedema.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
1	12	0	7.78	4.70	3.08	30.1
2	31	±	7.20	4.30	2.90	27.7
3	27	+	6.54	3.85	2.69	24.9
4	30	++	6.02	3.12	2.90	21.2

A consideration of the various groups in table 14 yields data of interest which are found to be of value when the classification of acute nephritis is undertaken.

Group one - no oedema.

In one case of this group the oncotic pressure was reduced to 22.3 mm. Hg. but in none of the others was it below 27.1 mm. Hg. The impression gained clinically of absence of oedema was confirmed by the fact that very little alteration in weight was noted during recovery. The type of acute nephritis specially associated with absence of oedema is that known as the acute focal variety. In that supposedly common condition blood pressure is not raised, there is no oedema and azotaemia is not found. The group of cases under consideration at present should therefore contain all the patients with acute focal nephritis. The following table (15) however shows that, while hyperpiesis was slight or absent in this group, azotaemia was not infrequent and was occasionally marked. Oedema while not present at the time of blood examination had been previously noted in 6 of the cases.

Of the 6 cases with no oedema only 2 had no azotaemia. In only one case (39) of this series therefore were oedema, hyperpiesis and azotaemia all absent.

Thus there is no evidence that acute focal nephritis exists as a clinical entity.

TABLE 15.

Group one - oedema absent.

Case.	Blood Pressure per cent. of normal.	Oedema prior to blood examination.	N.P.N. mgm.%	Oncotic Pressure. mm.Hg.	Duration of illness prior to blood examination.
39	100	0	25.0	34.6	2 days. ?
30	120	±	20.6	27.1	13 days.
50	110	+	67.4	28.5	14 days.
42	120	±	65.0	28.6	5 days.
16	130	0	34.5	33.8	12 days. ?
84	110	0	49.5	30.9	7 days.
85	110	0 ?	57.7	22.3	13 days.
96	130	±	36.3	32.9	6 days.
88	120	±	50.8	31.2	5 days.
100	120	0 ?	190.0	30.3	7 days.
72	120	0 ?	96.0	32.0	5 days.
51	-	±	28.2	28.2	19 days.

Group two - oedema slight.

In this group are placed those cases in which oedema was confined to puffiness of the face. Blood pressure was always above normal for age and non-protein nitrogen was above normal in 61 per cent. of cases. Gross haematuria was present in all the patients.

Serum oncotic pressure was below the lowest normal reading of 27.8 mm. Hg. in 55 per cent. of cases. 19.6 mm. Hg.

was the lowest level recorded. In 45 per cent. of cases in this group, therefore, oedema occurred with a serum oncotic pressure within normal limits. In every case where serum protein estimations were repeated a return to normal was found to occur save in case 53 where purpura was associated with the nephritis.

The behaviour of the serum proteins during the disease is illustrated in table 16.

TABLE 16.

Case.	Date.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
55	1.1.33	6.37	4.16	2.21	26.1
	5.1.33	6.84	4.45	2.39	27.8
	14.1.33	7.99	4.67	3.32	30.3
	3.2.33	7.02	4.76	2.26	29.5
44	7.7.31	6.77	3.81	2.96	25.1
	10.7.31	6.98	3.87	3.11	25.6
	23.7.31	8.24	4.96	3.28	31.9

Group three - oedema marked.

In the 27 cases of this group, a level of blood pressure of over 110 per cent. of normal was found in 25 patients (93 per cent.). Gross haematuria was present in all the cases save one, and azotaemia existed in fourteen (52 per cent.). Serum albumin and serum oncotic pressure in this group showed a greater degree of reduction than in Group two. The lowest readings were 2.47 gm. per cent. and 17.6 mm. Hg. respectively. In 85 per cent. of cases serum oncotic pressure was below the lower limit of normal. As in Group two a rise in serum albumin to normal levels was the usual finding on subsequent examination of the blood. Two typical examples are given in Table 17.

TABLE 17.

Case.	Date.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.
70	7.9.33	6.69	2.82	3.87	20.9
	26.9.33	6.90	4.23	2.67	27.0
	5.10.33	6.81	4.54	2.27	28.1
82	28.1.31	5.02	3.75	1.27	22.4
	19.3.31	7.73	4.95	2.78	31.1
	1.4.31	7.62	5.01	2.61	31.2

In two patients (81 and 37), however, the return to normal was interrupted by a fall which was rapidly made good. These cases present some additional features of interest.

CASE 81:-

Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Weight (Kg)	Blood pressure per cent. of normal.
30.10.32	8.30	4.04	4.26	28.1	96.7	20.0	166
3.11.32	6.71	4.32	2.39	27.1	51.7	19.1	130
7.11.32	5.79	3.47	2.32	22.3	49.1	18.8	110
11.11.32	7.31	3.87	3.44	26.1	30.5	18.3	110
29.11.32	7.81	6.29	1.52	36.7	25.0	17.1	110

In case 81 it is of interest to note that oedema was present on admission on 30.10 when serum oncotic pressure was 28.1 mm. Hg., i.e., within normal limits, but that on 7.11 in spite of a reduction in oncotic pressure to 22.3 mm. Hg. diuresis continued. It is suggestive that blood pressure had by then fallen to normal.

CASE 37:-

Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Oedema	Blood pressure per cent of normal.
28.1.32	6.38	4.17	2.21	26.0	29.8	+	150
2.2.32	7.99	5.60	2.39	34.1	72.0	∓	-
9.2.32	6.62	4.10	2.52	26.0	58.8	0 ?	110
25.2.32	6.30	4.16	2.14	25.9	45.4	0	90
12.12.32	6.71	4.62	2.09	28.3	20.0	0	100

In case 37 cerebral manifestations were present with much vomiting and it is conceivable that the rise in serum albumin on 2.2.32 may have been due to dehydration. Serum globulin however showed no increase. As in the previous case disappearance of oedema was apparently associated with fall in blood pressure whereas the serum oncotic pressure on 9.2.32 (oedema absent) was the same as on admission.

Group four - oedema very marked.

In 25 of the 30 cases in this group blood pressure was estimated on admission to hospital and in 21 patients (85 per cent.) a level of over 110 per cent. of normal was found. Azotaemia was present in 17 (57 per cent.) of the cases and gross haematuria in 80 per cent.. Fall of oncotic pressure was very frequently present; in 90 per cent. of the cases the level was below the lower limit of normal (27.8 mm.Hg.).

Furthermore in 30 per cent. of the cases serum albumin was below 2.5 grams per cent.. While in these cases the serum oncotic pressure reduction could account entirely for oedema, in the remaining cases of the group such a causal factor was obviously not solely responsible for the dropsy.

The data of this group require more detailed consideration since they are of importance for an understanding of the system of classification which it is proposed to adopt. The next chapter is devoted to a detailed survey of Group Four. Meanwhile the general findings in this chapter are summarized in the following table (18).

TABLE 18.

Summary of the findings in 100 cases.

Oedema.	No. of cases.	Per cent.of cases with calculated oncotic pressure below 27.8 mm.Hg.	Per cent.of cases with Azotaemia.	Per cent. of cases with Hyperpiesis.
0	12	8	58	*64
- +	31	55	61	*100
+	27	85	52	*93
++	30	90	57	*85

* Observations on the blood pressure were unfortunately omitted in some cases and these figures are percentages of the cases in which readings were taken.

Chapter 4.

The classification of cases with very marked oedema.

It is clear from the data of the previous chapter that cases of acute nephritis with marked oedema (Group Four) present features of dissimilar character. In the first place there is a small number in whom the blood pressure is not raised - this sub-group for reasons which will be given has been termed "nephrotic." The remainder, all of whom showed a rise of blood pressure, may be subdivided by the presence or absence of a reduction of serum protein. Those with no reduction have been placed in a sub-group called "hyperpietic." The majority of cases, however, show both a rise in blood pressure and a fall in serum protein and therefore may be termed "mixed type." These patients can be arranged according to degree of reduction of the serum proteins into two sub-groups:- (A) with serum albumin below 2.5 gm. per cent. and (B) with serum albumin between 2.5 and 4.45 gm. per cent. (the lower limit of normal).

NEPHROTIC SUB-GROUP.

The number of patients in this sub-group was four.* The details of the clinical and biochemical findings are given in full since they illustrate many points in the pathogenesis

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* Cases 99 and 181 are also discussed here. The former on admission had only moderate oedema. In the latter no observations were made on the serum proteins till after the development of empyema so that he is not included in the series of 100 patients.

of oedema. Meanwhile the common features may be summarized as marked reduction of serum albumin, gross albuminuria, absence of hyperpiesis and azotaemia and slight or no haematuria.

Case 38 admitted to hospital on 27.12.32, was a girl of 11 years who two weeks before admission developed oedema and cough. Some headache was felt at that time. On admission oedema was general but the child was not acutely ill. There was no fever although a mild degree of bronchitis was found. The heart and fundi presented no abnormality. Blood pressure was 90 per cent. of normal. The Wassermann reaction was negative. The urine contained much albumin, some casts and red blood corpuscles, but the guaiac reaction was negative. Within a week the red cells disappeared and have never been again observed. Blood chemistry on admission on 28.12.32 showed:-

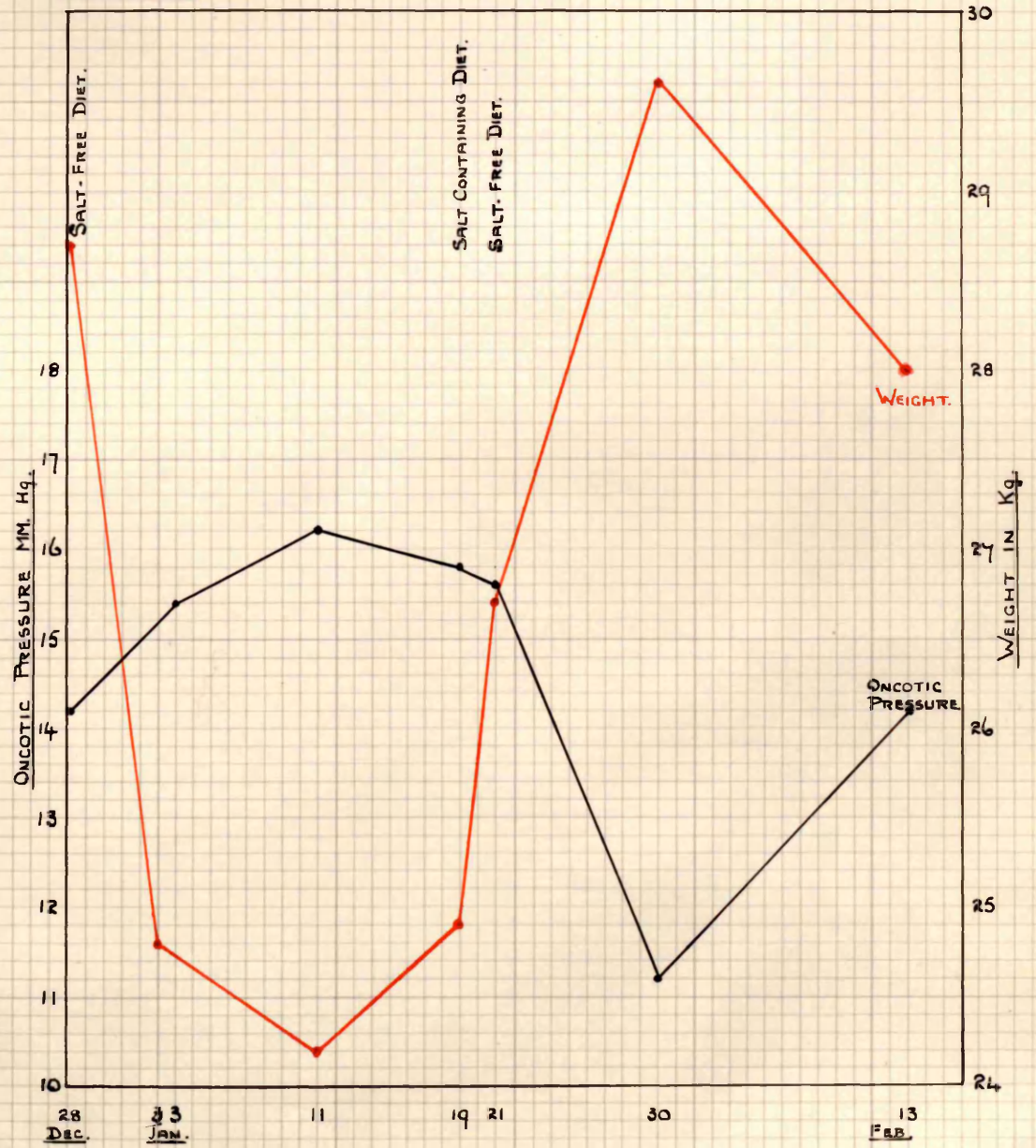
Total Protein.....	5.08	gm.%
Albumin.....	1.71	"
Globulin.....	3.37	"
Calculated Oncotic Pressure..	14.1	mm.Hg..
N.P.N.....	33.3	mgm.%.

Serum albumin was well below oedema level (2.5 gm. per cent.). Renal function as estimated by the urea concentration test on eleven occasions appeared to be good. (For details see Volume 2, p.43). Blood chemistry on 29 occasions during the past 19 months showed that the non-protein nitrogen of the blood was over normal on only one occasion and then but slightly - 44.4 mgm. per cent.. The Congo red test (p.75) for nephrosis was negative. Serum albumin and oncotic pressure have fluctuated but oedema has always been present in some degree save on 15.1.34 and 5.3.34 when oncotic pressure was 23.2 and 23.9 mm. Hg. respectively. At the last observation however on 7.6.34, serum proteins were:- Total protein 7.82, Albumin 5.39 and Globulin 2.43 gm. per cent. - within normal limits. Oedema was absent. Albumin in the urine which had always hitherto been profuse was but a trace. The blood pressure throughout has always been normal. In figure 20 is shown the relationship between oncotic pressure and oedema. The salient feature of this case is the marked fluctuation in oedema. Diuresis occurred shortly after admission and is to be chiefly attributed to the absence of NaCl from the diet although a slight rise in oncotic pressure did occur. It is probable that the rapid re-accumulation of dropsy which followed was brought about by the addition of

Fig.20 .

Relation Between Oedema and Oncotic Pressure.

Case 38.



salt to the diet on 19.1.33 but it will be noticed that the oncotic pressure was tending to fall and the weight to rise prior to this. Continued gain in weight after salt was omitted from the diet on 21.1.33 is attributable to a marked fall in oncotic pressure.

Case 58, a girl aged 9 years, was admitted on 13.3.33 with a history of generalized oedema of a week's duration. No urinary abnormality was detected by the mother. Oedema with ascites was present and the urine contained much albumin and scanty casts but no red blood corpuscles. There was some bronchitis but no fever. No abnormality was detected in the heart or fundi and the blood pressure was 110 per cent. of normal. Blood non-protein nitrogen was 20.0 mgm. per cent. The Wassermann reaction was negative. Because she was in contact with measles this patient was discharged 10 days later. On readmission the condition was unchanged and on 11.4.32 blood chemistry was:-

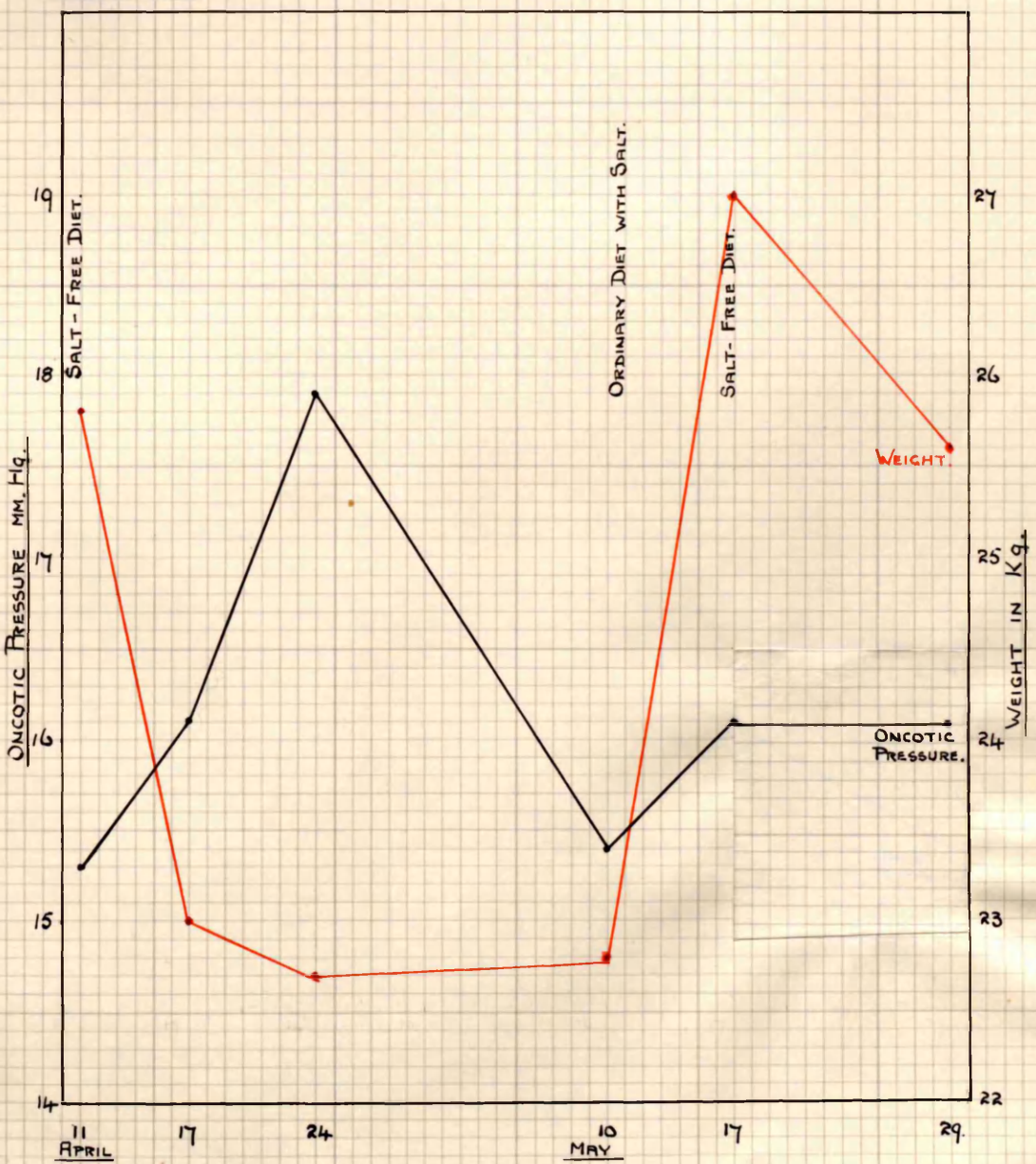
Total Protein.....	4.92	gm.%
Albumin.....	2.06	"
Globulin.....	2.86	"
Calculated Oncotic Pressure..	15.3	mm.Hg..
N.P.N.....	31.3	mgm.%.

Renal function as estimated by the urea concentration test on 3 occasions was good. Blood pressure throughout remained normal and no azotaemia was observed. Throughout the stay in hospital of three months' duration oedema was always well marked but in the out-patient department nine months after the onset of the disease oedema was observed to be much less, this state coinciding with the highest level of oncotic pressure noted - 20.2 mm. Hg.. Figure 21 shows the relationship between oedema and oncotic pressure. Diuresis on admission was due to the "salt-free" diet in association with rise in oncotic pressure from 15.3 to 17.9 mm. Hg. Fall in oncotic pressure to 15.4 mm. Hg. was observed on 10.5.33 without increase in oedema. On the administration of a salt-containing diet on the following day oedema rapidly returned to a marked degree, this in spite of a slight rise in oncotic pressure.

Fig. 21.

Showing Relation Between Oedema and Oncotic Pressure.

Case 58.



Case 4, a boy aged 7 years. He was admitted to hospital on 4.8.33. Two weeks before admission although he seemed to be well, generalized oedema appeared. On admission oedema was well marked and ascites was present. The heart and fundi were normal. The blood pressure was 120 per cent. of normal. Albuminuria was gross and scanty casts and R.B.C. were seen. The Wassermann reaction was negative. The non-protein nitrogen of the blood was 18.0 mgm. per cent. The Congo red test was negative.

In October 1933 and again in May 1934 a fleeting positive reaction with the Guaiac test was obtained for a few days but no change in the clinical condition or rise in blood pressure was observed. Renal function by the urea concentration test was good on 10.8.33 and 12.3.34.

Date.	Before Urea.	One hour after.	Two hours after.
10.8.33	1.24 gm.%	1.75 gm.%	3.32 gm.%
12.3.34	1.51 "	1.97 "	2.82 "

The first observations were made on the serum protein on 29.9.33 and showed:-

Total Protein.....	4.36 gm.%.
Albumin.....	1.92 "
Globulin	2.44 "
Calculated Oncotic Pressure..	13.9 mm.Hg..
N.P.N.....	36.7 mgm.%.

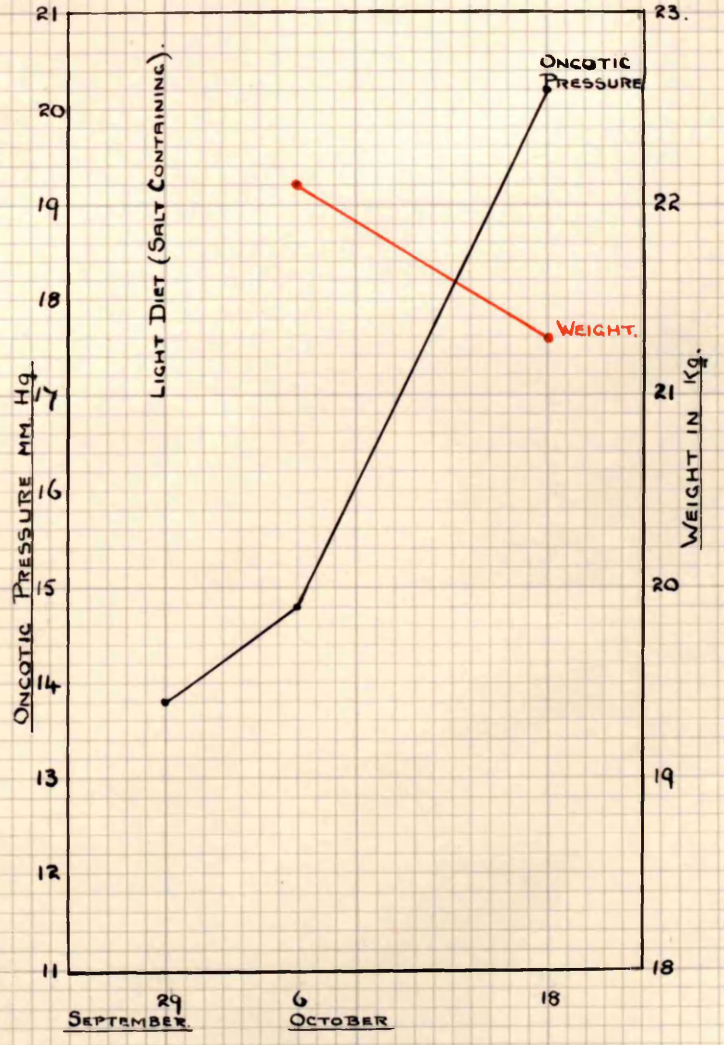
Figure 22 shows a fairly close correlation between serum oncotic pressure and oedema as estimated from fluctuations in the body weight.

Case 98, a girl aged 8 years, developed insidious oedema three months before admission. No abnormality in the urine was noted by the mother. On admission to hospital on 21.8.33 she was seen to be a very small child for her age with generalized oedema and ascites, and although some bronchitis was present she could not be described as acutely ill. The heart and fundi were normal. The urine contained much albumin and some casts and scanty red cells which disappeared in 5 days. The urine culture was sterile. Blood pressure was 120 per cent. of normal. The urea concentrating power of the kidney was apparently rather poor.

Fig. 22 .

To Show Relation Between Oncotic Pressure and Oedema.

Case 4.



	Urea grams per cent.
Before urea.....	1.96
1 hour after.....	2.19
2 hours after.....	2.39

Blood chemistry on 3.9.33 gave the following results:-

Total Protein.....	5.36	gm.%
Albumin.....	2.12	"
Globulin.....	3.24	"
Calculated Oncotic Pressure..	16.1	mm.Hg..
N.P.N.....	40.9	mgm.%.

One month after admission red blood corpuscles were again observed in the urine for 5 days. On 18.10.33 after a period of fever, b. paratyphosus B was isolated from the stool and the child was transferred to an isolation hospital. This infection was contracted from a patient in the ward and was mild in character. After dismissal from the fever hospital she was readmitted to R.H.S.C. still with oedema; the serum oncotic pressure was 19.8 mm.Hg. The condition of the urine and blood pressure was unchanged. No azotaemia was observed throughout the illness, the values for non-protein nitrogen varying from 40.9 mgm. per cent. on admission to 23.6 mgm. per cent. on 18.4.34. Figure 23 shows well the inverse relationship between oncotic pressure and oedema. The gain in weight of 3.0 Kg. on readmission was due at least in part to tissue building since oedema seemed less marked. The urea concentration test, poor on the first admission, was now good.

Case 99, a boy aged 7 years, was admitted to hospital with a history of oedema of seven months' duration. At the onset of the illness the urine was said to have been dark in colour.

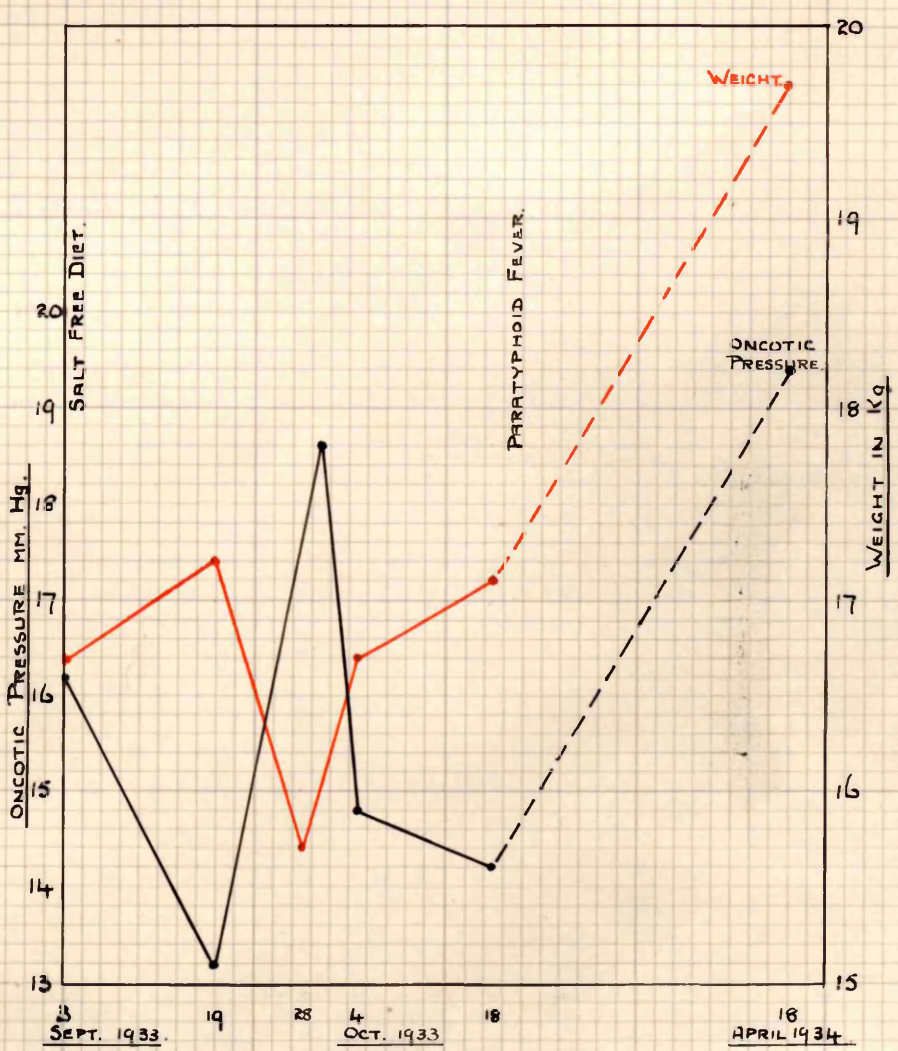
On admission on 10.3.34 oedema of the face and legs was present but no signs of ascites were detected. The heart, fundi and blood pressure showed no abnormality. The Wassermann reaction was negative. The urine showed much albumin, very scanty casts and no blood. Blood chemistry:-

Total Protein.....	6.86	gm.%
Albumin.....	2.47	"
Globulin.....	4.39	"
Calculated Oncotic pressure..	19.7	mm.Hg.
N.P.N.....	27.2	mgm.%.

Fig.23.

Relation Between Oedema and Oncotic Pressure.

Case 98.



The serum albumin was considerably reduced but in spite of the fact that globulin was markedly above normal, the serum oncotic pressure was just below the oedema level. Subsequently however (figure 24) serum oncotic pressure became further reduced and oedema became more marked.

A urea concentration test on 19.1.34 gave a good result and no azotaemia has been observed on six occasions over a period of three months. The Congo red test for nephrosis in this child was positive. Since admission to hospital oedema has always been present and serum oncotic pressure always below the oedema level.

Case 181, a boy aged 7 years, was admitted to hospital on 25.1.34. Three months before, on the eleventh day of an attack of scarlet fever, albuminuria was noted which lasted nine days. The doctor in charge states that neither oedema nor haematuria occurred during his stay in the fever hospital. For 14 days before dismissal the urine was clear of albumin. Six days after dismissal oedema appeared, but no other evidence of renal disease was manifest. On admission there was oedema of the face and shins. The heart, fundi and blood pressure showed no abnormality. The non-protein nitrogen of the blood was 22.5 mgm. per cent. The urine contained much albumin but no blood. The urea concentration test gave a good result. The Congo red test for nephrosis was positive in this child. Within a few days oedema became massive with marked ascites and three weeks after admission empyema developed. Following rib resection on 14.3.34 oedema disappeared although there was still much albumin in the urine. The non-protein nitrogen of the blood was 22.3 mgm. per cent. on 8.5.34 and the blood pressure was 100 per cent. of normal for the age. The serum proteins were:-

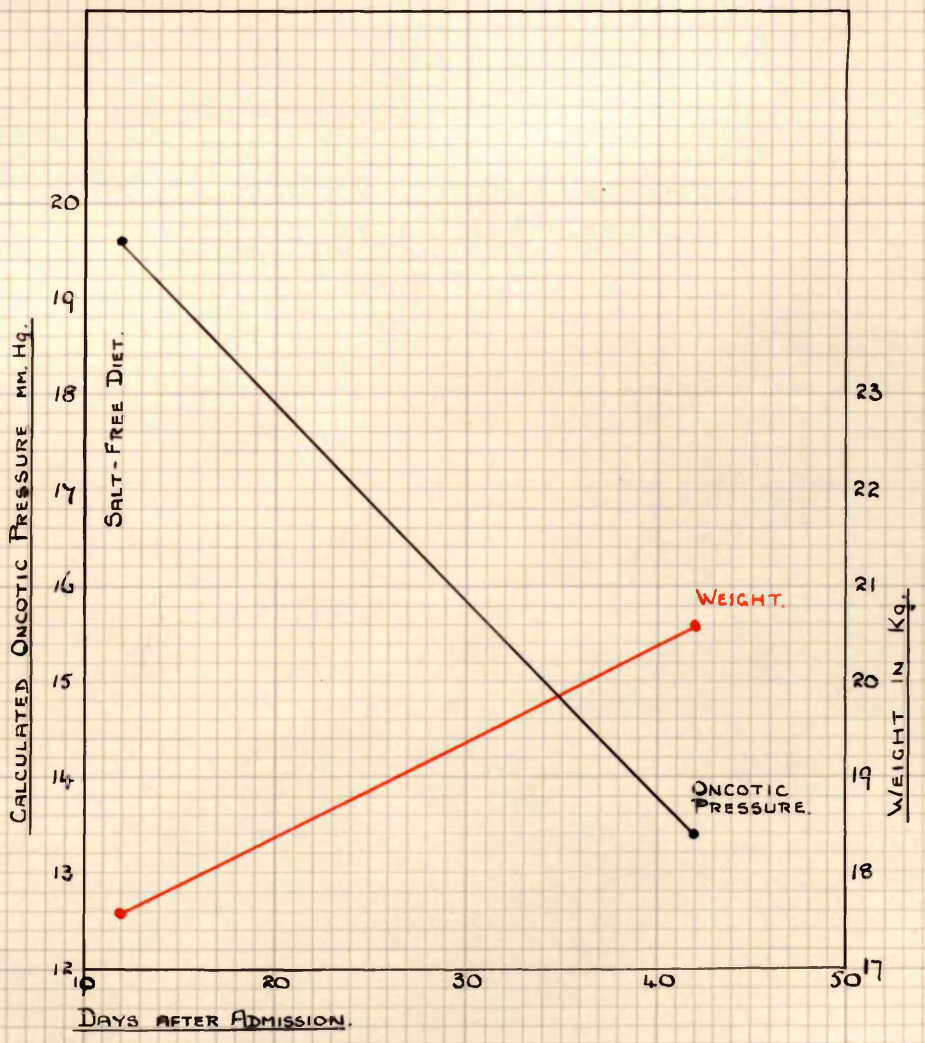
Total Protein.....	7.97	gm.%
Albumin.....	2.17	"
Globulin.....	5.80	"
Calculated Oncotic Pressure..	20.2	mm.Hg..

It is obvious that despite the absence of oedema there was still a marked reduction in serum albumin: the rise in globulin lessened the fall in oncotic pressure. Unfortunately the serum proteins were not estimated prior to operation but it seems likely that the rise in globulin occurring subsequent to the development of empyema led to the disappearance of oedema.

Fig. 24.

The Relation Between Oedema and Oncotic Pressure.

Case 99.



Summary.

In the group of cases classed as nephrotic the following features were noted in common. The onset of the disease was not attended by vomiting or any great degree of lassitude or even in several instances by loss of appetite. In no case was there evidence of gross haematuria. In three of the patients the urine was not tested till several months after the appearance of oedema but there was no history of any abnormality in the colour of the urine. In three cases no haematuria, even microscopic, was observed so that a diagnosis of true nephrosis would seem to be applicable (table 19). It must be remembered, however, that

TABLE 19.

Admission findings on nephrotic cases.

Case	Duration before admission	Haematuria		N.P.N. mgm.%.	Renal function. Urea Concentration Test.	Blood pressure per cent. of normal.
		Macroscopic	Microscopic			
4	18 days	0	+	18.0	good	120
38	2 weeks	0	+	33.3	good	90
58	1 week	0	0	20.0	good	110
98	3 months	0	+	40.9	fair	120
99	7 months	0 ?	0	27.2	good	120
181	6 months	0	0	22.5	good	110

these patients were not seen from the beginning of the illness. Furthermore it is to be noted that in the other three cases haematuria was by no means a constant feature, only occurring for a few days at a time. Apart from the evanescent appearance of blood in small amounts the clinical and biochemical findings of the six cases were similar. Accordingly the diagnosis of nephrosis cannot be entertained because of the occurrence of haematuria. Recently Ellis[1] described a type of acute nephritis - nephrotic nephritis - in which the first and often the only symptom was oedema. Haematuria was slight or absent, albuminuria was severe and hypertension and azotaemia not usually present. Hypo-albuminaemia was marked. The cases summarized in table 19 appear to comply with the type of case described by Ellis. In this series of patients azotaemia was not present and in no case was a rise in the non-protein nitrogen of the blood found at subsequent examination. Kidney function was on the whole normal. Blood pressure was but little above normal and might be attributed to emotion in a child newly admitted to hospital. In all the patients subsequent readings were constantly within normal limits. The heart and fundi in all cases showed no abnormality. The long duration of the oedema is a prominent feature of this sub-group. It is necessary to emphasize that oedema in every case in this group was always associated with a serum oncotic pressure below a level of 20.0

mm. Hg.. No close correlation between serum albumin and oedema was detected owing to the fact that considerable elevation of serum globulin not infrequently compensated for the albumin deficit but fluctuations in oedema were closely related to fluctuations in oncotic pressure.

According to Epstein[2] there exists a condition which he termed chronic nephrosis which is characterized by an insidious onset of oedema and proteinuria without cardiovascular changes, haematuria or impairment of renal function. Epstein[2] states that oedema is associated with a marked reduction of serum albumin and that the condition is not due to a defect in the kidney but to an upset of metabolism. (p.198). It is now recognised however that a picture clinically and biochemically indistinguishable from this can develop in the course of glomerulo-nephritis. (Leiter,[3] Peters[4] et alii). Shaw Dunn,[5] Christian,[6] Bannick,[7] Bell[8] and others indeed, believe that glomerulo-nephritis is always an antecedent factor in nephrosis and that unless intercurrent infection proves fatal, the cause of death is a progressive nephritis of interstitial type.

In the present series a previous attack of nephritis can almost certainly be ruled out; if these patients were suffering from glomerular nephritis its manifestations were certainly not those usually observed in that disease. No loss of renal function, rise of non-protein nitrogen or of blood pressure has been observed, but the duration of the

period of observation has been too short to determine whether progressive renal impairment will take place. At present two of the cases are much improved and no deaths have occurred. Recently Matthew[9] and Cameron by intravenous injection of congo red found that in nephrosis (2 cases) the dye appeared in the urine whereas in chronic parenchymatous nephritis (1 case) this did not occur. This, if confirmed, would seem to be an important diagnostic test. In four of the nephrotic cases in this series the test was made and dye was recovered from the urine in two cases (99 and 181). It is interesting to note that in these patients haematuria has never been detected in hospital. In conclusion it may be said that except for slight haematuria there was no essential difference between the cases which excreted congo red and those which did not. In three normal cases, six of acute nephritis with gross haematuria and one with diphtheritic myocarditis and oedema the dye did not appear in the urine.

THE HYPERPIETIC SUB-GROUP.

Three (10 per cent.) of the patients suffering from acute nephritis with marked oedema showed, in complete contrast to the nephrotic type of case, normal serum albumin and oncotic pressure. The following case histories demonstrate the characteristic features and course of this type of nephritis.

Case 77, a girl aged 7 years. Six days before admission she was out of sorts and 4 days later developed headache, began to vomit and showed oedema of the face. The urine was scanty and dark in colour. On admission the urine contained blood, albumin and casts. The patient was not acutely ill although signs of bronchitis were present. Oedema was general with ascites. The heart and fundi showed no abnormality.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure mm.Hg.	N.P.N. mgm.%.	Oedema	Blood Pressure per cent. normal.	Weight in Kilos.
17.12.33	7.65	5.19	2.46	31.9	52.0	++	188	20.9
23.12.33	-	-	-	-	-	0	120	17.9
30.12.33	-	-	-	-	25.0	0	110	17.0

Case 5, a boy aged 7 years. Five days before admission on 15.12.33 he developed oedema of the face: four days later the legs became oedematous and the urine was noted to be dark in colour. On admission oedema was general with ascites. The heart and fundi were normal. The urine contained blood, albumin and numerous casts.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Oedema	Blood Pressure per cent normal.	Weight in Kilos.
15.12.33	7.38	5.00	2.38	30.9	35.5	++	185	23.6
17.12.33	-	-	-	-	-	++	140	22.8
18.12.33	7.69	5.52	2.17	33.4	45.4	+	170	22.0
20.12.33	-	-	-	-	-	±	130	20.9

Case 65, a boy aged 5 years. Three days before admission he went off his food, complained of thirst and became swollen about the face. Next day the legs were swollen. On admission anasarca and ascites were marked. The heart and lungs showed no abnormality: fundi normal.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Blood pressure per cent. of normal.
27.12.33	6.98	4.45	2.53	28.0	120.0	190

Systematic records of blood pressure were not made in this case but no oedema was detectable 10 days after admission at which time the blood pressure was normal.

Summary.

The features of these cases are (1) the presence of marked oedema with normal serum oncotic pressure. (2) The disappearance of oedema concurrently with fall in blood pressure. (3) Rapid and apparently complete recovery in two cases (in the third (case 65) albuminuria has persisted but otherwise the child seems well.)

THE MIXED TYPE SUB-GROUP.

In the large majority of cases (77 per cent.) of acute nephritis with very marked oedema there is an association of rise of blood pressure and fall in serum oncotic pressure. Since the degree of fall in serum oncotic pressure has appar-

ently an influence upon the course and prognosis of the disease, a subdivision is made into mixed type A and mixed type B. In the former the serum albumin is at or below 2.5 gm. per cent. while in the latter the reduction is not so marked. The majority of the cases of the mixed type fall into the B category: only four present the characteristics of A as defined. These four cases show many features of considerable interest and are discussed in detail.

CATEGORY A.

Case 48, a girl aged 6 years. She was well till two days before admission when generalized oedema appeared. The urine was scanty in amount and red in colour. Though no definite complaint was made the child seemed ill. On admission to hospital on 15.6.33 she was sharply ill. The throat was very much inflamed and anasarca with ascites was present. The heart and fundi presented no abnormality. The blood pressure was 140 per cent. of normal. The urine contained much albumin and blood with many casts. The course of events is shown in table 20.

TABLE 20.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Oedema	Blood Pressure % Normal	Haematuria.
16.6.33	4.27	1.66	2.61	74.6	12.7	++	140	++
24.6.33	8.25	2.86	5.39	30.9	23.3	0	-	-+
13.7.33	8.26	5.92	2.34	28.3	35.8	0	130	-+
2.9.33	5.97	2.00	3.97	65.2	15.5	++	140	++
13.9.33	3.87	1.49	2.38	40.5	11.5	++	130	++
27.9.33	3.39	1.57	1.82	27.0	11.4	++	148	++
3.10.33	5.25	1.56	3.69	47.6	13.7	++	140	++
18.11.33	4.24	1.30	2.94	33.1	11.8	++	-	++
1.12.33	7.49	1.73	5.76	76.0	17.6	++	-	++

Renal function in this child would seem to have been poor but only two tests were made owing to the difficulty in persuading the patient to take urea.

UREA CONCENTRATION TESTS.

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
16.6.33	3.83	3.83	3.45
3.10.33	1.57	-	2.18

On 13.7.33 the child appeared to be progressing well although the blood pressure was still above normal and red blood cells were still present in the urine. But on 29.7.33 oedema reappeared for a few days and on 2.9.33 serum albumin, which had returned to normal, again showed a marked fall coincident with reappearance of very marked oedema. The blood in the urine again became gross in quantity and the non-protein nitrogen of the blood rose above normal level. Apart from fluctuation in non-protein nitrogen this state remained unchanged till death on 1.12.33. Drowsiness and marked abdominal distension and fever were present and it is possible that death was due to peritonitis or to uraemia. Permission for autopsy was refused.

Case 49, a boy aged 8 years. A month before admission he attended as an outpatient with pains in the knees and a purpuric rash on limbs, trunk and scrotum. There was no bleeding from mucous membranes and the spleen was not palpable. The capillary resistance test was negative. The urine at that time contained neither albumin nor blood and all symptoms disappeared in 18 days. Five days before admission he "felt cold." Next day oedema of the face and legs appeared, and the urine became scanty and contained blood. He was admitted to hospital on 24.4.33 with generalized oedema and ascites. No abnormality was detected in the heart or fundi and there was no purpura. The spleen was not palpable. The urine contained much albumin, blood, and many casts. Throughout the course of this case azotaemia was a marked feature and serum oncotic pressure was below oedema level, dropsy

being present throughout. Haematuria was never absent and blood pressure was raised. The biochemical findings are given in table 21.

TABLE 21.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % normal	Weight in Kilos.	Oedema.
25.4.33	6.25	2.51	3.74	50.0	19.0	130	23.8	++
28.4.33	6.07	2.28	3.79	77.9	17.8	110	24.5	++
2.5.33	6.01	2.06	3.95	88.2	16.9	120	24.2	++
6.5.33	Intussusception. Operation.				-	-	-	-
12.5.33	4.44	2.14	2.30	76.0	14.9	-	-	++
8.6.33	6.98	2.25	4.73	72.2	18.9	120	23.5	++
14.6.33	5.09	2.25	2.84	85.0	16.4	130	25.8	++
29.6.33	5.84	2.54	3.30	69.0	18.6	150	26.5	++
11.7.33	5.06	2.19	2.87	90.0	16.0	145	28.2	++
20.7.33	5.26	2.65	2.61	133.3	18.2	140	28.2	++

Renal Function. The urea concentration test, performed on one occasion only (8.6.33) gave a poor result.

Before urea.	1 hour after.	2 hours after.
1.08 gm.%	1.33 gm.%	1.75 gm.%

It can be seen from from the table that changes in oedema in this case did not show the correlation to variations in serum oncotic pressure as was found in the nephrotic sub-group. This would suggest in view of the

history of purpura that capillary damage might have played a part in the pathogenesis of oedema. On physical examination however there was no evidence of this. The ascitic fluid obtained at operation yielded the following figures on analysis.

Total Protein.	Albumin.	Globulin.
0.9% gm. %.	0.61 gm.%	0.37 gm. %.

It seems more probable that increase of oedema on 29th June in spite of rise in oncotic pressure was associated with increase in the level of the blood pressure on that date. This point is dealt with more fully in chapter 5.

During the course of the nephritis an enteric intussusception developed and a foot of gangrenous bowel was successfully removed. No effect on the nephritis was apparent save some temporary loss of oedema due presumably to drainage of fluid through the incision. Death occurred after an illness of three months' duration. The last few days of the illness were marked by drowsiness, air-hunger and convulsions. Abdominal paracentesis showed that there was no infection of the ascitic fluid. Permission for autopsy was refused.

Case 29, a boy aged 10 years. Ten days before admission became listless and began to vomit. Four days later his mother noted that the urine was scanty in amount and dark in colour and oedema of the face appeared. On the day before admission he was drowsy and some twitching of the limbs was seen.

7.9.33. On admission oedema was generalized with ascites. There was no fever but the throat was inflamed. He was

drowsy but quite conscious when aroused. Cardiac dulness was within normal limits: a basal V.S. murmur was audible. The fundi showed no abnormality. In the urine there was much albumin and blood and many casts. The blood pressure was 148 per cent. of normal for the age. In the course of 6 days, vomiting ceased and blood pressure fell to 132 per cent. of normal but it was observed that non-protein nitrogen which was 280.0 mgm. per cent. on 8.9.33 was still 222.0 mgm. per cent. (13.9.33). On 16.9.33 vomiting recurred, he became very drowsy and cyanosed and blood pressure rose again to 164 per cent. of normal. No enlargement of cardiac dulness was observed. Oedema which had been steadily diminishing was less marked than it had been since admission (the weight confirms this (Table 22). By venipuncture 100 c.c. of blood were withdrawn and by lumbar puncture 25 c.c. of clear cerebrospinal fluid. Blood CO_2 was 56.8 vols. per cent. - within normal limits. It is interesting to observe that non-protein nitrogen had again fallen, being now 133.0 mgm. per cent. in spite of the increase in the severity of the uraemic manifestations. Rapid improvement in the clinical condition followed the removal of blood and spinal fluid. One month (4.10.33) later serum albumin, which had been rising steadily from 2.39 gm. per cent. on admission, showed a slight fall from the level observed on the previous observation (28.9.33) and blood pressure was still slightly raised. Six months after the onset of the illness (19.3.34) however serum albumin, oncotic pressure, non-protein nitrogen and blood pressure were all within normal limits and the urine contained merely a trace of albumin. The urea concentration test however remained poor. The blood chemistry findings are given in table 22.

TABLE 22.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % normal	Oedema	Weight in Kilos.
8.9.33	7.62	2.39	5.23	280.0	20.5	148	++	26.8
13.9.33	7.52	3.44	4.08	222.0	24.6	132	++	25.6
16.9.33	7.61	3.69	3.92	133.0	25.8	164	+	24.0
28.9.33	6.27	3.96	2.31	30.4	25.0	146	±	22.0
4.10.33	7.36	3.57	3.79	23.0	24.9	120	0	21.1
19.3.34	8.31	5.39	2.92	20.0	33.7	110	0	-

Urea Concentration Tests.

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
13.11.33	0.66	1.63	2.50
23.3.34	1.63	1.93	1.95

Case 62, a boy aged 4 years. About two weeks before admission he developed oedema which gradually became more marked. No abnormality in the urine was observed by the parents. On admission to hospital on 20.4.34 there were generalized oedema and ascites. The heart and fundi were normal. Much albumin was present in the urine and sufficient blood to give a positive guaiac reaction for the first two days. Since then red blood corpuscles were scanty and the guaiac test negative till 31.5.34 when macroscopic haematuria reappeared. This was still present on dismissal on 25.6.34. The systolic blood pressure was 150 per cent. of normal. In table 23 are given the blood chemistry findings.

TABLE 23.

Date.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Weight in Kilos.	Blood Pressure % of normal.
21.4.34	3.96	2.03	1.93	45.7	13.8	18.7	150
24.4.34	5.97	1.94	4.03	19.0	16.3	18.2	-
23.5.34	4.01	2.22	1.79	53.6	14.6	19.2	140
6.6.34	5.70	1.19	4.51	60.1	12.8	20.9	-

The urea concentration test on 23.4.34 was poor.

Before urea..... 1.24 gm.%
1 hour after..... 1.40 "
2 hours after..... 2.02 "

This patient was removed from hospital by his parents on 25.6.34 The general condition was unchanged.

The characteristic features of Category A of the mixed type may be summarized as follows:-

(1) Persistent low oncotic pressure of the serum.

(2) Persistent elevation of blood pressure.

(3) Persistent azotaemia.

(4) Persistent haematuria.

(5) Poor urea concentrating power.

(6) Grave prognosis.

Of the four cases, two are already dead, one is still gravely ill, and one, although dismissed from hospital, has marked impairment of renal function.

CATEGORY B.

The remaining 63 per cent. of cases with massive oedema fall into this category. The characteristics are illustrated in tables 24a and 24b. The changes in blood pressure and biochemistry throughout the illness are indicated by the findings in 5 cases reported more fully in table 24b.

TABLE 24a.

Case	Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of normal.	Oedema
76	10.10.33	6.58	2.72	3.86	34.8	20.4	150	++
66	14.7.33	6.46	3.11	3.35	17.0	21.8	164	++
33	1.6.31	6.03	3.36	2.67	24.8	22.2	170	++
56	17.3.32	6.31	2.91	3.40	39.6	20.9	158	++
46	21.6.31	5.95	3.48	2.47	23.4	22.5	-	++
69	1.5.31	5.40	2.78	2.62	43.1	18.9	-	++
75	11.10.33	6.84	4.07	2.77	44.7	26.2	150	++
1	7.9.33	6.64	3.54	3.10	36.3	23.8	145	++
9	28.5.32	4.44	3.01	1.43	20.7	18.5	-	++
24	31.3.33	8.52	3.79	4.73	136.0	27.6	-	++
15	15.1.31	6.02	3.71	2.31	56.1	23.5	205	++
71	21.3.32	6.34	2.45	3.89	35.3	18.9	130	++
12	30.1.31	5.60	3.60	2.00	40.0	22.6	-	++
37	19.2.34	6.57	3.29	3.28	49.0	23.7	140	++

TABLE 24b.

Case	Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of normal.	Oedema
27	3.5.31	4.61	2.81	1.80	18.2	18.2	130	++
	3.6.31	8.17	5.05	3.12	27.2	32.1	100	0
13	14.3.34	6.71	3.54	3.17	35.7	23.9	190	++
	16.3.34	6.37	3.58	2.79	31.0	23.6	180	+
	19.3.34	8.01	4.16	3.85	30.4	28.3	140	±
	23.3.34	8.01	4.59	3.42	31.7	30.0	120	0
25	12.12.33	6.17	4.19	1.98	48.7	25.8	148	++
	15.12.33	8.71	5.60	3.10	32.2	36.0	150	+
	18.12.33	8.56	3.57	4.99	32.4	26.6	90	0
	27.12.33	6.87	4.72	2.15	34.4	28.9	90	0
93	27.3.34	5.86	3.07	2.79	89.2	20.8	144	++
	3.4.34	7.84	4.97	2.87	21.5	31.3	110	0
8	15.5.31	5.79	3.18	2.61	47.7	21.4	145	++
	23.5.31	7.68	5.23	2.45	45.5	32.1	-	0

The features of Category B are as follows:-

(1) Serum albumin although always reduced was only once below 2.5 gm. per cent. In all cases its return to normal was rapid.

(2) Azotaemia, present in 57 per cent. of the cases, was as a rule not marked and was always a fleeting manifestation.

(3) Elevation of blood pressure and haematuria were only observed in the first few days of the illness.

(4) Urea concentrating power, poor as a rule in the acute phase, generally soon returned to normal.

(5) The prognosis was good. One death occurred, in Case 15. Here death was ascribed to pulmonary oedema developing during uraemia at the onset of the illness. None of the other cases showed more than a trace of albumin in the urine on dismissal.

The following schema, elaborated in table 25, indicates the classification which has been adopted in the cases of nephritis with very marked oedema.

It is obvious that in this classification cases with little or no oedema will fall into the mixed type B category or the hyperpietic group.

Normal blood pressure - nephrotic.

Raised blood pressure.

- Normal serum albumin - hyperpietic.
- Reduced serum albumin - mixed type.
  - Albumin < 2.5 gm.%. CATEGORY A.
  - Albumin > 2.5 gm.%. CATEGORY B.

TABLE 25.

Type.	Per cent of cases	Serum Albumin.	Non-protein Nitrogen.	Haematuria.	Urea Concentration test.	Blood Pressure	Oedema.	Prognosis.
Nephrotic	13.3	Below 2.5 gm.%	Normal throughout	Never macroscopic.	Good throughout	Normal throughout	Associated with fall in oncotic pressure below oedema level. Persistent.	Long slow course.
Hyperpietic.	10.0	Normal.	Raised. It rapidly falls to normal.	Present at first	Poor early ?	Raised early.	Associated with hyperpiesis. Disappears rapidly.	Good.
Mixed type CATEGORY A	13.3	Below 2.5 gm.%	Usually raised throughout or for a longer period.	Present and persisting.	Poor throughout	Raised throughout	Associated with fall in oncotic pressure below oedema level and hyperpiesis. Tends to be prolonged.	Fatal issue in 3 to 6 months in 2 cases out of 4.
Mixed type CATEGORY B	63.3	2.5-4.45 gm.% Only once below 2.5 gm.%. Rapid return to normal.	May be raised or normal. If raised rapidly falls to normal.	Present at first	Usually poor early.	Raised early.	Associated with fall in oncotic pressure and hyperpiesis. Short duration.	Good.

Chapter 5.

The reciprocal rôle of hyperpiesis and reduction of oncotic pressure in the pathogenesis of oedema.

According to Starling's[1] hypothesis oedema may be produced by fall in serum oncotic pressure or by increase of capillary pressure. This view has been largely accepted as far as the oedema of nephrosis or chronic glomerulo-nephritis is concerned. In acute nephritis however fall in serum oncotic pressure below oedema level is the exception rather than the rule and many workers depart from Starling's[1] theory and invoke other factors to explain oedema. Some of these views have already been discussed and some arguments against their adoption advanced. In this chapter will be submitted evidence to show that the dropsy of acute nephritis can also be explained on the basis of Starling's[1] hypothesis.

It has already been demonstrated that neither reduction of serum albumin nor rise in blood pressure will separately explain the production of oedema in every case of acute nephritis. In the present series of 100 cases, only 10 showed a reduction of serum albumin below 2.5 gm. per cent.. These figures correspond to the findings of van Slyke[2] and his co-workers who report a similar group of 30 per cent. in 23 cases. In their series all but three patients had hypertension and in two of these the blood pressure was not estimated until oedema had disappeared. Moore[3] and van Slyke

found no direct relation between blood pressure and serum protein except that a very high blood pressure was not present when the serum albumin was less than 60 per cent. of normal. In the present series while the blood pressure was not raised in the nephrotic group, moderate hyperpiesis was present in Mixed Type, Category A, in which the serum albumin was less than 2.5 gm. per cent..

It may be objected at the onset that dropsy is a rare occurrence in uncomplicated hyperpiesia. It seems reasonable, however, to assume that while the gradual rise of blood pressure is unable to overcome the elastic resistance of the tissues, the sudden rise of blood pressure in acute nephritis does overcome tissue resistance and produce oedema. It is probable that not the height of the blood pressure, but the rapidity with which the height is reached is the determining factor.*

A further objection is that of Mufson[4] who stated that the blood pressure is not a measure of the capillary pressure and gave figures to show that there is no mathematical relation between them. He measured capillary pressure in five cases of acute nephritis and found it to be high. Oedema however was only present when serum total proteins were

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* Increase in hydrostatic pressure due to circulatory failure has already been considered (p. 35). It was there concluded that in only 2 per cent. of cases could the production of oedema in acute nephritis be contributed to by that factor.

low. It is of interest to note that oedema was not present in Mufson's[4] cases where the systolic blood pressure was below 140 mm. Hg.. Measurement of capillary pressure has not been undertaken in this work since at best it is a difficult procedure especially in children in whom the results are of very doubtful value.

Observations on blood pressure have been made at the same time as blood was taken for estimation of the serum proteins. In figure 25 are charted the findings for systolic blood pressure, (as a percentage of the normal for the age), oncotic pressure of the serum and degree of oedema. From these results the following two points emerge:-

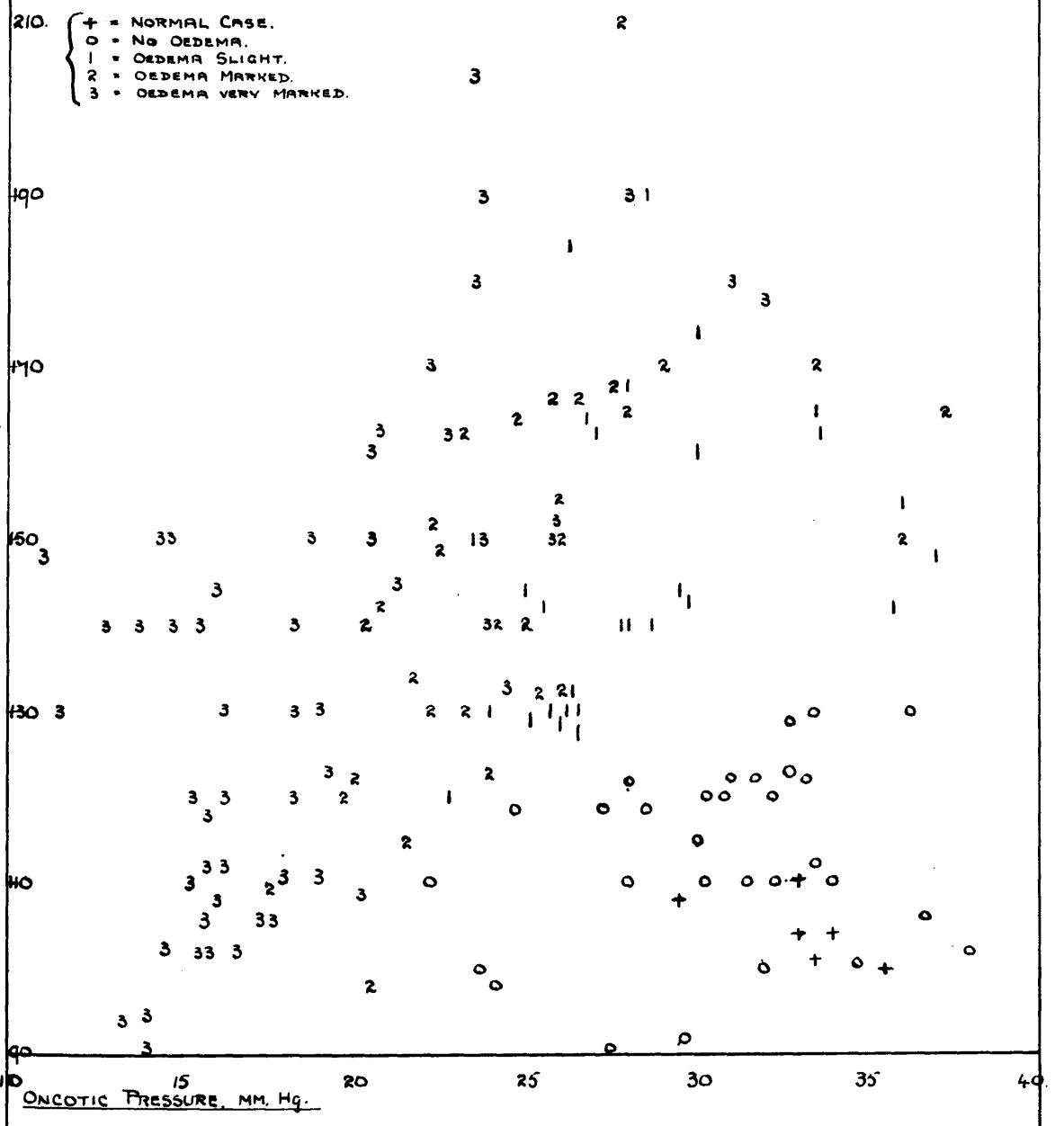
(1) When blood pressure was normal oedema was not found when serum oncotic pressure was 21.0 mm.Hg. or above.

(2) With normal serum oncotic pressure - 27.8 mm. Hg. being the lower limit - oedema did not occur with blood pressure under 138 per cent. of normal.

The hypothesis which has just been submitted would explain the presence of oedema. It is thus evident that a moderate fall in oncotic pressure together with a moderate rise in blood pressure promote marked oedema, whereas a fall of oncotic pressure of the same magnitude would not alone produce oedema. It is intelligible also how in some patients with acute nephritis oedema is a marked feature during the stage of hypertension irrespective of the level of serum oncotic pressure. It is interesting to note that van Slyke[2]

Fig.25.

The Relationship of Serum Oncotic Pressure to Degree of Oedema in Acute Nephritis.



quotes two cases of acute nephritis aged 3 and 29 years with oedema and normal serum proteins. The systolic blood pressure was 130 and 150 mm. Hg. respectively, the former reading being about 180 per cent. of normal for the age.

These results would appear to justify the contention that the oedema of acute nephritis in children can be explained as the resultant of the forces produced by changes in serum oncotic pressure and blood pressure.

Chapter 6.

The rôle of sodium chloride in the pathogenesis of oedema.

While changes in hydrostatic and oncotic pressure play the main part in the production of oedema, there is no doubt that administration of NaCl is attended by the appearance or increase of oedema in many cases of nephritis. In illustration of this point the following cases are quoted.

Case 58. This child was admitted to hospital with very marked oedema which on a diet of milk very rapidly diminished but did not entirely disappear. Four weeks after admission to hospital a salt-containing diet was permitted and in 6 days, the child gaining 4.2 Kg. in weight, oedema again became massive. Figure 26 shows that the oncotic pressure of the serum fell slightly before the aggravation of oedema and rose very slightly during its accumulation.

Case 38. In figure 27 a similar association existed between the administration of salt in the diet and increase in oedema. A fall in oncotic pressure took place during the increase of oedema.

From these cases one concludes that the administration of salt to a nephritic patient, whose oncotic pressure is very low, results in an aggravation of oedema.

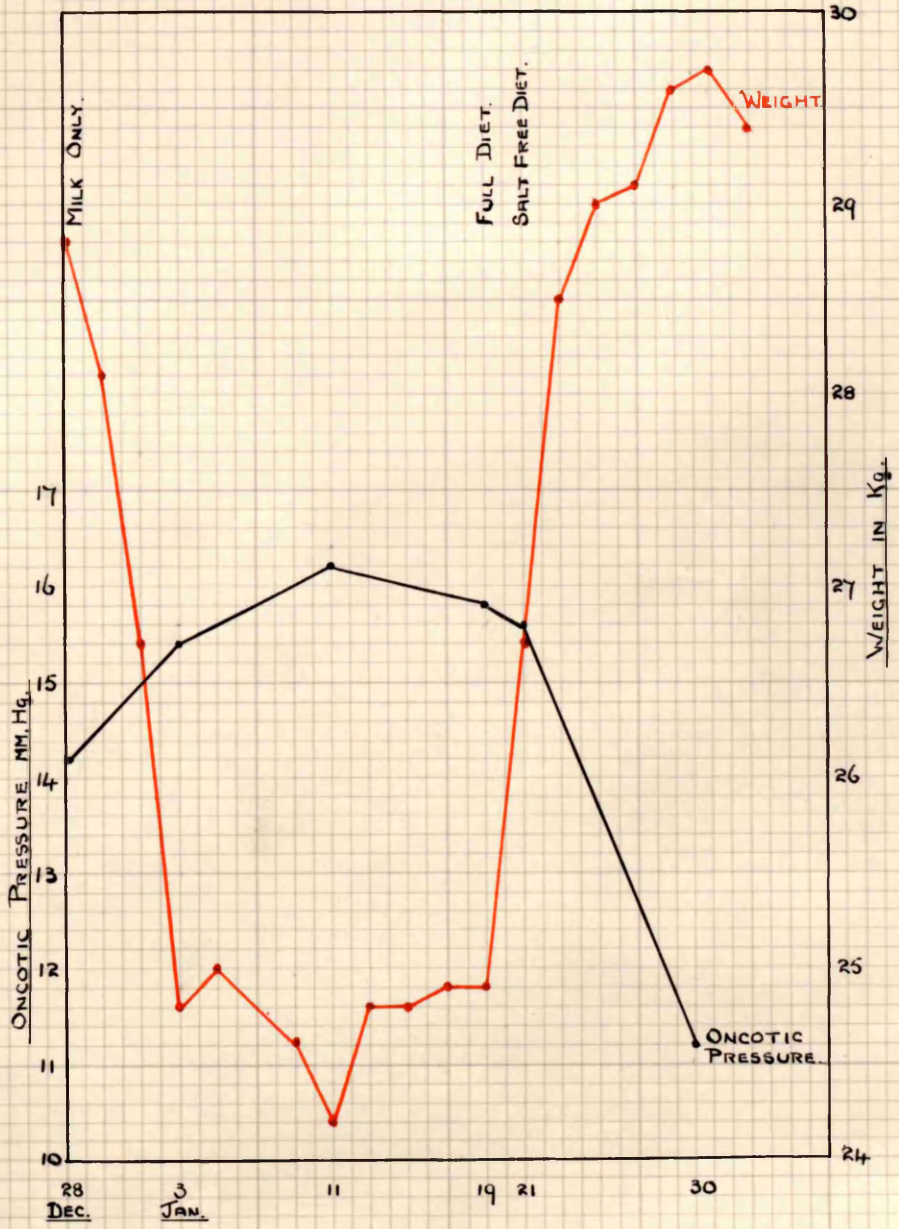
The results of salt administration to cases where serum oncotic pressure and blood pressure are normal, or the former but slightly reduced, are quite different as is clear from the following cases.

Case 37. This child had acute nephritis complicated by uraemia, marked oedema being present. The blood pressure was elevated and serum oncotic pressure was slightly below normal (figure 28). On the 13th day after admission a full diet

Fig. 27.

Increase of Oedema on the Addition of Sodium Chloride to the Diet.

Case 38.



The Failure of Salt to Produce Oedema in Cases where Oncotic Pressure is Normal or Only Slightly Reduced.

Fig. 28.

Case 37.

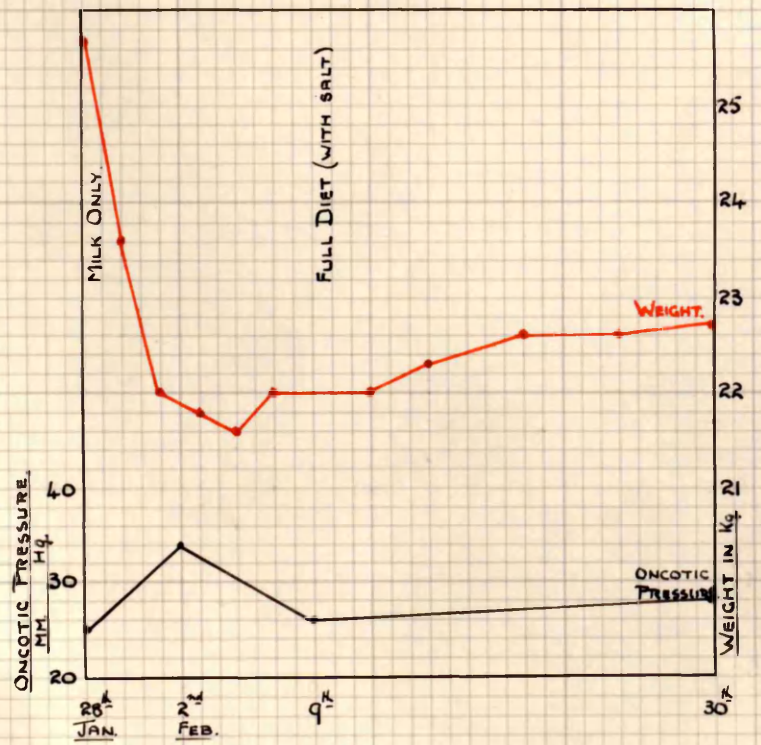
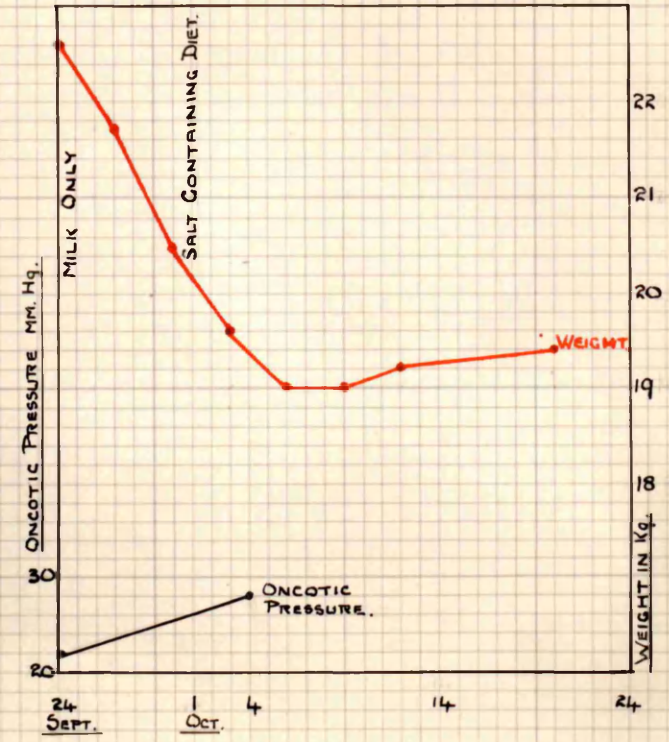


Fig.29.

Case 73.



(with salt) was given. No return of oedema was observed and the slight rise in weight which did occur was undoubtedly due to tissue replenishment and was observed to continue throughout convalescence.

Case 73. In this patient acute nephritis with marked oedema was present. The blood pressure was elevated and serum oncotic pressure moderately reduced (figure 29). A salt containing diet was allowed 7 days after admission. Fall in weight continued. The serum oncotic pressure 10 days after admission was found to be within normal limits.

It may be concluded therefore that in acute nephritis aggravation of oedema is produced by NaCl administration only when the serum oncotic pressure is low. That this is not the result of any renal impairment is shown very clearly by estimating the 2 hourly output of water, urea and chloride.

Figure 30 shows in the healthy subject (case 158) the great variations in the 2 hourly samples of urine, of Cl, urea and volume. In contrast to this a case (134) with marked renal impairment shows a completely different state of affairs.

Case 134, a boy aged 7 years. Since birth enuresis had been present and the mother complained also of his smallness of stature. He was found to be very small for his age but otherwise appeared to be healthy. The urine contained a trace of albumin. The blood pressure was not greatly raised - 120 per cent. of normal. On ophthalmoscopic examination a slight degree of optic neuritis was found. The non-protein nitrogen of the blood was 96.0 mgm. per cent.. Nine months after dismissal from hospital the child died at home. Convulsions, probably of uraemic origin, were present for some days before death. Figure 31 shows that the variations found in the normal case were entirely absent in the 2 hourly samples. This indicated a high degree of renal impairment in excretion of the urinary solids including Cl.. Oedema in this case was absent. It might be anticipated, if retention of chloride were due to the kidney, that the nephrotic type of case would give similar

Fig. 30.

To Show the Large Variations in Excretion of Urinary Solids in the Normal Kidney.

Case 158.

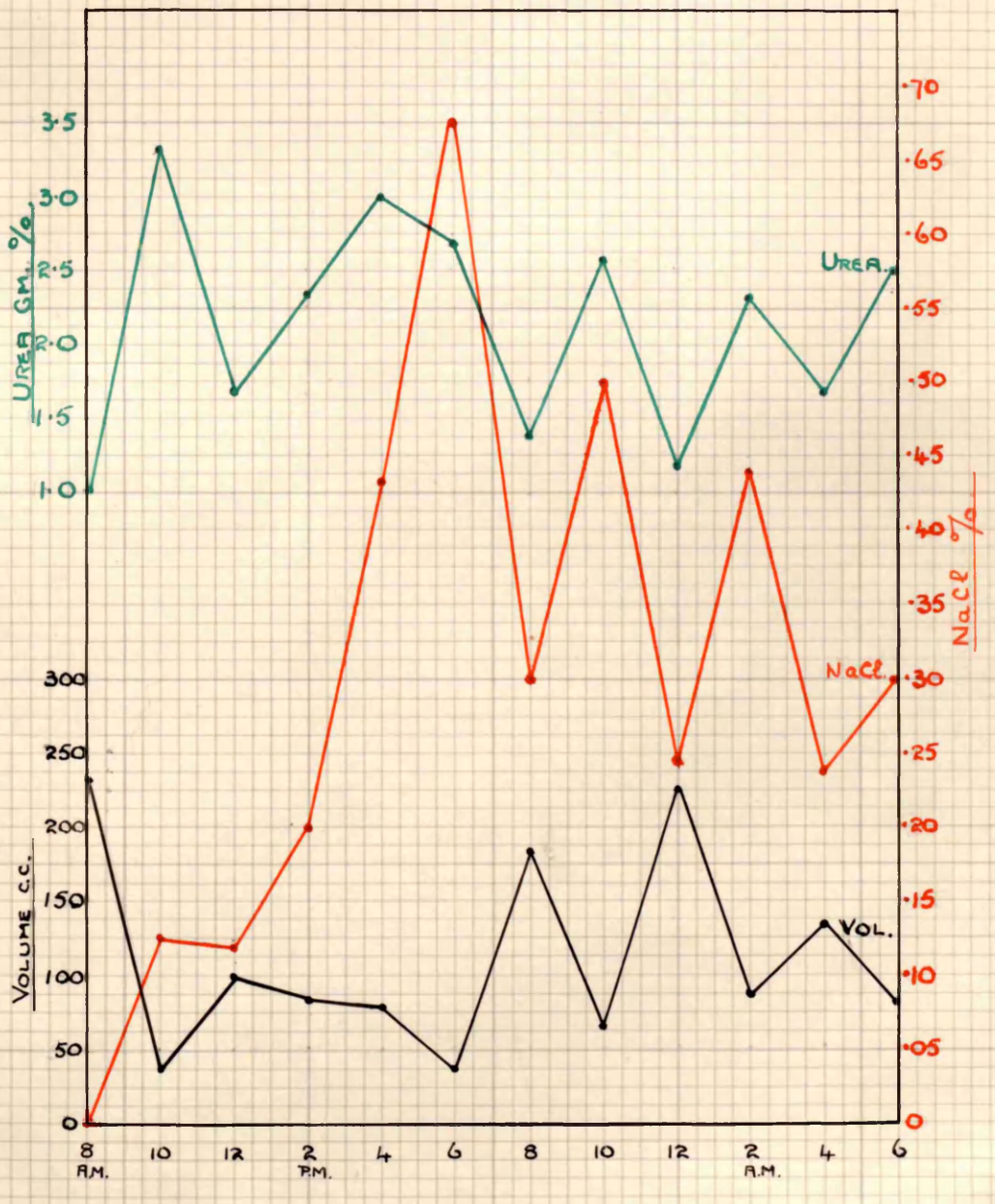
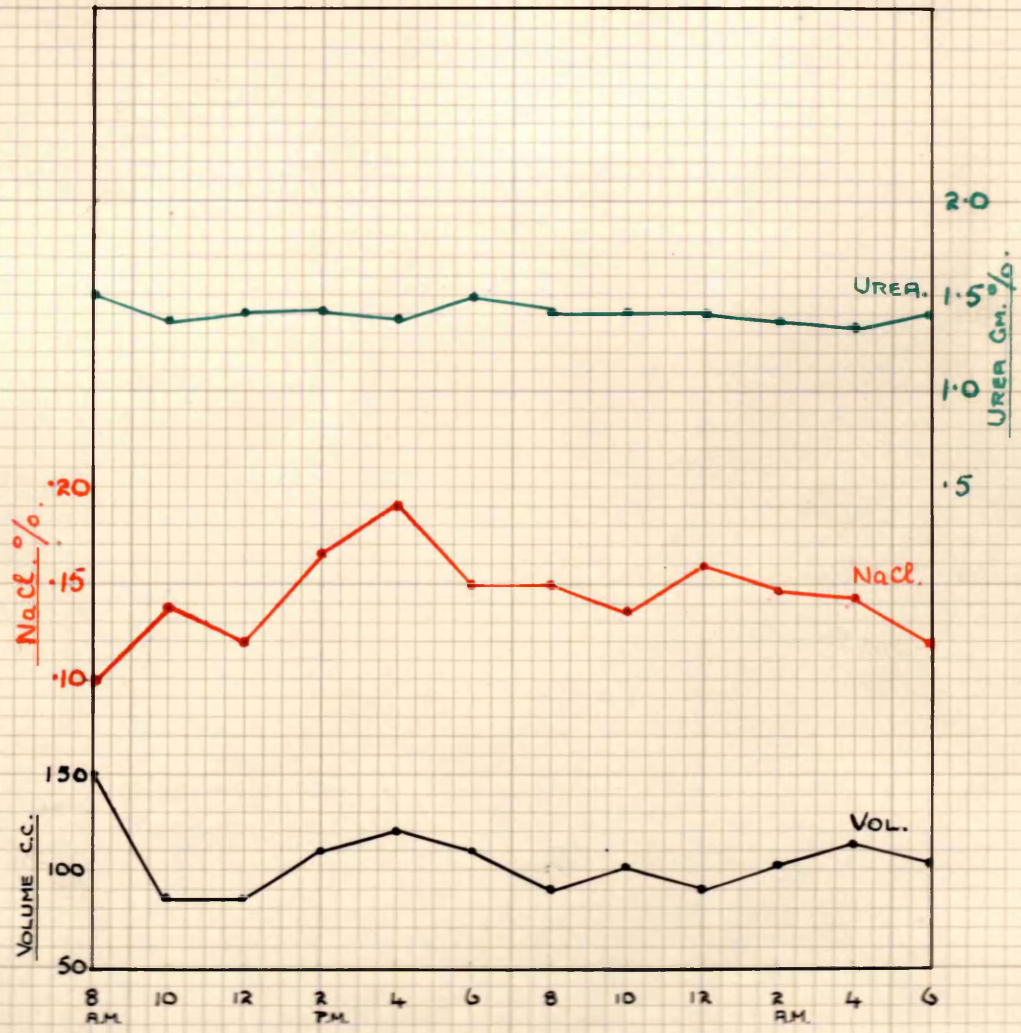


Fig. 31.

To Show Impairment of Excretion of Urinary Solids in Renal Dwarfism.

Case 134.



findings. Such is not the case.

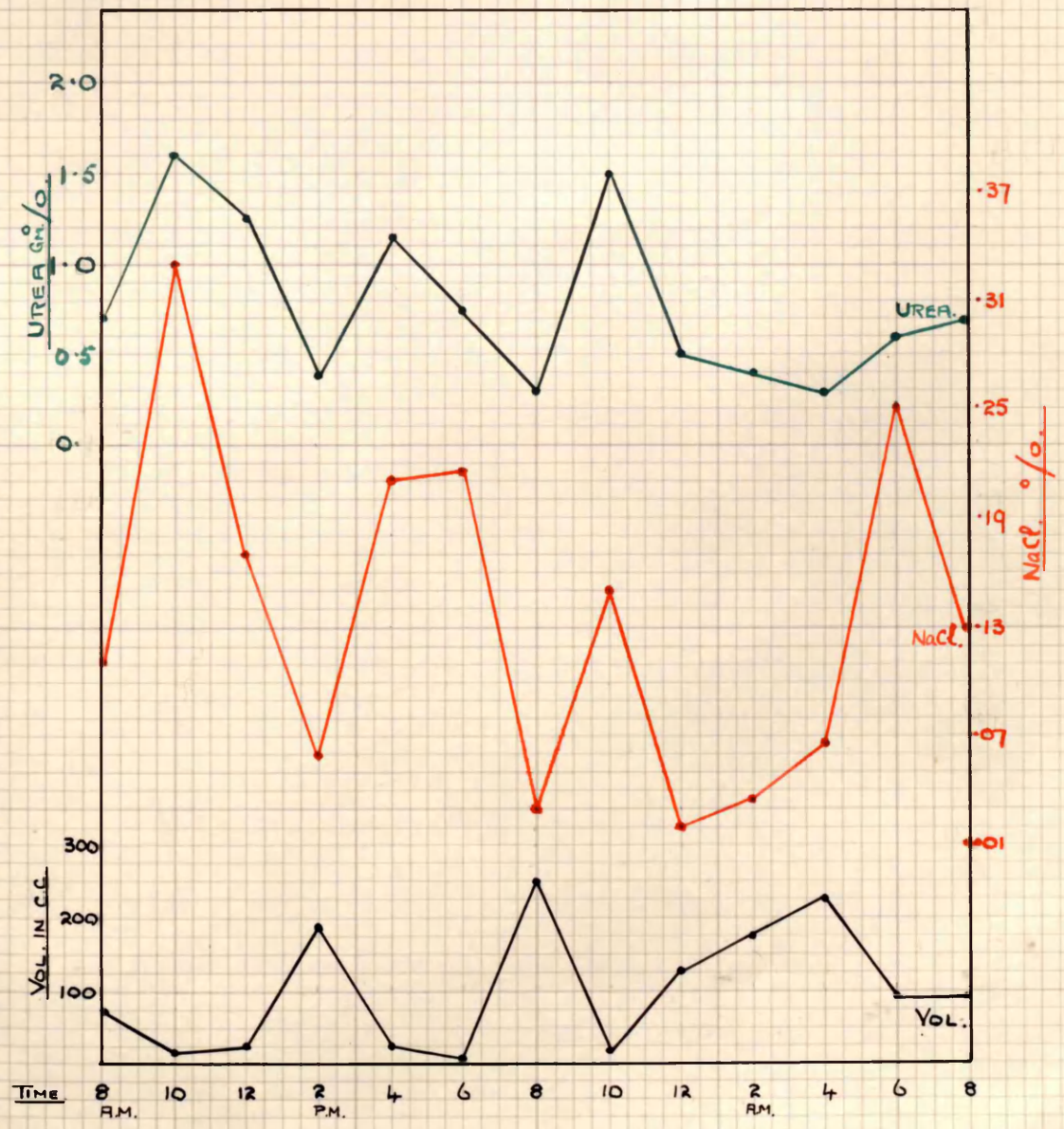
Case 99. This patient presented the features of the nephrotic type of nephritis. Figure 32 shows clearly that fluctuations as seen in the normal subject occurred also in this patient.

From a consideration of these figures confirmation is given to the view that in the nephrotic type of patient the power of the kidney to excrete chloride is unimpaired so that it is unlikely that the low output of chloride is due to inability of the kidney to excrete this substance.

Fig. 32.

To Show the Variations (Resembling the Normal) in the Excretion of Urinary Solids by the Kidney in Nephrotic Nephritis.

Case 99.



Chapter 7.

Some observations on the treatment of oedema in acute nephritis.

As long ago as 1889 Henoch[1] advocated sweating and purging with milk diet in acute nephritis and Goodhart[2] in 1890 while following similar lines stressed the importance of a low protein diet. Osler[3] in the 1909 edition of his text-book put forward no new treatment while Cruickshank[4] and Beaumont[5] and Dodds in 1934 adopted the older views. It can thus be seen that little new has been advocated in the treatment of oedema within the past 50 years as far as acute nephritis is concerned. Most workers however have observed not infrequently that in certain cases of acute nephritis oedema remains instead of rapidly disappearing. It is proposed first of all to consider the treatment of those types of acute nephritis with moderate or no diminution of serum proteins and thereafter to deal with the groups showing marked hypoalbuminaemia.

HYPERPIETIC AND MIXED TYPE B GROUPS.

The course of oedema in the acute nephritis of these types is brief and apparently depends on the duration of the hyperpiesis and the time taken for oncotic pressure to return to normal when a reduction is present.

All cases of nephritis received magnesium sulphate by mouth and in addition 62 per cent. received hot air baths

twice daily. It is difficult to assess the value of the latter and Christian[6] states that sweating is not now considered advisable in the treatment of acute nephritis. The impression gained in this investigation was that the disappearance of oedema was not accelerated by its use. Unless fluids are restricted its value seems doubtful. Boyd,[7] Aldrich[8] and others dealing with children held that patients from whom fluid was withheld were more acutely ill than others to whom it was allowed ad lib.. On the other hand, Christian,[6] Ellis,[9] and others advocate a restricted fluid intake in the early days of the disease. The patients under discussion in this paper received unrestricted fluids, and this did not appear to prolong the period of dropsy.

The question of diet has assumed more importance since Peters[10] et alii suggested that too long continued protein restriction might lead to prolongation or return of oedema through continued or subsequent fall in serum albumin. At the start of the illness however most workers agree that diet should be minimal, many advocating only water and fruit juice for a few days.

In this series the diet from admission was milk, or half milk and half water, the latter being usually increased to whole milk in a few days, until there was no oedema, hyperpiesis or haematuria save for an occasional red cell in the urine. These amounts of milk represent a daily protein intake of 47.0 to 17.0 grams, depending on the age of the patient.

The higher figure was probably ample but the lower was almost certainly inadequate. In the hyperpietic and mixed type B. cases no significant fall in serum albumin occurred during the course of the disease irrespective of whether the diet was half milk or whole milk. In the one case with serum albumin below 2.5 gm. per cent. no further observation was made on the blood but oedema disappeared rapidly on a milk diet containing 47.0 gm. of protein per day. As far as acute nephritis of the hyperpietic and mixed type B groups is concerned, serum proteins if normal, remained normal, and if reduced, rapidly returned to normal, irrespective of the amount of protein in the diet.

During the acute phase the diet of milk contained 1-2 grams of NaCl per day depending on whether the half milk or whole milk régime was followed. Boyd[7] states a "salt-free" diet should be continued during convalescence for several months. It has been shown however (figures 26, 27, 28, 29) that retention of chloride with formation of oedema depends on the level of oncotic pressure, at least after the acute phase has passed, and the rationale of Boyd's[7] procedure seems doubtful, at any rate where the reduction of serum protein is not marked.

NEPHROTIC AND MIXED TYPE A GROUPS.

While it is manifest that in the majority of cases of acute nephritis in children oedema is a transient phenomenon it has been noted by Peters[10] and his co-workers and by Ellis[9]

and others that dropsy may be of a much more obstinate character. These workers have indicated that the persistence of oedema is associated with a marked and persistent fall in serum oncotic pressure. Since it seems that oedema can be attributed directly to this, a rational line of treatment would appear to be an attempt to restore oncotic pressure to normal.

A. Attempts to raise serum oncotic pressure.

High protein diet.

The instigator of this form of treatment was Epstein[11] who gave large amounts of protein, 120-240 grams daily and claimed good results. It has however met with varied reception, Aldrich,[12] Schwarz[13] and Kohn, and Davison[14] and Salinger for example met with little success with its use in nephrosis in childhood. Ellis[9] employs a high protein diet on theoretical grounds but has never seen a cure in nephrotic nephritis which he could attribute to any form of treatment. Osman[15] also reports little success following its employment. Much difficulty in gauging the effect of treatment occurs owing to the fact that rise of serum protein may apparently be spontaneous. Amberg[16] in children has reported good results on a diet containing 2-3 grams of protein per Kg. of body weight per day, while Peters[17] and his co-workers in a series of cases of nephrosis and of the nephrotic syndrome in adults achieved success in raising serum oncotic pressure and dissipating oedema

by a moderately high protein diet not exceeding 125 gm. daily. They attributed the favourable results in part at any rate to the making good of protein starvation since a high degree of malnutrition was present in their cases. One gm. of protein per kilo of body weight was given daily in addition to an amount sufficient to cover the loss in the urine; the total was increased by 20.0 gm. per day when appetite improved. But in the cases quoted the period of treatment extended over one or more years before an oedema-free stage with normal serum proteins was reached. Furthermore the rise of serum albumin was not a continuous one and some possibility of spontaneous cure must be considered. Bannick[18] and Keith, indeed, report cures while the patients were on low protein diets.

Figures 33 and 34 show the effects of administration of a protein-rich diet to nephrotic cases. In Case 58 (figure 33) while on milk oncotic pressure tended to fall whereas an upward tendency was observed on diets with higher protein content. This child was dismissed on ordinary diet but still with low oncotic pressure and oedema. Six months later in the outpatient department serum oncotic pressure was 20.2 mm. Hg., the highest level noted, the diet being unchanged. In Case 38 (figure 34) a diet rich in protein was given for a period of 40 days - an initial rise in oncotic pressure was observed but this was followed by a reduction. This child also was dismissed on ordinary diet and observations since dismissal showed that on 7.6.34 the serum oncotic pressure was normal

Fig. 33

To show the Effect of High Protein Diet.

Case 58.

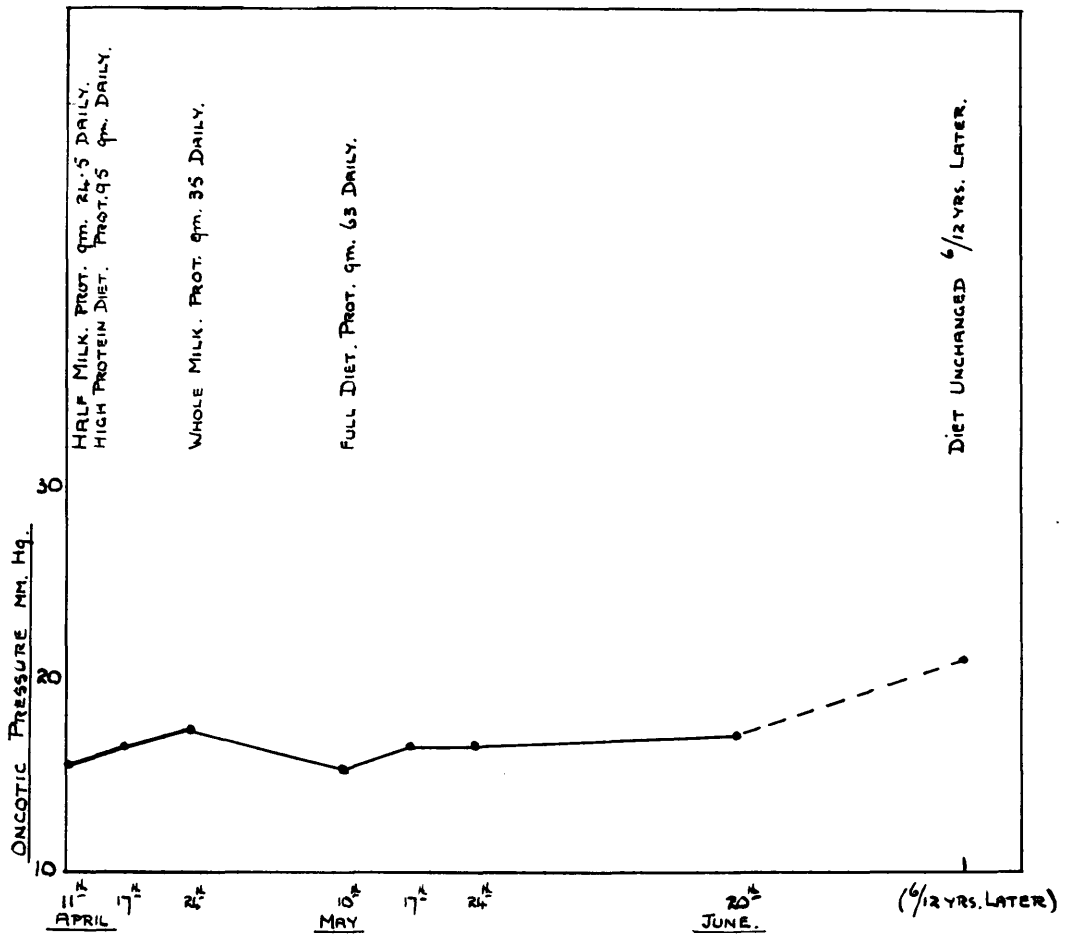
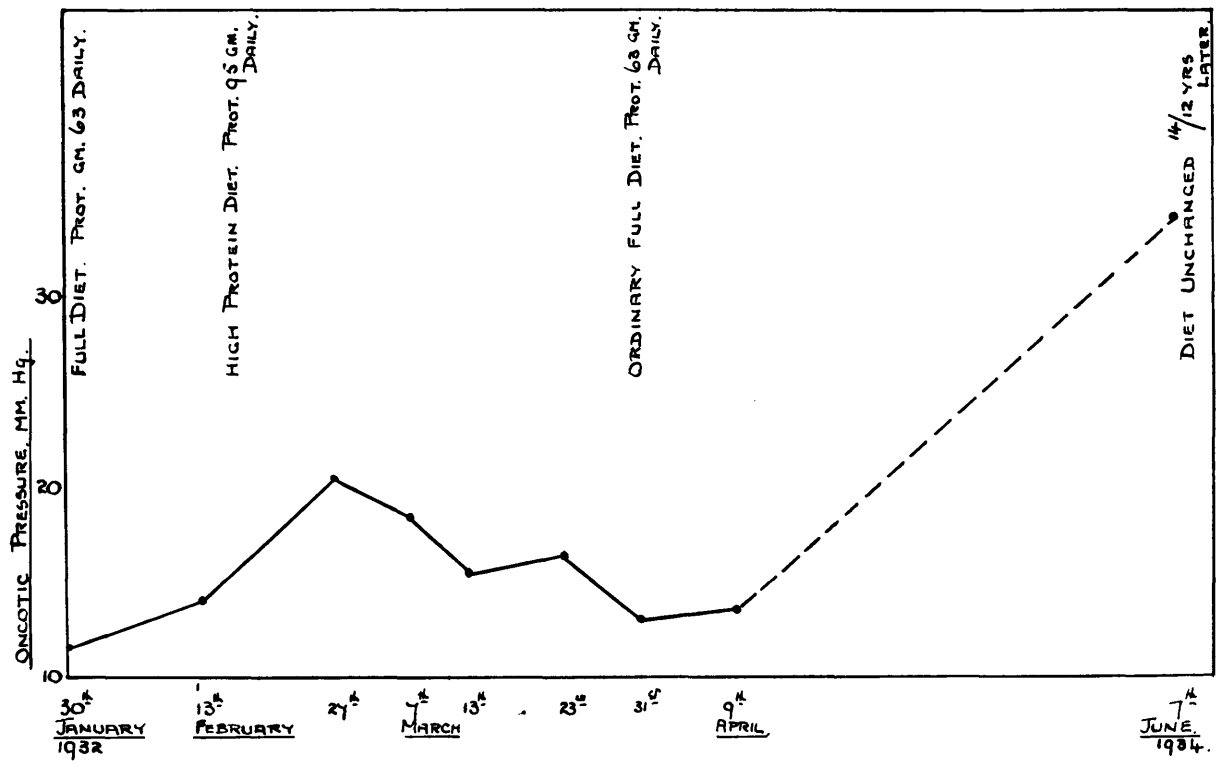


Fig. 34.

To Show Failure of High Protein Diet.

Case 38.



for the first time in twenty-nine estimations. The diet was unchanged. Case 193 was an infant (figure 35) to whom a high protein diet was given with apparent success. The rise in oncotic pressure however was not checked when high protein diet was omitted four weeks later and in this case also a spontaneous tendency to recovery seems probable since a reduction of the protein intake by 75 per cent. did not interfere with the return of serum proteins to normal. In the cases quoted it seems more than doubtful if high protein diet had any influence on the serum oncotic pressure but in view of the findings of Peters[17] et alii it might be claimed that the periods of trial were short.

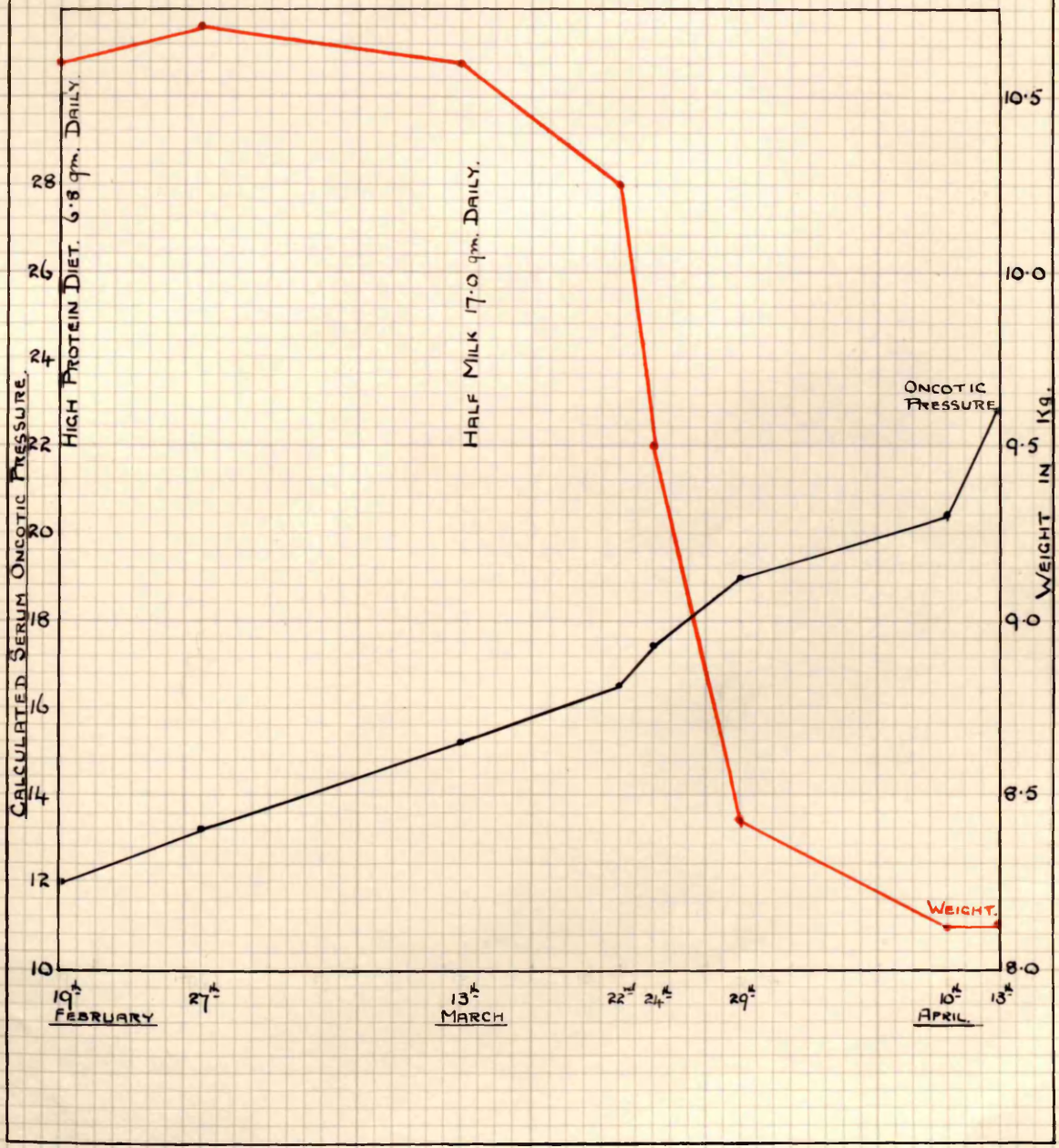
A further argument against the necessity of a high protein diet may be adduced from consideration of a case in which return to normal level of oncotic pressure was apparently spontaneous and high protein diet had not been used. Case 191:- an infant aged 1 year and 4 months. The blood chemistry findings were:-

Date.	Total Protein. gm.%	Albumin. gm.%	Globulin. gm.%	Calculated Oncotic Pressure. mm.Hg.	Daily Protein Intake. gm.
8.9.32	4.51	2.92	1.59	18.3	37.0
14.9.32	5.63	2.25	3.38	17.1	37.0
15.5.33	7.31	5.32	1.99	31.8	50 + for 8 months.

Fig.35.

Relation of Oncotic Pressure of the Serum to Oedema:

Treatment by High Protein Diet.



In cases where impairment of renal function with azotaemia is present in association with a serum albumin content of the blood below 2.5 gm. per cent. there seems to be some doubt as to the safety of administering a high protein diet. Bennett[19] states that if used at all great caution should be observed presumably because of the risk of increasing accumulation of nitrogenous waste products. On the other hand Peters[20] and van Slyke found that following the use of moderately high protein diets in haemorrhagic nephritis of the nephrotic type with impaired renal function some improvement actually occurred in the excretory power of the kidney. They quote the work of Peters,[21] Bulger, Eisenman and Lee to show that non-protein nitrogen was not increased in either blood or urine when sufficient protein was given to cover the metabolic requirements and the albumin lost in the urine.

In the following patient (Case 48), mixed type A nephritis, a very adequate protein diet was given throughout the illness. The amount of protein per day varied from 44 to 64 gm..

From the figures it can be seen that the amount of protein in the diet had no apparent effect on the serum proteins. The point of this case would seem to be that a very marked reduction of serum albumin took place after a period of two months on a protein intake quite sufficient for needs of the child, indicating that adequate protein in the diet failed to prevent fall in serum albumin.

Case 48.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Daily Protein Intake in gm..
16.6.33	4.27	1.66	2.61	12.8	74.6	44.0
24.6.33	8.25	2.86	5.39	23.3	30.9	44.0
29.6.33	-	-	-	-	-	60.0
13.7.33	8.26	5.92	2.34	35.8	28.3	60.0
2.9.33	5.97	2.00	3.97	16.5	65.2	44.0
13.9.33	3.87	1.49	2.38	11.5	40.5	44.0
27.9.33	3.39	1.57	1.82	11.4	27.0	44.0
3.10.33	5.25	1.56	3.69	13.7	47.6	64.0
11.10.33	-	-	-	-	-	50.0
18.11.33	4.24	1.30	2.94	11.8	33.1	60.0
1.12.33	7.49	1.73	5.76	17.6	76.0	60.0

Case 49.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Daily Protein Intake in gm.
25.4.33.	6.25	2.50	3.75	19.0	50.0	33.0
28.4.33	6.07	2.28	3.79	17.8	77.9	33.0
2.5.33	6.01	2.06	3.95	16.9	88.2	33.0
12.5.33	4.44	2.14	2.30	15.0	76.0	33.0
8.6.33	6.98	2.25	4.73	18.9	72.2	33.0
14.6.33	5.09	2.25	2.84	16.4	85.0	60.0
29.6.33	5.84	2.54	3.30	18.6	69.0	33.0
11.7.33	5.06	2.19	2.87	16.0	90.0	33.0
20.7.33	5.26	2.65	2.61	18.2	133.0	33.0
24.7.33	Died					

Consideration of the figures of Case 49 shows that oncotic pressure fluctuated while the diet was whole milk; no improvement occurred on high protein diet.

Case 29. The point of interest in this case is the considerable rise in oncotic pressure on a diet of milk.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Daily Protein Intake in gm.
8.9.33	7.62	2.39	5.23	20.5	280.0	40
13.9.33	7.52	3.44	4.08	24.6	222.0	40
16.9.33	7.61	3.69	3.92	25.8	133.0	40
28.9.33	6.27	3.96	2.31	25.0	30.4	40
4.10.33	7.36	3.57	3.79	24.9	25.0	40

While little can be said as to the effects of high protein diet in raising oncotic pressure, fluctuations in an upward direction were observed even on a low protein intake. On ordinary diet for the age apparently complete recovery was also observed in infants. Low protein diet was not given over any lengthy period and its effect on the serum proteins has consequently not been observed. It cannot therefore be said with any measure of certainty that the protein intake had any influence on the serum oncotic pressure level on the cases of this series.

Protein Shock.

Aldrich[12] in a paper on the treatment of nephrosis in childhood observed that complete disappearance of oedema followed recovery from acute febrile infections complicating the disease, while improvement was claimed by Gautier[22] after measles and mastoiditis respectively in two cases. In this series loss of oedema followed empyema but albuminuria persisted while serum oncotic pressure was just above oedema level (Case 181). In Aldrich's[12] paper no estimation of serum proteins was made and Gautier's[22] figures show but a slight rise, mainly in serum albumin. Leiter[23] quotes a case reported by Karácsony[24] in which oedema was not relieved by diuretics but twice disappeared following an attack of lobar pneumonia. Aldrich,[12] Gautier,[22] and Leiter[23] all suggest that foreign protein therapy might be of value but no references to its employment have been found in the literature.

Numerous workers have found that serum globulin is increased in infections such as enteric fever, pneumonia, pyogenic infections generally, syphilis, tuberculosis, malaria and other diseases. Following plasmaphaeresis, Leiter[25] and Darrow[26] have found that serum globulin regenerates more rapidly than does albumin on cessation of the bleeding. It is probable therefore that cure of nephrotic oedema which has been observed following infection is associated with rise in serum oncotic pressure due to increase in serum globulin. The suggested rationale of protein shock therapy in the treatment is

to stimulate production of serum protein, and two cases of the nephrotic type were treated by intravenous injections of triple typhoid vaccine with this object in view.

Case 99. Four injections of vaccine were given. No marked febrile reaction followed, the maximum temperature observed being 101°F. rectally. A blood sample was taken prior to injection of the vaccine into a cervical vein. While serum globulin showed marked variations, serum albumin remained constantly at a low level and was unchanged one month after the last protein shock: the oedema was unaltered. Figure 36 shows the effect on the serum proteins.

Case 4. In this patient blood was taken before injection of vaccine and also on the following day. Figure 37 shows that on the day following the first protein injection serum albumin fell slightly and serum globulin was increased. Globulin then fell and albumin increased. After subsequent injections, however, entirely the reverse was seen on every occasion. As far as oedema was concerned great diuresis began on the day following the third injection, oncotic pressure having risen from 12.2-18.5 mm.Hg.(Figure 38). Relapse however took place almost immediately and oedema was worse than before treatment, with serum oncotic pressure falling to 9.9 mm. Hg..

Fremont-Smith,[27] Morrison and Makepeace found that stasis occurred in the capillaries after intravenous injection of T.A.B. vaccine: Drinker[28] and Field commenting on this finding suggest that leakage of protein would occur through increase of capillary permeability. Following 5 injections of vaccine in Case 4 the results do not altogether substantiate this view since on four occasions a rise in oncotic pressure, though temporary, did occur. It is interesting to observe however that the oncotic pressure subsequent to protein shock reached a much lower level than before treatment, suggesting a possible damage to the capillaries.

Fig. 36.

Serum Albumin and Globulin in a Case of Nephrotic Nephritis Treated by Protein Shock.

Case 99.

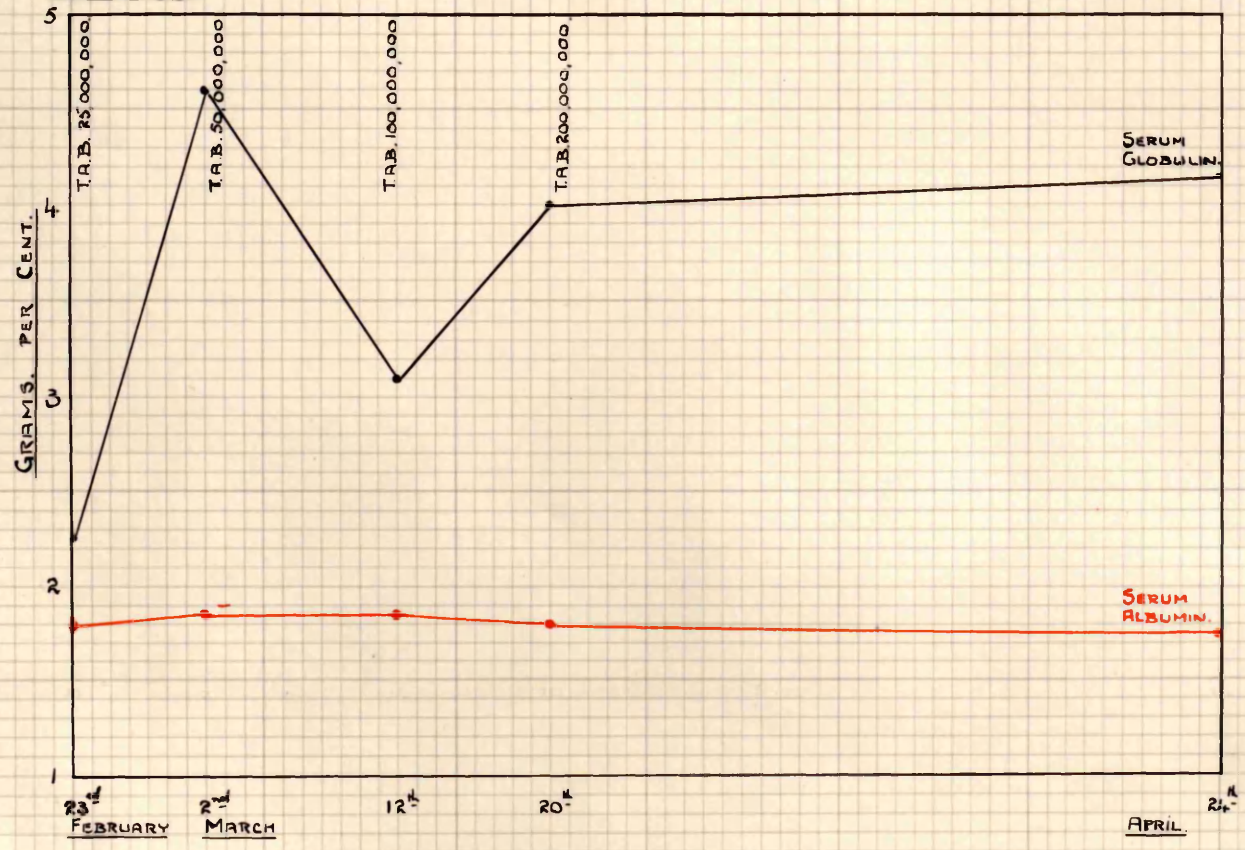


Fig. 37.

Fluctuations Observed in Serum Albumin and Globulin in a Case of Nephrotic Nephritis Treated by Protein Shock.

Case 4.

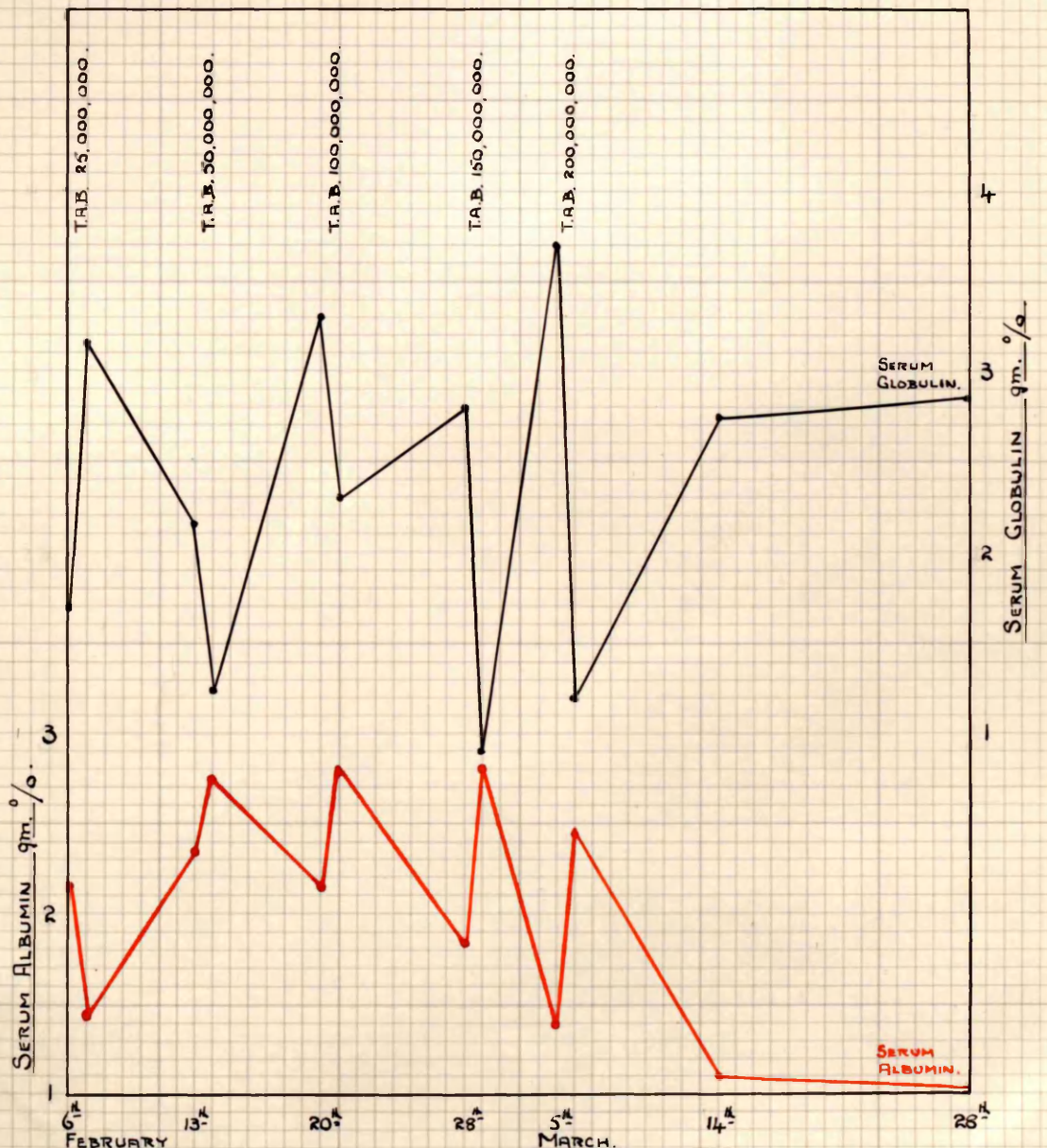
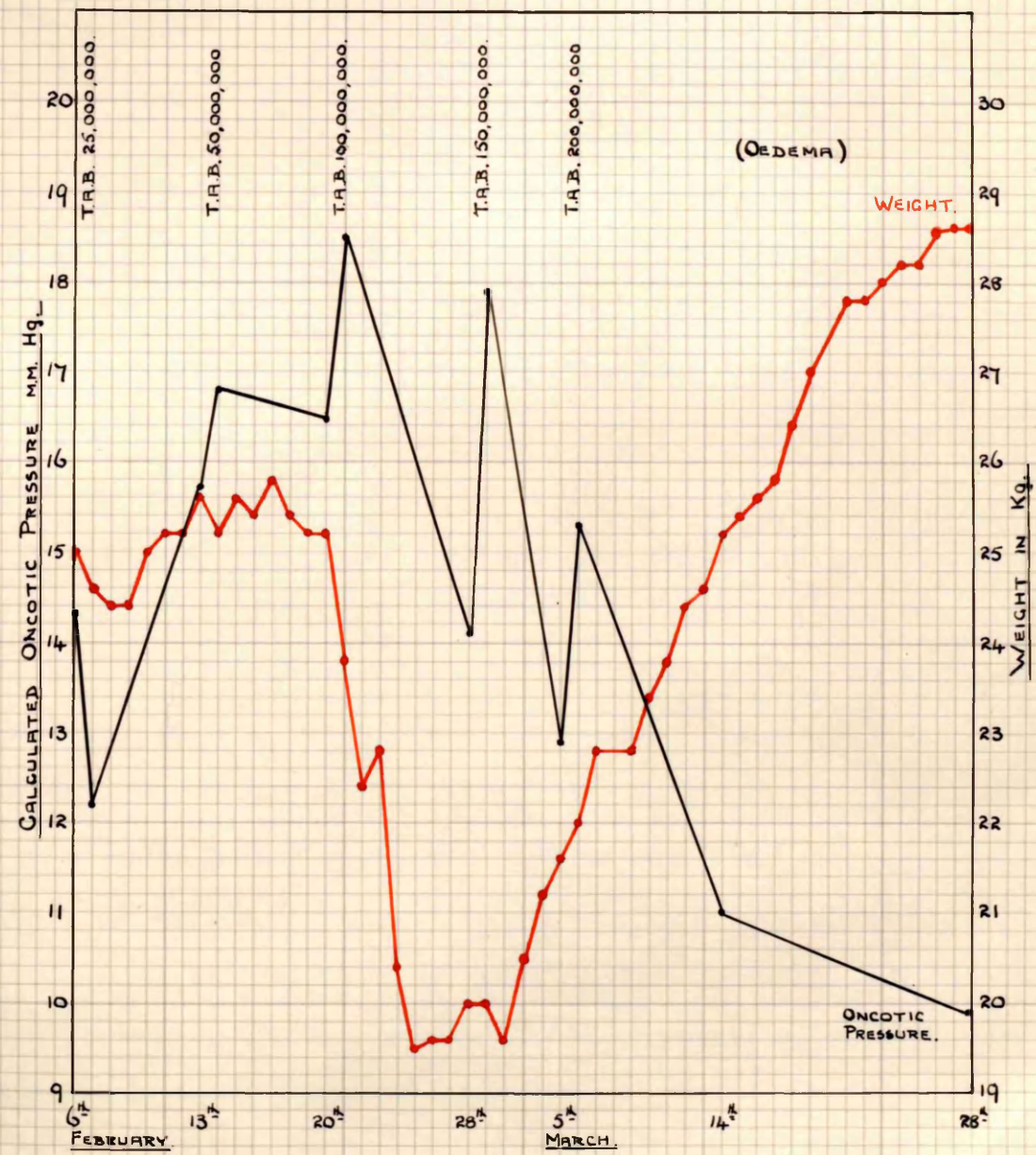


Fig. 38.

Relation of Oedema to Serum Oncotic Pressure in Case of Nephrotic Nephritis Treated by Protein Shock.

Case 4.



Injections of gum acacia or blood transfusion.

Epstein[11] in one of his original papers suggested that blood transfusion should be tried in nephrosis although he admitted that improvement was but temporary. According to Leiter[23] such a measure fails because the amount of plasma protein injected is insufficient to raise the oncotic pressure of the patient to a significant height, and moreover, quoting Maclean,[33] he says that the glomerular capillaries are more permeable than normal to colloids. Hartmann[29] and his co-workers found that blood transfusion in their cases failed to raise the plasma proteins. Treatment by repeated injections of gum acacia in 6 cases was followed by apparently complete cure in one, great improvement in another and temporary improvement in two.

In case 38 (nephrotic type of nephritis) 24.1 grams of acacia in 7 per cent. solution in normal saline were given intravenously (one gm. per Kg. of the estimated true weight) according to the technique of Hartmann[29] and his co-workers. Fifteen minutes after injection the child's face appeared to become more swollen and rather cyanosed, the eyes were suffused and violent vomiting occurred. The temperature rose to 102°F. In view of this rather alarming reaction and the absence of improvement in the serum oncotic pressure or oedema this form of treatment has not been repeated.

B. Other forms of treatment.

Other forms of treatment which do not depend primarily on increase of serum oncotic pressure have also been suggested by various workers. Several of these methods have been tried on a few patients with intractable oedema.

Massive doses of alkali in treatment of cases of the chronic parenchymatous type have been advocated by Osman[30] who claims good results. Equal parts of potassium and sodium citrate and potassium and sodium bicarbonate are given commencing with a daily dose of 60 grains of the mixed salts increasing gradually to 960 per diem. He states that oedema increases at first but with increasing alkalinity of the urine diuresis ensues and eventually complete disappearance of oedema and albuminuria occurs in favourable cases. The treatment according to him must be maintained till diuresis ensues and if relapse occurs alkali must be recommenced. Gradual withdrawal of alkali should be practised. Osman[30] admits that in cases of exceptional severity the alkaline treatment is only partly successful. Albright[31] and Bauer by administration of sodium bicarbonate were able to induce diuresis in a case of nephrosis and Hastings[32] et alii in two cases of nutritional oedema and one of nephrosis treated by sodium bicarbonate observed exacerbation of oedema followed by diuresis. Serum albumin, however, remained between 2.0 and 2.8 gm. per cent. and oedema returned when the alkali was stopped.

This form of treatment is based upon the finding of its promoter that plasma bicarbonate is frequently reduced in nephritis. Peters[20] and others however have reported that the alkaline reserve in nephrotic cases is either unaltered or if low with but a slight deviation from normal. The findings in the Royal Hospital for Sick Children (p.43) with regard to the CO_2 content of the blood in nephritis are in complete agreement with those of Peters.

In the course of this investigation two cases have received treatment as suggested by Osman,[30] save that sodium bicarbonate was the alkali used.

Case 4, figure 39, where the results of the therapy are given, shows that 8 days after the intake of alkali had reached 960 grains daily, a marked diuresis occurred. Weight then remained stationary with perhaps a slight tendency to increase. The child received bicarbonate for 42 days but was never oedema-free. When alkali was omitted weight increased steadily and estimation of the serum proteins showed that the oncotic pressure was 14.1 mm. Hg..

It is obvious therefore that sodium bicarbonate has only a temporary effect in removing oedema unless the serum oncotic pressure rises.

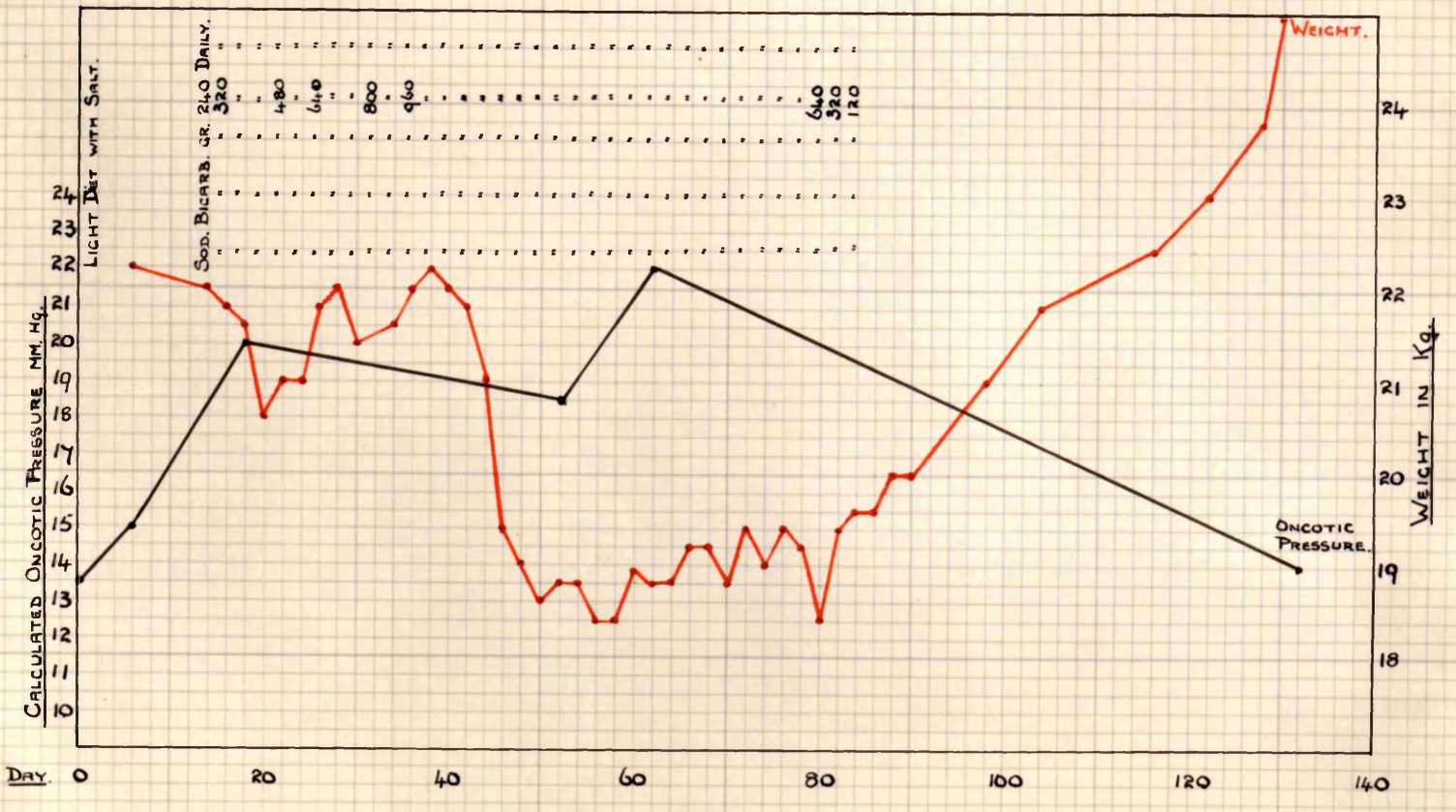
In the other case on whom this form of treatment was tried observations were interrupted after 11 days by the development of vomiting and diarrhoea. No improvement, however, was noted.

In one case therefore this form of treatment (after a protracted trial) was unsuccessful. The interesting observation was made that frequently no albumin whatever was detected

Fig. 39 .

Treatment with Massive Doses of Alkali.

Case 4.



by Esbach's method of quantitative estimation during the period that alkali was given unless a large amount of acetic acid was used to neutralize the urine. If this was done the percentage of albumin present in the urine was found to be reduced during diuresis owing to the larger amount of water passed, but in both the cases the total daily amount of albumin lost was not significantly less.

"Salt-free" diet.

Leiter[23] in a review of nephrosis states that salt restriction may lead to diuresis or prevent further increase in oedema. Patients may thus be kept oedema-free by a salt-poor diet even although plasma protein deficiency may be still present.

Osman[15] found that the "salt-free" diet is of little permanent benefit in nephritis of the chronic parenchymatous type and Aldrich[12] observed that on occasions oedema actually increased during its use. In the literature reports as to the efficacy of salt restriction are conflicting but the position has been clarified by the work of Peters[17] et alii who found that oedema associated with a serum total protein above 4.0 gm. per cent. might be eliminated by a "salt-free" diet with or without diuretic drugs. With a total protein below 4.0 gm. per cent. such treatment was usually ineffectual.

In all the cases of the nephrotic and mixed type A

Fig.40.

Fluctuations in Oedema on Salt-Free Diet.

Case 98. Oedema present throughout.

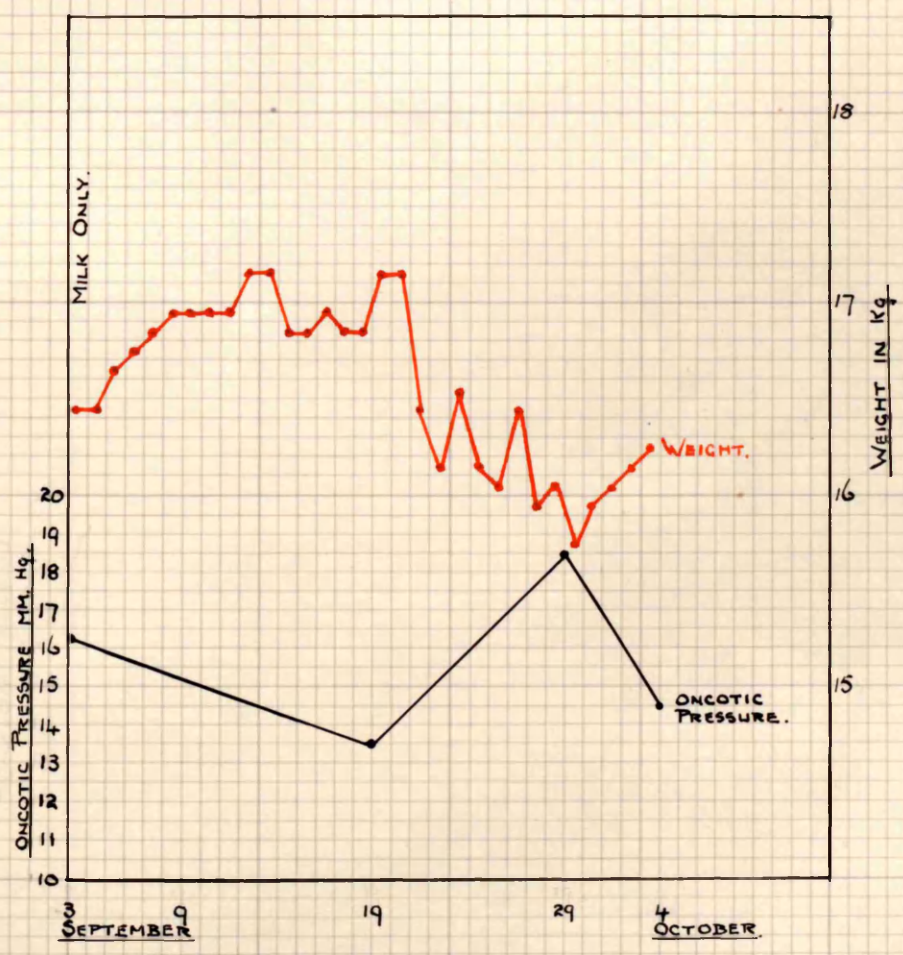
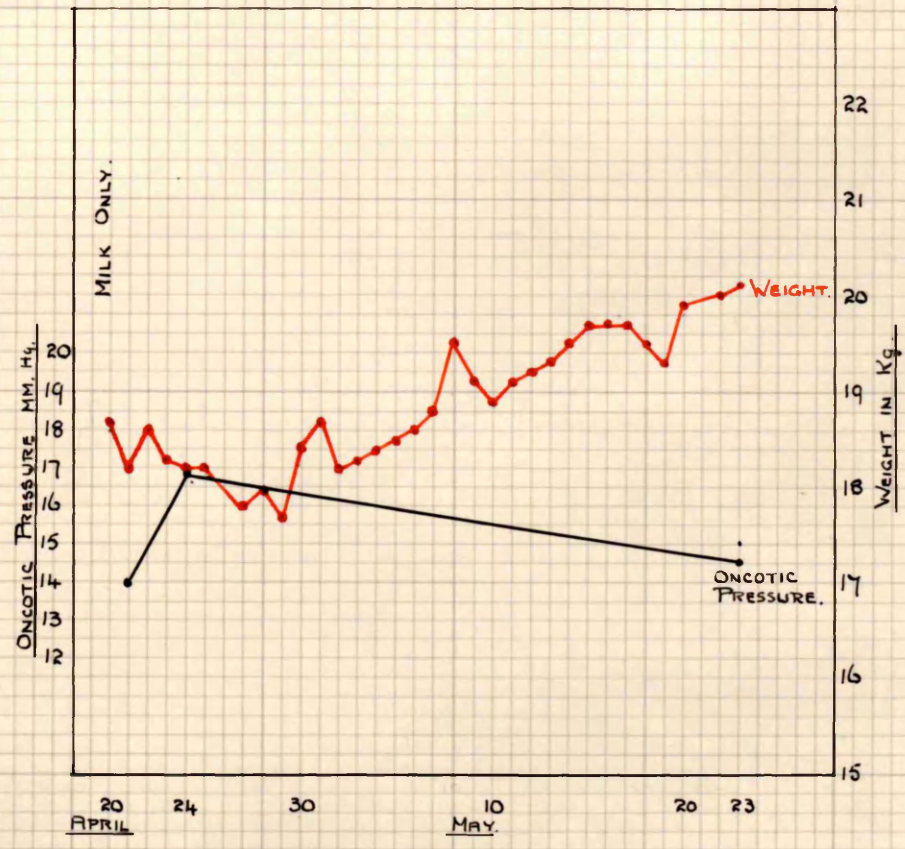


Fig. 41 .

Increase of Oedema on Salt Free Diet.

Case 62.



group under consideration a "salt-free" diet was employed and in none was complete disappearance of oedema noted, even temporarily, as a result of its use unless serum oncotic pressure rose above oedema level. Marked improvement however was not infrequent but subsequent addition of sodium chloride to the diet was associated with an exacerbation of oedema (Chapter 6, figures 26, 27) even if serum oncotic pressure level remained constant. Figures 40 and 41 on the other hand show cases in which oedema increased on "salt-free" diet. The explanation of this is the fall in oncotic pressure. Presumably even the small amount of NaCl in the diet was retained along with water to form oedema.

It is apparent that successful results with a salt-free diet in nephritis are obtained in cases where hyperpiesis with or without a moderate fall in oncotic pressure is present. As Ellis[9] states these cases will recover whatever treatment be given. In other words salt retention depends upon the fall in serum proteins. Peters[17] and his co-workers found that salt restriction and the use of diuretics were only palliative measures in treatment of nephrotic oedema which remained or tended to recur unless and until the serum protein rose above oedema level.

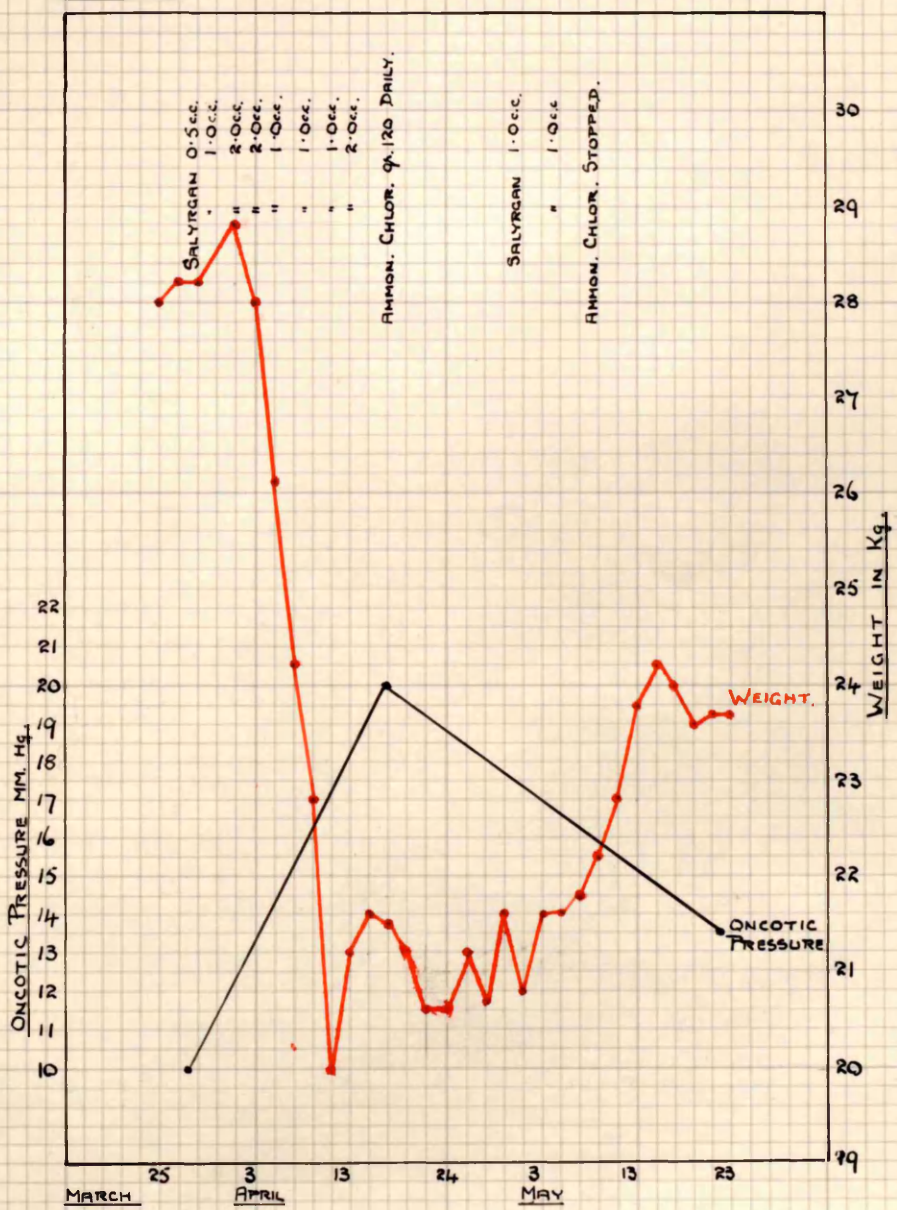
Salyrgan.

The use of mercurials in the treatment of nephrotic oedema has been justified by Bannick[18] and Keith who found them safe in the absence of evidence of reduced renal function. They

Fig. 42.

Treatment by Salyrgan.

Case 4



may be given intramuscularly or intravenously, alone or in conjunction with ammonium or calcium chloride which is started three days before the first injection of mercurial.

Figure 42 shows that in case 4 very pronounced diuresis occurred which at first sight would suggest an excellent result for salyrgan, the form of mercury used. Examination of the blood however revealed the fact that during the period of administration serum oncotic pressure had risen from 10.0 mm. Hg. to 21.3 mm. Hg. and a subsequent tendency for oedema to increase was associated with fall in serum oncotic pressure. It seems unlikely that any rise in oncotic pressure should be attributed to salyrgan and the apparent benefit in case 4 from mercurial injections must in large part be attributed to a spontaneous rise similar to that observed in the same case while receiving no treatment. (Figure 22).

Thyroid.

In view of the lowered basal metabolic rate present in nephrosis Epstein[34] and others have advocated the administration of this substance in large doses. Since, however, in oedematous states generally, the basal metabolic rate is reduced, as was pointed out by Peters[17] and his co-workers, it is unlikely that any special benefit will accrue from its use in nephrosis. These workers and Platt[35] and others have found no diuresis or rise in plasma proteins to follow its exhibition in such cases. In one patient (case 4) of this

series thyroid was given in gradually increasing doses to a maximum of 16½ grains per day. At this point diarrhoea developed and the drug was stopped. During administration oedema actually increased till the onset of diarrhoea when 2.0 Kg. in weight were lost but speedily regained when the motions returned to normal. No observations were made on the serum proteins at this time.

Calcium.

In the nephrotic type of nephritis a reduction of the calcium of the serum is present as was pointed out by Kohn;[36] Salvesen[37] and Linder showed that the reduction was at the expense of the fraction bound to serum protein. In view of this parathyroid extract has been used in the treatment of nephrosis apparently with the object of raising serum calcium, thereby diminishing the permeability of the capillaries and lessening the urinary excretion of protein. In the literature however the results indicate that following its use diuresis is rare and rise in serum calcium is not maintained. Presumably with the same object calcium has been administered in the form of calcium gluconate. O'Donnell[38] and Levin reported cure or improvement with loss of oedema in three cases but from their case reports it would seem doubtful if the good results could be ascribed to the treatment: two of the cases received only one dose of 10 c.c. each whereas the third received 155 c.c. over 24 days. Hoffman[39] and Post

following the administration of 100 mgm. of calcium (in the form of calcium gluconate) by intravenous injection on eight consecutive days observed no lasting rise in serum calcium and no alteration in serum protein: diuresis did not occur from its employment.

In this series two patients (cases 4 and 62) received treatment by intramuscular injection of 10 c.c. of calcium gluconate. Table 26 shows the findings.

TABLE 26.

Case	Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	Serum Calcium mgm%	Number of Injections.
4	22.5.34	5.21	1.50	3.71	13.5	6.4	7
	6.6.34	4.84	1.93	2.81	14.5	9.1	
62	23.5.34	4.01	2.22	1.79	14.6	8.4	8
	6.6.34	5.70	1.19	4.51	12.8	9.1	

From table 26 it can be seen that no significant alteration occurred in the level of serum albumin or oncotic pressure while serum calcium was raised to normal. The increase in serum globulin in case 64 was not presumably associated with the treatment since it was observed to occur apparently spontaneously in other patients. Oedema in both subjects remained massive.

Summary.

Of the forms of treatment employed none was successful in effecting disappearance of oedema. Salt restriction, salyrgan, and massive doses of alkali caused diminution of oedema for short periods but it is felt that no permanent benefit ensued because serum oncotic pressure remained below oedema level. Calcium gluconate and thyroid were useless. Attempts to raise serum proteins by diet and by protein shock also failed. Spontaneous cure, apparently complete, associated with rise in serum proteins to normal was observed in three infants and one child. Empyema in one instance was followed by loss of oedema associated with rise of serum oncotic pressure due to increased globulin. After paratyphoid fever in another case oedema was somewhat less and oncotic pressure, although still below oedema level, higher than before the attack.

On theoretical grounds a moderately high protein intake seems advisable and the diet should be salt-free. In so far as the greater the oedema, presumably the greater the risk of infection, any measure which may cause diminution in oedema even although temporary is strongly indicated.

Chapter 8.

The importance of serum protein estimations in the immediate prognosis of acute nephritis.

Still[1] made the observation that in the first few days of an attack of acute nephritis it was impossible to foretell the outcome. Gainsborough[2] and Wilbur[3] and Davidson were of the same opinion and found that it was impossible to foretell whether rapid recovery would ensue or the patient remain oedematous for months. In his study of the oncotic pressure in nephritis, Mayrs[4] found in one acute case that oedema was associated with a very low figure and that the subsequent course of the case was protracted. Van Slyke[5] and his co-workers in 23 cases concluded that the prognosis was independent of the severity of the symptoms or signs in the first few weeks with the single exception of the level of the plasma albumin. When this was at a low level most of the cases became chronic with protracted oedema. On the other hand Harrison[6] and Wyllie stated that only in hydraemic types of nephritis, with gross oedema, were plasma proteins low. In "acute" and "acute haemorrhagic" nephritis they were generally within normal limits and from their observations they concluded that estimation of the plasma protein was generally superfluous as a guide to treatment or an aid to classification.

On the whole little attention has been paid in the literature to serum protein estimations as an index of prog-

nosis but a consideration of the course of the nephritis in the present series of 100 patients would indicate that when oedema is present an estimation of serum albumin may be of some assistance even at an early stage in the disease. This is indicated in table 27. In the column "well" are included patients free from oedema and with at most a trace of albumin in the urine: azotaemia and hyperpiesis were absent and renal function was within normal limits.

TABLE 27.

The relation of the serum albumin level (initial observations) to prognosis.

Serum albumin. gm.%	Number of cases.	Well.	Still ill.	Died.
> 4.45	24	21	1	2 (a)
4.45-2.51	66	63	-	3 (b)
< 2.51	10	2	6	2

From this, which is admittedly a small number of cases, it would appear that the prognosis is better in those patients

(a) Case 92 Died of lobar pneumonia and acute nephritis.
Case 97 Died of pneumococcal meningitis complicating acute nephritis.

(b) Case 15 Died of acute pulmonary oedema complicating uraemia in acute nephritis.
Case 64 Died of pneumococcal meningitis complicating acute nephritis.
Case 100 Died of broncho-pneumonia complicating uraemia in acute nephritis.

in whom serum albumin was not reduced below 2.51 gm. per cent.. Although death occurred in five cases where such a reduction of serum albumin was not present, the fatal issues were due rather to the complications than to Bright's disease. In the remaining two fatal cases death ensued after a period of months in which oedema, hypertension and azotaemia were present. The patient with normal serum albumin who has been classified as "still ill" has a marked degree of albuminuria (tests show that this is not orthostatic in origin) but otherwise shows no abnormality. Six cases remain in which serum albumin was 2.5 gm. per cent. or less on admission. Of these four have for months shown oedema of varying degree and massive albuminuria. A fifth has azotaemia and hypertension in addition to oedema and albuminuria. The sixth patient still shows poor renal function and albuminuria after a long illness characterized by oedema, azotaemia and hypertension.

Chapter 9.

Acute nephritis in infancy.

Although the subject of nephritis has been studied from many aspects, comparatively few reports are extant on the manifestations of the disease as it occurs in infancy. Henoch[1] recognised the existence of both acute and chronic nephritis in infants and noted that oedema was its most prominent manifestation. In the edition of his text-book published in 1899 Holt[2] described the symptomatology of what he termed acute exudative nephritis in children under 2 years but included as synonymous titles acute desquamative nephritis, acute parenchymatous nephritis and acute septic interstitial nephritis. In the condition he described the onset was abrupt with high fever and vomiting, while oedema was exceptional, being present in only 6 out of 23 cases and then slight in degree and only towards the termination of the disease. Dyspnoea was observed frequently but was ascribed to anaemia. Muscular twitchings were common and convulsions occurred in 3 cases. Albuminuria, which was frequently absent early in the attack, was rarely gross. Although casts were not usually numerous, many pus and endothelial cells were seen together with red blood corpuscles in moderate numbers. The mortality was very high. At post-mortem the kidneys presented a mottled appearance due to the aggregation of pus cells and even abscesses were often found. It seems evident that Holt[2] was describing pyelonephritis and in later editions of his book

he did not include these symptoms in his description of acute parenchymatous nephritis. Spence[3] also states that oedema is rare and emphasizes the presence of marked dyspnoea which he attributes to nephritic acidosis. He considers azotaemia an important diagnostic feature, the level of the non-protein nitrogen in the blood occasionally being as high as 100-150 mgm. per cent. He states the prognosis is grave. Such a description might include any condition associated with severe toxaemia and dehydration, since albuminuria, acidosis and azotaemia are not uncommon features in these conditions. However Spence[3] mentions the presence of casts and blood cells in the urine.

A series of cases reported by Boyd[4] were hydraemic in type and resulted in almost 100 per cent. cure unless fatal secondary infection occurred. Still[5] mentions the occurrence of nephritis with oedema in an infant 5 days old. In 49 cases of acute nephritis in children, Paterson[6] and Wyllie record 7 of parenchymatous type occurring between the age of one and 3 years. Of Lyttle[7] and Rosenberg's series of 74 cases of acute glomerular nephritis, 17 acute diffuse and 8 acute tubular, 3, 1 and 2 cases respectively occurred under 2 years. Levy[8] found 17 cases of nephritis in infants under a year in 1,000 admissions to hospital over a period of 10 years. Of these 17, 14 died giving a mortality rate of 82 per cent. as against one of 19 per cent. for total admissions. These cases he divides into three groups of different etiology:-

(a) Nephritis complicating erythrodermia desquamativa, - 5 cases. All of these died, 4 of the primary disease and 1 of sepsis.

(b) Nephritis occurring in the course of congenital syphilis - 6 cases. In 3 there was albuminuria with casts and scanty red blood corpuscles in the urine and oedema. A fourth had more marked haematuria and slight oedema. The remaining 2 cases showed signs similar to the first 3 but Levy[8] considers that they developed nephritis as a result of treatment for syphilis. All died.

(c) Nephritis in the course of an acute infection or nephritis sui generis - 6 cases. Of these, 3 followed broncho-pneumonia, enteritis or erysipelas. They showed marked albuminuria and oedema and are classed as degenerative in type. All died. Three other cases of nephritis arose spontaneously and were considered to be examples of acute glomerular nephritis. Oedema and albuminuria were less marked and haematuria was more prominent than in the cases of the degenerative type.

Levy[8] concludes that nephritis in infancy is a rare disease. On the other hand, Brown[9] in Toronto found 14 cases under 18 months in 109 cases of nephritis in children over a period of 5 years.

Gray[10] describes a case of nephritis in an infant aged 8½ months of 5 weeks' duration during which oedema was constantly present. The albumin in the urine measured 10-19 gm. per litre during the last 12 days of life and enough blood was usually present to give a positive reaction to the guaiac test. Casts were numerous. The Wassermann reaction was negative. At autopsy tubular degeneration was present and doubtful glomerular changes. This case is classified by Gray as nephrotic nephritis.

Osman[11] discusses the effect of large doses of alkali on a child aged 11 months with oedema which appeared 14 days before admission to hospital. Albumin exceeded 6 gm. per litre. Casts were numerous but no blood was seen. For 17 days potassium citrate and sodium bicarbonate, 120 grains of each, were given daily. Oedema then disappeared but possibly the gastro-enteritis which developed played a part in depleting the tissues of fluid. Recovery was apparently complete.

Saldun[12] describes a case of lipoid nephrosis in an infant. Oedema was marked and albumin in the urine reached 30 gm. per litre. The presence or absence of haematuria is not indicated. The Wassermann test was negative. Weight was lost during the course of the disease with diminution of oedema. The blood chemistry findings were:- Total proteins 7.80, albumin 3.18, globulin 4.62 gm. per cent., urea 14.0 mgm. per cent. Unfortunately the date of the blood chemistry findings with reference to the degree of oedema is not mentioned. On the development of broncho-pneumonia death occurred with generalised convulsions, seven weeks after the onset of the nephrosis. Further references to blood chemistry are given in 2 cases commencing under 18 months described as acute tubular nephritis (nephrosis) by Wolbach[13] and Blackfan. Insidious onset of anasarca was the main feature. Albuminuria was marked and haematuria absent. The total protein content of the plasma was 5.8 gm. per cent. and 3.2 gm. per cent. and non-protein nitrogen 55 mgm. per cent. and 44 mgm. per cent.

respectively. At the post-mortem examination tubular degeneration was observed. The glomeruli were normal in one case and in the other there were slight changes which were attributed to septicaemia.

Mackay[14] and Johnstone describe a case of lipoid nephrosis of 17 years' duration starting at the age of one year and four months. Up to the time of death, which was due to streptococcal peritonitis, renal function tests were normal and cardiovascular changes were absent. Ehrich[15] describing the pathology of the same case found the kidneys large while microscopic examination revealed hyalinisation of 50 per cent. of the glomeruli, the others being apparently normal.

Congenital Syphilis.

From a perusal of the literature the impression is gained that there is close causal relationship between syphilis and nephritis in infancy. Spence[3] suggests that the presence of nephritic oedema in an infant should lead the observer to suspect syphilis. Four of his 5 cases died and the 5th recovered on arsphenamine injection. Paterson[16] states that syphilitic nephritis is the commonest cause of oedema in infancy but other manifestations of syphilis are very commonly present. Boyd's[4] 5 cases, in which congenital syphilis was present, were clinically indistinguishable from acute mixed nephritis. Although the spleen was palpable in all cases the only other manifestation of syphilis was a rash which was present in one case and positive reactions to Wassermann's test.

All these children died. Post-mortem, however, well-marked evidence of congenital syphilis was present. Still[5] quotes 2 cases with both clinical and pathological evidence of syphilis and nephritis. According to Pfaundler[17] and Schlossmann post-mortem examination gives unmistakable evidence of the disease. Spence[3] and Hutchison[18] believe the skin and nasopharyngeal lesions found in congenital syphilis to be the indirect cause of the nephritis. Paterson and Wyllie[6] report 3 cases with oedema and albuminuria in which the Wassermann reactions were positive. All died. Of the 17 cases of nephritis in infancy reported by Levy,[8] 6 had congenital syphilis, in 2 of which he attributes the nephritis to mercurial treatment.

It is evident therefore from the literature that congenital syphilis may be a cause of nephritis in infancy but conclusive proof has not been adduced that renal oedema, in the absence of manifest signs of lues, is due to syphilis.

In this part of the work are discussed the cases of nephritis, 10 in number, occurring in infants under 18 months admitted to the Royal Hospital for Sick Children during the past 3 years. The cases described constitute 0.4 per cent. of total admissions to the medical wards of the same age period and 5.5 per cent. of all cases of acute nephritis under 13 years.

Case 193, a boy aged 9 months. Good family history. Normal pregnancy and labour. He was breast-fed and throve well till a week before admission when oedema, first noticed in the face, appeared. On admission on 18.2.33 he was found to be a fairly well-nourished child, afebrile, with marked anasarca and ascites present. The Wassermann reaction was negative. Urine - Albumin 20 parts Esbach: the guaiac reaction was positive. Casts and red blood corpuscles were very numerous.

The biochemistry of this case is of particular interest because of the fact that 9 observations were made on the serum proteins during the course of the disease until recovery was established. As can be seen from Table 28 a close relation exists between the serum oncotic pressure level and the extent of the oedema. A high protein diet

TABLE 28.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Weight in Kilos.	Remarks.
19.2.33	3.67	1.80	1.87	28.0	12.5	10.5	Oedema ++
27.2.33	4.24	1.80	2.44	27.0	13.3	10.7	Oedema ++
13.3.33	3.92	2.38	1.54	27.2	15.2	10.7	Orchitis. Fever.
22.3.33	4.34	2.19	2.15	20.0	15.0	10.3	Orchitis. Fever.
24.3.33	6.22	2.16	4.05	25.3	17.5	9.5	Oedema less.
29.3.33	6.78	2.24	4.54	25.0	18.7	8.4	Testicular abscesses.
10.4.33	5.83	2.93	2.89	41.6	20.2	8.2	No oedema.
13.4.33	5.86	3.54	2.32	37.0	22.7	-	No oedema.
25.9.33	6.99	4.18	2.81	27.0	26.9	-	No oedema. Urine clear.

containing 68 gm. protein per day or about 8 gm. per kilo. body weight was given for 4 weeks. From the time of the first observation calculated serum oncotic pressure rose steadily. When it reached 20.2 mm. Hg. no oedema was observed (Table 28 and figure 35). At that point the albumin in the urine had fallen to 1 gm. per litre.

At first glance cure in this case may seem to be due to the administration of a diet high in protein for which some observers claim good results in the treatment of nephrosis and the nephrotic syndrome of glomerulo-nephritis. It is, however, well known that spontaneous rise of serum proteins may occur and in this case after 4 weeks of high protein feeding the diet was changed to half milk, providing only 2.0 gm. of protein per kilo. body weight (see figure35) and this did not interfere with the rise of serum proteins. It is also known that infections may cause a rise in serum globulin (Peters[19] and Eisenman). In this case the development of suppurative orchitis probably accounted for the very high globulin found on 24.3.33 and 29.3.33. (Table 28). If the theory of Epstein[20] and others that the nephrotic syndrome is a metabolic upset be correct and that the normal production of serum proteins is interfered with then it is possible that an infection may act as a stimulus to the production of serum proteins, but the possibility of rise in serum albumin being spontaneous must not be lost sight of as a steady rise occurred from the first blood observation. The

non-protein nitrogen of the blood was normal save on the occasion when it reached 41.6 mgm. per cent.. This slight rise above the normal level was possibly associated with the suppurative process.

No red blood corpuscles were seen after the 8th day in hospital. Seven months after the onset of the illness the child appeared to be perfectly well. The urine contained no abnormal constituents and serum proteins were normal.

Case 186, a female aged 1 year and 3 months. An only child of healthy parents who was breast-fed till 9 months and throve well. Six weeks before admission both ears discharged pus for 4 weeks and the child became pale, listless and vomited occasionally. Four weeks before admission a purulent nasal discharge began. No history of oedema. Admitted to hospital on 7.9.33. She was a pale child who was fairly well nourished. Face puffy; slight pitting over the tibiae present. Nothing abnormal was detected in the heart, lungs, nervous system or abdomen. Ophthalmoscopic examination was negative. The urine contained 3.5 gm. of albumin per litre, red blood cells were exceedingly scanty and some casts were seen. Culture of the urine was negative.
9.9.33. Body weight remained stationary but slight fever developed, temperature reaching 100°F. with the appearance of a purulent nasal discharge. The Wassermann reaction was negative. The systolic blood pressure was 98 mm. Hg.. Oedema was unchanged.
18.9.33. Oedema absent. Passage of loose green stools commenced on 17.9.33 with frequent vomiting.
21.3.33. Child removed from hospital against advice.
1.2 Kg. in weight was lost during the past 4 days. Enteritis was still present.
On 14.10.33 the child was seen as an out-patient. Since the last note enteritis had continued and the baby appeared to be very dehydrated and ill. A catheter specimen of urine showed no albumin, casts or blood. The mother refused to leave the child in hospital and the child died at home 5 days later. (No examination of the blood was made on 14.10.33).

Blood Chemistry Findings.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Oedema	Remarks.
9.9.33	3.80	2.40	1.40	29.2	15.2	+	
18.9.33	5.21	2.13	3.08	28.0	16.0	-	Enteritis.

It can be seen that rise in serum oncotic pressure was but slight. Even at as low a level as 16.0 mm. Hg. oedema was absent. It is probable that the dehydrating influence of the enteritis played a large part in the disappearance of the oedema.

Case 194, a boy 6 months old. The first pregnancy ended in a miscarriage. The patient's three brothers and sisters were well and the family history was good. Breast-fed for 1 month, he afterwards received Nestlés milk. At 5 months old he took chicken-pox which was followed a week later by enteritis. Two weeks later generalized oedema was observed and he was admitted to hospital on 16.6.31.

Patient was a well-nourished infant with oedema involving the face, sacrum, scrotum, thighs and legs. Ascites was present. In the lungs some rhonchi were found. In the heart and nervous system no abnormality was detected. The urine contained 11 gm. of albumin per litre and the guaiac reaction was positive. Numerous red blood corpuscles and casts were present. Urine culture was negative. The stools were loose and green. Ophthalmoscopic examination was negative. On 16.6.31 the systolic blood pressure was 85 mm. Hg..

Blood chemistry: Total protein..... 4.09 gm.%
Albumin..... 1.63 "
Globulin ..... 2.46 "
Calculated Oncotic Pressure.. 12.4 mm. Hg.
Non-protein nitrogen..... 27.5 mgm.%.

From the day of admission enteritis continued and the child steadily lost weight - 2.3 Kg. - became dehydrated and died on 24.6.31.

Post-mortem examination showed enteritis and hypostatic congestion of lungs. A mixed type of nephritis was present. On histological examination the changes were chiefly tubular. No evidence of congenital syphilis was found.

Case 192, a male aged 1 year and 4 months. The tenth child of healthy parents. Second child was still-born. The family history was not relevant. Breast-fed and throve till 11 months when he developed ? encephalitis and was in the Royal Hospital for Sick Children for 6 weeks. At that time the Wassermann reaction of blood and cerebrospinal fluid was found to be negative. The urine contained no abnormal constituents. On dismissal he appeared to have made a good recovery. A week before second admission generalised oedema was observed but no abnormality of the urine was observed by the mother. Readmitted to Royal Hospital for Sick Children on 30.8.32 with oedema of the face, sacrum and legs. Ascites was also present. The urine contained much albumin, 14 gm. per litre and the guaiac reaction was positive. Numerous red blood cells and casts were present. Urine culture was negative.

31.8.32. Blood chemistry.

Total proteins.....	4.54 gm.%.
Non-protein nitrogen...	24.1 mgm. %

During a stay in hospital of 22 weeks oedema was present in varying degree for 16 weeks. It diminished during administration of ammonium chloride, during a febrile period due to otitis media but also at other times for no apparent reason; the reduction of oedema could not be related to any form of diet or therapeutic measure. Haematuria persisted for 15 weeks. Albuminuria was present throughout and the child was dismissed as a chicken-pox contact while the urine still contained much albumin. Blood was absent.
6.6.33. The child reported in the out-patient department much improved. A cough had been present for 2 weeks. No oedema had been observed. The temperature was 100°F. and numerous rhonchi were audible in both lungs. The urine contained a trace of albumin but no casts nor red cells were seen.

Blood chemistry.	Total Protein.....	9.95 gm.%
	Albumin.....	5.83 "
	Globulin.....	4.12 "
	Calculated Oncotic Pressure..	37.8 mm. Hg.
	Non-protein nitrogen.....	25.0 mgm.%.

While in this case serum albumin and serum globulin were not estimated separately during stay in hospital it can be seen that there was a rise of serum total protein to above normal level. This is due to increase in both albumin and globulin, the high globulin being probably explained by the presence of the respiratory infection which later was found to be whooping cough.

Case 188, a male aged 4 months. The family history was good. He was breast-fed and throve till 2 weeks before admission when puffiness of the face was noted. Admitted to hospital on 4.2.33 with oedema of face, sacrum and legs and some ascites. The heart, lungs and nervous system showed no abnormality. The urine contained much albumin but casts were not numerous and red cells were very scanty. The urine culture was negative.

6.2.33. Blood chemistry.

Total Protein.....	4.84	gm.%
Albumin.....	1.60	"
Globulin.....	3.24	"
Calculated Oncotic Pressure..	13.3	mm. Hg.
Non-protein Nitrogen.....	50.0	mgm.%.

12.2.33. Numerous loose stools were passed during stay in hospital and on 14.2.33 he became comatose and began to have convulsions. Lumbar puncture was performed and the cerebrospinal fluid was found to be normal. Death occurred on the same date.
Post-mortem examination showed marked oedema of the brain. No evidence of congenital syphilis was found. Areas of intense congestion were present in the small bowel. Both kidneys were swollen and the capsule was slightly adherent: histologically subacute nephritis was present with well-marked tubular involvement and extensive proliferation of the interstitial tissue with foci of round-cell infiltration.

There are two possibilities:- (a) the convulsions may have been terminal and due to an intense toxaemia arising from bowel infection: (b) the convulsions may have been symptomatic

of true uraemia and it is somewhat significant that the only instance of convulsions in patients under 18 months occurred in the child whose kidneys showed interstitial changes. This together with the increased concentration of non-protein nitrogen in the blood lends some support to this view.

Case 191, a boy aged 1 year and 4 months. He was a healthy infant who was breast-fed for 1 month, from that age received cow's milk till 1 year and then a mixed diet. Four weeks before admission he began to refuse food and two weeks before admission oedema of the face was noted. On admission on 7.9.33 he was found to be a small child with a moderate degree of oedema of the legs, face and sacral region. Ascites was present. The blood pressure was 100 mm. Hg. systolic. Ophthalmoscopic examination was negative. The urine contained albumin up to 12 gm. per litre but red cells were very scanty although casts were numerous. The Wassermann reaction was negative. Urine culture was negative. As previous experience had shown that fatal enteritis was very prone to supervene in such cases, this child was dismissed from hospital although the urine still contained albumin, 4 gm. per litre, and there was still slight oedema. On dismissal the child attended the out-patient department and was observed to weather an attack of diarrhoea shortly afterwards. Two weeks following dismissal the urine was found to be quite free of albumin. The oedema had disappeared entirely during the attack of diarrhoea and never returned. Since that time the child has been perfectly well.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Wt. Kg.	Remarks.
8.9.32	4.51	2.92	1.59	28.5	18.3	8.4	Oedema +
14.9.32	5.63	2.25	3.38	35.7	17.1	7.7	Oedema ±
15.5.33	7.31	5.32	1.99	31.2	31.8	-	Oedema 0. Urine clear.

The diminution in oedema at the time of the second observation (14.9.32) while serum oncotic pressure had fallen slightly may be explained by the fact that while in hospital the child was receiving a diet of milk, containing much less salt than is found in mixed diet. The rise in globulin on 14.9.33 may have been indicative of regeneration of the serum proteins but more probably was a reaction to the bowel infection.

Case 190, a male aged 1 year. He was an only child of healthy parents who was breast-fed and throve till 2 weeks before admission when oedema was observed. Admitted to hospital on 26.10.31. The patient was a big child with marked oedema involving the face, chest wall, lumbar region and legs. Ascites also was present. The heart, lungs and nervous system showed no abnormality. Ophthalmoscopic examination was negative. The systolic blood pressure was 98 mm. Hg.. The urine contained much albumin and the guaiac test was positive. Casts and red cells were numerous. Urine culture was negative.

Blood chemistry.	Total Protein.....	4.23	gm.%
	Albumin.....	1.96	"
	Globulin.....	2.27	"
	Calculated Oncotic Pressure..	13.9	mm.Hg..
	Non-protein Nitrogen.....	36.3	mgm.%.

On the day after admission severe enteritis developed, much oedema was lost but some was still present along with much albumin and blood in the urine when the child died 6 days after admission. Permission for an autopsy was refused. This child died of enteritis complicating nephritis.

Case 189, a female aged 7 months. The family history was good. She was fed on whole cow's milk and progressed well till 3 weeks before admission when swelling of the face was noticed and a week before admission the abdomen became prominent. Admitted to the Royal Hospital for Sick Children on 23.6.31. She was a small child with moderate oedema of feet: slight ascites and puffiness of the face were present.

The urine contained much albumin - 11 gm. per litre - scanty casts and red cells. Culture of the urine was negative. 27.6.31. The child died, stools being frequent and vomiting persistent for the past 4 days. No oedema was then apparent, 1.70 Kg. having been lost in 4 days. No blood examination was made on this case.
Autopsy:- A few patches of broncho-pneumonic consolidation were present in the lungs. No evidence of congenital syphilis was found. Histological report:- Early acute glomerulo-nephritis with marked cloudy swelling of the tubular epithelium present.

Case 187, a male aged 8 months. The family history was good. He was breast-fed and throve till 4 weeks before admission when generalised oedema was observed. The urine at that time was reported to be dark in colour. Admitted to hospital on 17.10.31 with a marked degree of oedema involving face, legs and lumbar region. Slight ascites was present. Examination of the heart, lungs and nervous system showed no abnormality. The urine contained albumin, 15 gm. per litre, the guaiac reaction was negative and red cells were scanty. Casts were fairly numerous.

21.10.31. Blood chemistry.

Total Protein.....	6.78	gm.%
Albumin.....	2.66	"
Globulin.....	4.12	"
Calculated Oncotic Pressure.	20.4	mm. Hg..
Non-protein Nitrogen.....	29.1	mgm.%.

On 22.10.31 oedema was much less but fever, present since day after admission, increased steadily and signs of pneumonia were noted on 23.10.31. The stools became loose and the child lost oedema rapidly and died nine days after admission.
Autopsy:- Both lungs showed broncho-pneumonia. Brain oedematous. No evidence of syphilis detected. Histological report of kidneys:- Early acute glomerulo-nephritis was present with well-marked swelling of the convoluted tubules.

This child died of pneumonia complicating acute nephritis. From the high serum oncotic pressure level it is likely that blood examination was carried out after diuresis had begun. This is borne out by the rapid loss of oedema which was observed on the following day. Presumably the pneumonia was responsible

for the increase in globulin which compensated for the deficiency in albumin and thus allowed serum oncotic pressure to reach a level compatible with diuresis.

Case 195, a boy aged 1 year and 1 month. The first and third pregnancies ended in still-births. He throve till a fortnight before admission when oedema developed and the urine was observed to be dark in colour. Admitted to hospital on 5.4.34 with generalised oedema and ascites. No abnormality was detected in the heart or lungs. The urine contained albumin - 20 grams per litre - and much blood: casts were numerous. The Wassermann reaction was negative. The child was afebrile till the development of a cellulitis of the abdominal wall on 29.4.34 which proved fatal on 1.5.34.

Blood Chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Weight in Kilos.
6.4.34	4.32	2.46	1.86	16.1	65.2	10.5
11.4.34	4.91	2.52	2.39	17.2	39.9	10.3
1.5.34	4.27	1.39	2.88	11.7	29.1	10.8

In this case a moderate degree of azotaemia was present on the first blood examination but not subsequently. Permission for autopsy was refused.

Summary.

The course of the disease was, in the absence of infection, afebrile, and the infants were comparatively bright and did not present the features of a toxaemic illness. The urine contained large quantities of albumin and casts. Haema-

turia would seem to vary in amount with the duration of the illness. It was present in every case on admission as seen in table 29 where the findings are summarized. Cardio-vascular changes were absent. Blood pressure records, made in only 4 instances, were of questionable value as the infants invariably cried during the determination. Oedema with ascites was marked in all the cases save one, where it was confined to the face and legs.

There is one feature in this small series which appears to be more constant in its occurrence than in the nephritis of

TABLE 29.

Case	Urine on Admission.				Duration of illness prior to admission. Weeks.	Result.
	Albumin gm. per litre.	Reaction with guaiac.	Micro-scopic blood.	Casts		
193	20.0	+	+	+	1	Well.
186	3.5	0	$\bar{+}$	$\bar{+}$	12	Death. Enteritis.
194	11.0	+	+	+	1	Death. Enteritis.
192	14.0	+	+	+	1	Well.
188	+++	0	$\bar{+}$	+	2	Death. Enteritis.
191	12.0	0	$\bar{+}$	+	4	Well.
190	+++	+	+	+	2	Death. Enteritis.
189	11.0	0	$\bar{+}$	+	3	Death. Enteritis.
187	15.0	0	$\bar{+}$	+	5	Death. Pneumonia.
195	20.0	+	+	+	2	Death. Cellulitis.

Oedema present in all cases.

older children. That is the obstinacy of the oedema. The dominating feature was the great reduction of serum proteins and the persistence of oedema and heavy albuminuria. This contrasts with the state of affairs in nephritis of older children in whom the persistence of oedema is the exception rather than the rule and this apparently is the feature which gives the nephritis of infancy its grave prognosis, the tendency to infection in all oedematous subjects being well known. Eight of the 10 cases showed infection of the respiratory or alimentary tract while in hospital, the 9th developed a double streptococcal orchitis and the 10th a cellulitis.

One might also comment on the absence of uraemic signs. In one case (188) generalized convulsions did occur and death followed after a period of coma. In view of the elevation of the non-protein nitrogen of the serum and the histological findings (extensive interstitial changes) in this case the diagnosis might be one of true uraemia. In no instance did the pseudo-uraemic or hypertensive type of convulsions, seen so frequently in older children, occur.

Syphilis was apparently not a factor. In 5 cases the Wassermann reaction was negative and at post-mortem in other 4 no evidence of lues was found. In the 10th case the Wassermann reaction was not done and permission for a post-mortem examination was refused but there was no evidence of congenital syphilis either from the history or from the clinical examination. Syphilis should not be diagnosed merely from the presence

of oedematous nephritis in infancy in the absence of serological or definite post-mortem evidence.

Perhaps the most salient feature of this investigation is that the serum albumin was reduced below 3.0 gm. per cent. in all the infants in which the serum proteins were estimated. (See table 30). In all the cases which recovered it was observed that a return to the normal level occurred as the oedema disappeared. In an other patient permission to

TABLE 30.

Ten cases of acute nephritis in infants under 18 months. Initial observations on admission.

Case	Age in years	Oedema	Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%
193	9/12	++	3.67	1.80	1.87	12.5	28.0
186	1,3/12	+	3.82	2.40	1.42	15.2	29.2
194	7/12	++	4.09	1.63	2.46	12.4	27.5
192	1,4/12	++	4.87	-	-	-	24.1
188	4/12	++	4.83	1.60	3.23	13.3	50.0
191	1,4/12	++	4.52	2.92	1.60	18.3	28.5
190	1	++	4.23	1.96	2.27	13.9	36.3
189	7/12	++	-	-	-	-	-
187	8/12	++	6.78	2.66	4.12	20.4	29.1
195	1,1/12	++	4.32	2.46	1.85	16.1	65.2
22 normals under 2 years.			7.08	4.95	2.13	30.1	40.0
24 normals over 2 years			7.42	5.15	2.27	31.5	40.0

obtain a sample of blood after recovery from nephritis was refused but the child was oedema free and the urine contained no albumin.

Non-protein nitrogen was above normal in 2 cases only, (case 188) in which it reached a level of 50 mgm. per cent. and (case 195) 65.2 mgm. per cent.. It may be concluded that azotaemia is not generally present.

Chapter 10.

The "uraemia" of acute nephritis.

During the course of this study a number of cases were met with which showed cerebral manifestations early in the course of acute nephritis. Of recent years it has become fashionable to apply the term hypertensive encephalopathy to the cerebral manifestations which not uncommonly occur in the early stage of an attack of acute nephritis. It is almost certain that no true renal insufficiency, as occurs in chronic interstitial nephritis, is present in these patients and the symptoms have by many authorities been attributed to oedema of the brain.

Nobécourt[1] states that the condition is a common one in acute nephritis of childhood and occurs early in the disease. The prognosis is good. Oedema is not a marked feature but by weighing it can be demonstrated that a considerable degree of fluid retention occurs. He makes the important statement that although apparently all the factors found in uraemic cases may be present cerebral manifestations do not necessarily occur. While the non-protein nitrogen of the blood may be normal Nobécourt believes that hypertension is the chief factor in the production of uraemia which he says is due to spasm of the cerebral vessels. Aldrich[2] in a series of 28 cases found haematuria and hypertension present in all. The lowest blood pressures recorded were 118 and 125 mm. Hg. systolic in two

cases aged 3 years and 9 years respectively. He also is of the opinion that the cause is cerebral oedema which may be intracellular. A considerable proportion of his cases showed azotaemia, some with a non-protein nitrogen level of well over 100 mgm. per cent.. Holt[3] states that a blood pressure of 140 mm. Hg. or more is found in association with uraemia. Non-protein nitrogen on the other hand may be normal but is not infrequently greatly increased during a uraemic attack. Where death occurs early a convulsion or myocardial failure is the cause, whereas later pneumonia is frequently responsible for the fatal issue. Boyd[4] stresses the importance of high non-protein nitrogen of the blood in differentiating true uraemia from cerebral manifestations due to oedema of the brain. In the latter she says there is no marked degree of azotaemia. Blackfan[5] and McKhann conclude that uraemia is prone to occur when the blood pressure reaches 140 mm. Hg. but state that the rapidity of the rise is also of importance. One of their cases, aged three years, was an apparent exception as uraemia occurred with a blood pressure of only 118 mm. Hg. If however the normal at three years is allowed to be 70 mm. Hg., 118 mm. Hg. is 170 per cent. of normal for the age. In their cases azotaemia, sometimes marked, occurred in about 50 per cent.. They believe that oedema in nephritis is intracellular and that cerebral manifestations may be due to imbibition of fluid by the cells of the brain. Evans[6] reports an incidence of 8 per cent. in 90 cases of acute nephritis of

which four were fourteen years old or under. All showed rise of blood pressure, haematuria and oedema but in only one was there azotaemia, which was not marked. Ophthalmoscopic examination showed merely fulness of veins, no haemorrhages being seen. Convulsions were present in all the cases, improvement taking place, with fall in blood pressure, following venesection and lumbar puncture. He considered the prognosis to be good. Kylin[7] sums up in regard to pathogenesis. In favour of cerebral oedema being the cause he makes the following points:-

(1) A limited fluid intake without salt is the best form of treatment.

(2) The pressure of the cerebrospinal fluid is usually raised.

(3) Oedema is the rule.

(4) Lumbar puncture results in clinical improvement.

On the other hand against cerebral oedema being the cause he states that:-

(1) Oedema may be absent.

(2) Cerebrospinal fluid pressure may be normal.

(3) Oedema may be marked without uraemia.

Kylin[7] however holds that uraemia may occur without rise in blood pressure.

In the present series of 100 cases 12 patients showed manifestations of uraemia. The clinical and biochemical findings are discussed in detail.

Case 7, a male aged 10 years. Six days before admission he developed oedema of the hands and face and four days later complained of headache and began to vomit frequently. On the same night convulsions began. On admission on 6.5.33 he was comatose: oedema of the face only was present: blood pressure was 140 per cent. of normal. The urine contained much blood and a moderate quantity of albumin: on ophthalmoscopic examination he showed dilatation of the retinal veins. Blood (50 c.c.) was removed by venipuncture: lumbar puncture under chloroform anaesthesia was also performed, 50 c.c. of fluid being withdrawn under increased pressure. By next day the boy was apparently normal mentally and no further fits occurred.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure per cent. normal	Remarks.
6.5.34	6.84	4.41	2.43	23.2	27.6	140	Uraemia. Oedema +
8.5.34	6.71	5.04	1.67	51.7	30.4	114	No uraemia No oedema.

A urea concentration test on 8.5.34 only two days after admission gave the following result:-

Before urea..... 3.45 gm. %
1 hour after.... 4.12 "
2 hours after... 4.52 "

No further test was carried out. A small quantity of albumin in the urine was present on dismissal on 1.6.33.

Case 40, a boy aged 8 years. Five days before admission he complained of headache and began to vomit. Drowsiness was marked and next day oedema of the face was noted. Twelve hours before admission convulsions began. On admission on 17.5.34 he was drowsy and complained of headache: oedema of the face and feet was present. Much albumin and blood were present in the urine. Ophthalmoscopic examination showed fulness of the retinal veins. Blood pressure was 166 per cent. of normal. 60 c.c. of blood and 25 c.c. of cerebrospinal fluid under in-

creased pressure were removed. The blood pressure then fell to 140 per cent. of normal but rose again to 170 per cent. of normal on the next day. Convulsions recurred and on 19.5.34 blindness developed and a hemiplegia appeared involving the right arm, leg and face. Lumbar puncture was again performed and 80 c.c. of blood were removed. The blood pressure fell to 130 per cent. of normal and no further convulsions occurred. On 6.6.33 the blood pressure was at a normal level. The paralysed leg still showed weakness on 10.7.34 but complete recovery had occurred by 23.8.34. The cerebro-spinal fluid in this case gave normal findings and the Wassermann reaction of the blood and fluid was negative.

Blood chemistry:-

Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Blood Pressure % of Normal.	Calculated Oncotic Pressure. mm.Hg.	Remarks.
17.5.33	8.86	3.67	5.19	82.2	166	27.4	Convulsions Vomiting marked. Oedema ±
19.5.33	11.14	4.36	6.78	92.3	170	33.5	Condition unchanged.
6.6.33	-	-	-	34.2	110		No uraemia. No oedema.

Urea concentration tests gave the following results:-

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
29.5.33	1.13	1.17	1.30
12.6.33	1.37	1.40	1.60
5.7.33	1.40	1.75	1.78

A trace of albumin was still present in the urine on dismissal on 8.9.33.

Case 55, a boy aged 12 years. Four days before admission he began to have severe headaches. Three days after, oedema of the face appeared, he became drowsy and said that he could not see.
Admitted on 1.1.33, he was a well-nourished boy who was delirious and apparently blind. Oedema was limited to the face. The urine contained much albumin and blood. Ophthalmoscopic examination revealed fulness of the retinal vessels and two small haemorrhages in the right fundus. The blood pressure was 184 per cent. of normal. Blood (150 c.c.) and cerebrospinal fluid (20 c.c.) were removed, the latter under increased pressure. On the same evening the blood pressure was 146 per cent. of normal. By 3.1.33 vision was still impaired but drowsiness was much less and by 5.1.33 drowsiness was gone and blood pressure was almost normal.

Blood chemistry:-

Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of Normal.	Remarks.
1.1.33	6.37	4.16	2.21	30.0	26.1	184	Uraemia. Oedema ∓.
5.1.33	6.84	4.45	2.39	31.1	27.8	120	No uraemia. No oedema.
14.1.33	7.99	4.67	3.32	42.3	30.3	110	
3.2.33	7.02	4.76	2.26	27.2	29.5	110	

The urea concentration test one month after admission to hospital gave the following result.

6.2.33.	Before urea.....	1.55 gm.%
	1 hour after....	2.48 "
	2 hours after...	2.31 "

Recovery was apparently complete, the urine being free of albumin on dismissal on 9.2.33.

Case 81, a boy aged 8 years. Four days before admission he developed oedema of the face and legs. Two days later he became very drowsy and vomited frequently. On admission on 30.10.32 oedema of the face and legs was present, drowsiness

was marked, and a few hours later he took a convulsion. The blood pressure was 170 per cent. of normal. Ophthalmoscopic examination showed no abnormality of the fundi. Haematuria and albuminuria were marked. After the removal of blood (80 c.c.) and cerebrospinal fluid (25 c.c.), the latter under increased pressure, the blood pressure fell to 125 per cent. of normal. By 3.11.32 all drowsiness was gone and on 7.11.32 the blood pressure was normal.

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of Normal.	Remarks.
30.10.32	8.30	4.04	4.26	96.7	28.1	160	Uraemia. Oedema +.
3.11.32	6.71	4.32	2.39	51.7	27.1	130	No uraemia
7.11.32	5.79	3.47	2.32	49.1	22.3	110	No uraemia
11.11.32	7.31	3.87	3.44	30.5	26.1	110	No uraemia
29.11.32	7.81	6.29	1.52	25.0	36.7	110	No uraemia

Urea concentration tests gave the following results:-

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
29.11.32	0.92	1.86	2.55
4.1.33	1.06	2.14	3.67

On dismissal the urine contained no albumin. Recovery was presumably complete.

Case 37, a boy aged 10 years. Four hours before admission he began to have convulsions following cough and fever of 10 days' duration. On admission on 28.1.33 he was very drowsy but could be roused. Oedema of legs and face was present and

the urine contained much blood and albumin. Cardiac dulness was increased to right and left of the mid-line and a V.S. murmur was audible. The liver was 3 fingers-breadth below the costal margin. No ascites was detected. The blood pressure was 150 per cent. of normal. Ophthalmoscopic examination revealed no abnormality. Under chloroform anaesthesia, blood (80 c.c.) and cerebrospinal fluid (50 c.c.), the latter under increased pressure, were withdrawn. On 30.1.33 blood pressure was still 156 per cent. of normal but the patient was clearer mentally and cardiac dulness was within normal limits. An uninterrupted recovery followed.

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of normal.	Remarks.
28.1.33	6.38	4.17	2.21	29.8	26.0	180	Uraemia. Oedema + .
2.2.33	7.99	5.60	2.39	72.0	34.1	-	No uraemia.
9.2.33	6.62	4.10	2.52	58.8	26.0	110	No uraemia. No oedema.
25.2.33	6.30	4.16	2.14	45.4	25.9	110	No uraemia.

Urea concentration tests gave the following results:-

Date	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
2.2.32	1.23	1.87	0.3
10.2.32	1.65	2.41	2.75

On dismissal on 24.3.32 a trace of albumin was still present in the urine but otherwise the child was quite well.

Case 100, a boy aged 11 years. He was well till a week before admission when he lost his appetite, complained of headache and began to vomit occasionally. On the day before admission he complained of dimness of vision and in the evening twitching of the legs was observed. Two hours before admission generalized convulsions began and he lost consciousness. On admission on 15.7.33 he was unconscious. No oedema was detected. A catheter specimen of urine contained blood, albumin and epithelial casts. The heart was normal. In the lungs much râle was audible at both bases but chiefly the right. The blood pressure was 130 per cent. of normal. Blood (110 c.c.) and cerebrospinal fluid (40 c.c.) were withdrawn, the latter under slightly increased pressure. Intravenous injection of 25 c.c. of 10 per cent. magnesium sulphate caused no improvement and the patient died seven hours after admission.

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of Normal.
15.7.33	10.06	3.98	6.08	190.0	30.4	130.

At autopsy an acute nephritis was found affecting both glomeruli and tubules. In addition there was broncho-pneumonia affecting both the lungs with areas of consolidation chiefly of the right lower lobe.

Case 185, a boy aged 10 years. A week before admission oedema of the face was observed. Six days later he complained of headache, dimness of vision, and began to vomit. On admission on 23.12.32 he was found to be a well-nourished boy who was rather drowsy and complained of headache. Much oedema was present with some ascites: occasional twitching of the face was noted: the urine contained blood, albumin and casts; the heart was normal. The blood pressure was 150 per cent. of normal. Blood (130 c.c.) and cerebrospinal fluid (30 c.c.) were withdrawn, the latter under much increased pressure. This had an immediate good effect, headache being relieved and twitching not recurring. Ophthalmoscopic examination showed undue prominence of the retinal vessels.
27.12.33. The blood pressure was 118 per cent. of normal.

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % normal	Remarks.
24.12.32	7.47	-	-	80.0	-	150	Uraemia. Oedema ++ .
27.12.32	6.72	-	-	49.0	-	118	No uraemia.
12.1.33	7.73	4.66	3.07	89.5	29.9	90	No uraemia. No oedema.
19.1.33	6.23	3.87	2.36	30.0	24.6	-	No uraemia.
30.1.33	6.19	3.53	2.66	37.7	23.1	98	No uraemia.
1.3.33	7.34	4.66	2.68	26.0	29.4	-	No uraemia.

Urea concentration tests gave the following results:-

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
12.1.33	1.73	1.73	1.73
30.1.33	1.46	1.82	2.08
1.3.33	1.76	1.76	2.10

The urine on dismissal contained a trace of albumin but otherwise the boy was well.

Case 29, a boy aged 10 years. Ten days before admission he became listless and began to vomit. Four days later the face became puffy and the urine was observed to be dark red in colour. On the day before admission twitching of the arms and legs was observed. On admission on 7.9.33 the child was rather drowsy and oedema was marked with ascites. The cardiac dulness was not increased but a basal V.S. murmur was present.

The urine contained much blood and albumin. On retinoscopy no abnormality of the fundus was detected. The blood pressure was 148 per cent. of normal for the age. Though there was still some vomiting and drowsiness no twitching was noted and the blood pressure fell to 132 per cent. of normal by 13.9.33. It was however observed that the non-protein nitrogen which reached the high level of 280.0 mgm. per cent. on admission was still 222.0 mgm. per cent. on 13.9.33. On 16.9.33 the boy became cyanosed and much more drowsy and the pulse rate rose. Cardiac dulness was not increased. Vomiting increased in frequency but no convulsions were observed. The blood pressure rose to 164 per cent. of normal. Blood (100 c.c.) and cerebrospinal fluid (25 c.c.) were withdrawn, the latter under increased pressure. Non-protein nitrogen in this specimen of blood was 133.0 mgm. per cent. showing a marked fall in spite of the increase in the severity of the uraemic manifestations. CO_2 was 56.8 vols. per cent. Following the removal of blood and cerebrospinal fluid he became less drowsy and cyanosed: the blood pressure fell to 134 per cent. of normal. Next day it rose to 144 per cent. of normal without any recurrence of uraemic symptoms. 28.9.33. No uraemic manifestations were present but blood pressure was still 146 per cent. of normal.

Blood chemistry:-

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of normal.	Remarks.
8.9.33	7.62	2.39	5.23	280.0	20.5	148	Oedema ++ . Drowsy.
13.9.33	7.51	3.44	4.08	222.0	24.6	132	Oedema + . Drowsy.
16.9.33	7.61	3.69	3.92	133.0	25.8	164	Oedema + . Vomiting. Very drowsy.
28.9.33	6.27	3.96	2.31	30.4	25.0	146	Oedema + . No uraemia.
4.10.33	7.36	3.57	3.79	23.0	24.9	120	No oedema. No uraemia.
18.11.33	-	-	-	31.8	-	120	No oedema.
19.3.34	8.31	5.39	2.92	20.0	33.7	110	No oedema.

Urea concentration tests gave the following results:-

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
10.10.33	0.6	1.63	2.5
23.3.34	1.63	1.93	1.95

In this patient a positive guaiac reaction was obtained for nearly 6 months after the onset of the illness and a trace of albumin was still present on dismissal on 23.3.34 although by that time no red blood cells were observed.

Case 12, a boy aged 8 years. Five days before admission he complained of sore throat. Swelling of the face and legs appeared two days later and the urine was observed to be dark red in colour. On the day of admission vomiting was frequent. On admission on 29.1.31 generalized oedema and ascites were present. The heart and lungs were normal: the urine contained much blood and albumin: very drowsy and apparently blind. The blood pressure in this case was not taken. Blood (200 c.c.) and cerebrospinal fluid (25 c.c.) were withdrawn, the latter under increased pressure. Almost immediately a beneficial effect was noted. On 2.2.31 the systolic blood pressure was 110 per cent. of normal and retinoscopy was negative. No evidence of uraemia was then present and recovery was uninterrupted.

Blood chemistry:- 29.1.31.

Total Protein.....	5.60	gm.%
Albumin.....	3.60	"
Globulin.....	2.00	"
Calculated Oncotic Pressure	22.6	mm. Hg..
Non-protein Nitrogen.....	40.6	mgm. %.

No renal function tests were made. He was dismissed with the urine free of albumin on 2.4.31.

Case 15, a girl aged 4½ years. Seven days before admission she developed oedema of the face and legs. Two days before admission she became acutely ill; cough was a prominent feature. Admitted on 14.1.31. Oedema was general with ascites: cyanosis was marked and much râle was present at the bases of the lungs: she was very drowsy. The blood pressure was 200 per cent. of normal and on ophthalmoscopic examination the retinal veins were observed to be prominent. The urine contained much albumin and blood. On 15.1.31 her condition became worse and the child was unconscious. Blood (80 c.c.) and cerebrospinal fluid (40 c.c.) were withdrawn, the latter under moderate increase of pressure. No improvement resulted and the child died 12 hours later.

Blood chemistry:- 15.1.31.

Total Protein.....	6.02 gm. %.
Albumin.....	3.71 "
Globulin.....	2.31 "
Calculated Oncotic Pressure	23.5 mm.Hg..
Non-protein Nitrogen.....	56.0 mgm.%.
Blood Pressure % of Normal...	200.0

Autopsy showed acute nephritis affecting both tubules and glomeruli. The heart was normal but marked pulmonary oedema was present.

Case 88, a boy aged 11 years. Three days before admission he was observed to be puffy about the eyes and the urine was noted to be dark. On the day before admission he began to have convulsions. Admitted on 8.2.31. Oedema of the face only was present and the patient was drowsy and very irritable when roused. The heart and lungs showed no abnormality. A catheter specimen of urine showed blood and albumin to be present. After admission convulsions recurred and blood (180 c.c.) and cerebrospinal fluid (30 c.c.) were removed. On 8.2.31 further convulsions occurred and a further 60 c.c. of blood were withdrawn and the blood pressure, not previously taken, was found after venipuncture to be 120 per cent. of normal. Ophthalmoscopic examination showed congestion of the retinal veins to be present. Thereafter no further uraemic manifestations were observed and the blood pressure fell to within normal limits.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure per cent. of normal.
9.2.31	6.71	5.32	1.39	50.8	31.3	-
17.2.31	-	-	-	32.4	-	98

Urea concentration tests gave the following results:-

Date.	Before urea. gm.%	1 hour after. gm.%	2 hours after. gm.%
11.2.31	4.08	3.60	2.22
17.2.31	2.68	2.22	1.20

On dismissal on 1.4.31 the urine was free of albumin and the child was well.

Case 41, a boy aged 9 years. On 14.12.33 he developed otitis media and some days later became rather drowsy. On 7.1.34 he complained of headache and began to vomit and eight hours later took a convulsion. From then he did not recover consciousness and had several more convulsions. Lumbar puncture at home on the day of admission showed a normal fluid under increased pressure. On admission he was a well-nourished boy with some puffiness of the face and oedema of the legs. He was quite unconscious. No abnormality was detected in the heart or lungs. The urine contained much blood, albumin and many casts. The blood pressure was 130 per cent. of normal. The right knee-jerk was exaggerated, clonus was present and the plantar response was flexor. Ophthalmoscopic examination was negative. 100 c.c. of blood were removed without any immediate benefit resulting.
9.1.34. There was now no evidence of a pyramidal tract lesion but as he was still very drowsy and vomiting frequently 30 c.c. of cerebro-spinal fluid, under increased pressure, were removed and a further 100 c.c. of blood.
10.1.34. He was much less drowsy. The blood pressure was now 96 per cent. of normal.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Blood Pressure % of Normal.	Remarks.
8.1.34	8.36	3.51	4.85	88.2	26.1	130.0	Oedema + . Uraemic.
10.3.34	-	-	-	31.2	-	100.0	No oedema.

A urea concentration test gave the following result:-

10.3.34.	Before urea....	1.4 gm. %.
	1 hour after...	2.12 "
	2 hours after..	2.28 "

On 24.3.34 the child was dismissed well, the urine containing neither blood nor albumin.

Summary.

The findings are summarized in table 31.

Oedema was found in all but one of the cases and was well marked in seven of them: it behaved as in acute nephritis without cerebral manifestations. The fact that it was frequently observed after disappearance of uraemia and that in case 29 it had diminished when cerebral manifestations reached a maximum indicate that cerebral oedema is not a likely cause of this type of uraemia. Furthermore in the nephrotic cases of the present series uraemia was not seen and it is known that at autopsy in such cases oedema of the brain is marked.

Cardio-vascular manifestations. Cardiac enlargement was encountered in one case only. Examination of the fundi in eleven of the cases showed fulness of the veins of the retina in six patients. In case 55 only was haemorrhage observed.

The blood pressure when taken before venipuncture and lumbar puncture was never below 140 per cent. of normal save in one

TABLE 31.

Admission findings in cases showing cerebral manifestations of acute nephritis.

Case	Sex	Age yrs.	Blood Pressure % of normal.	Oedema	Haematuria	Total Protein gm.%	Albumin gm.%	Globulin gm.%	N.P.N. mgm.%	Calculated Oncotic Pressure. mm.Hg.	Ophthalmoscopic examination.
7	M.	10	140	∓	+	6.84	4.41	2.43	23.2	27.6	Vessels prominent.
40	M.	8	166	+	+	8.86	3.67	5.19	82.2	27.4	Vessels prominent.
55	M.	12	184	∓	+	6.37	4.16	2.21	30.0	26.1	Haemorrhages.
81	M.	8	170	+	+	8.30	4.04	4.26	96.7	28.1	Nil.
47	M.	10	150	+	+	6.38	4.17	2.21	29.8	26.0	Nil.
100	M.	11	130	0	+	10.06	3.98	6.08	190.0	30.4	Not examined.
185	M.	10	150	++	+	7.47	-	-	80.0	-	Vessels prominent.
29	M.	10	148	++	+	7.62	2.39	5.23	280.0	20.5	Nil.
12	M.	8	-	++	+	5.60	3.60	2.00	40.6	22.6	Nil.
15	F.	4½	200	++	+	6.02	3.71	2.31	56.0	23.5	Vessels prominent.
18	M.	11	-	∓	+	6.71	5.32	1.39	50.8	31.3	Vessels prominent.
41	M.	10	130 *	∓	+	8.36	3.51	4.85	88.2	26.1	Vessels prominent.

* Lumbar puncture performed 4 hours before admission to hospital.

patient (Case 100). Much higher levels however than that were frequently observed in patients with acute nephritis who presented no cerebral manifestations. Apart from the fact that case 15, with the highest blood pressure in the series, developed pulmonary oedema, little prognostic value could be attached to the height of the blood pressure. There was also no relation between the blood pressure and the non-protein nitrogen of the blood. The findings in this paper agree with Nobécourt[1] that there is no definite level of blood pressure above which uraemic manifestations appear. In contrast to Kylin's[7] statement that uraemia may occur in acute nephritis without rise in blood pressure, it is worth noting that no case occurred with a blood pressure below 130 per cent. of normal.

Serum proteins showed no consistent alteration, moderate reduction in serum albumin and oncotic pressure being the most constant finding. In case 29 serum albumin was below 2.5 gm. per cent. on admission but subsequently rose gradually. Very high globulin readings of over 6.00 gm. per cent. were observed in two patients (cases 100 and 40), in one of whom bronchopneumonia was present.

Non-protein nitrogen ranged from 23.2 to 280.0 mgm. per cent. and was within normal limits in 33 per cent. of cases only. No relation was made out between the non-protein nitrogen level and either oedema or the severity of the symptoms. In cases 7, 55, 37 and 40 non-protein nitrogen rose after the uraemic

manifestations had ceased and in case 29 it actually fell from 280 mgm. per cent. to 133.0 mgm. per cent. while the uraemic state became more marked. One must conclude from the erratic behaviour of non-protein nitrogen with regard to uraemia that there is no apparent causal relationship between them.

Sex. All cases save one were males.

Prognosis. Of the twelve cases death occurred in two but as the uraemic manifestations were complicated by pulmonary oedema and broncho-pneumonia respectively the prognosis may be considered good if treatment is energetic.

PART IV.

OBSERVATIONS ON THE PATHOGENESIS OF THE FALL IN SERUM PROTEINS.

Chapter 1.

Cardiac oedema.

From the survey of the literature already given (p.13) it appears that an alteration in serum proteins is not infrequent in oedema associated with cardiac decompensation. All reports agree that the change consists of a fall in serum albumin, while the percentage of globulin, when altered, is increased. According to Payne[1] and Peters, 49 observations on heart disease without oedema showed little alteration in serum proteins and even when decompensation with dropsy was present cases not infrequently occurred showing no change. Since the protein fractions were not equally reduced in their series they argued that hydraemia was not a factor and that albuminuria could not be held responsible for the fall because never more than a trace was observed. While suggesting increased capillary permeability as a possible factor, the chief agent in producing reduction of serum albumin they considered to be malnutrition, which condition was well marked in all cases which showed low serum albumin. The cause of the malnutrition they attributed to anorexia, nausea and vomiting. Serum albumin was never below 2.5 gm. per cent. and the dropsy was attributed to a combination of increased back pressure and

diminished oncotic pressure, being more marked in the presence of both factors.

In the cases reported by Govaerts[2] and Fahr[3] and Swanson, albuminuria was slight or absent, while Starlinger[4] and Winands observed similar changes and also found no evidence of blood dilution, the haematocrit readings being normal.

In the following pages details are given of 9 cases of oedema of cardiac origin, 7 being due to rheumatic infection, one to diphtheria and one to congenital heart disease with decompensation.

Case 105, a girl aged 6 years. Three days before admission on 2.1.34 swelling of the face was noted. On admission on 2.1.34 oedema of face and legs was present with slight ascites. The heart was slightly enlarged to the left and to mid-sternum on the right side: the sounds were very soft and foetal in character. Slight cyanosis and frequent vomiting were present. The urine contained albumin 2.5 parts Esbach and numerous casts but no blood was found. The diagnosis was made clear by the subsequent development of loss of knee-jerks with the appearance of palatal and finally diaphragmatic paralysis. On the development of pneumonia the patient died. Before death albuminuria had largely disappeared and cardiac dulness had returned to normal with the disappearance of oedema. At autopsy the kidneys were apparently normal.

Blood chemistry. 3.1.34.

Total Protein.....	6.22 gm.%
Albumin.....	5.08 "
Globulin.....	1.14 "
Calculated Oncotic Pressure..	29.5 mm.Hg.
Non-protein Nitrogen.....	53.7 mgm.%
Blood Pressure % of Normal...	88

The congo-red test for nephrosis was negative. A urea concentration test on 3.1.34 gave the following result:-

Before urea.....	2.83 gm.%
1 hour after.....	2.10 "
2 hours after.....	3.40 "

Case 106, a girl aged 10 years. Cardiac decompensation appeared about 2 years after an attack of arthritis, one month before admission on 12.1.34 when oedema was present but no ascites. After admission the child became worse with marked oedema (including the face), orthopnoea, and cyanosis. The heart was much enlarged with V.S. and V.D. murmurs at the apex. The liver was much enlarged and great ascites was present. The urine on admission contained no albumin but was not again examined. There was no vomiting. On 21.1.34 the child died, permission for autopsy being refused.

Blood chemistry. 21.1.34.

Total Protein.....	6.38	gm. %
Albumin.....	4.05	"
Globulin.....	2.33	"
Calculated Oncotic Pressure...	25.5	mm. Hg.
Non-protein Nitrogen.....	45.0	mgm. %
Blood Pressure % of Normal....	110.0	

Case 107, a boy aged 5 years. Admitted to hospital on 25.8.32 with rheumatic endocarditis, but no decompensation. On 13.9.32 pericarditis appeared and generalized oedema (including the face) was noted from 12.12.32 till death on 8.2.33. During the last weeks albumin was present in the urine reaching on one occasion 3.5 parts Esbach but generally being merely a trace. Vomiting was fairly frequent in this case - once or twice a week and more often towards the termination of the illness.

Blood chemistry. 1.2.33.

Total Protein.....	6.48	gm. %
Albumin.....	2.41	"
Globulin.....	4.07	"
Calculated Oncotic Pressure..	18.9	mm. Hg.
Non-protein Nitrogen.....	33.0	mgm. %.

Case 108, a girl aged 4 years. This child had an attack of rheumatic arthritis 18 months before admission. When admitted to hospital on 10.1.34 rheumatic arthritis and endocarditis were present but there was no decompensation. On 4.2.34 cardiac dulness was observed to be increased and on 9.2.34 oedema of face and legs and ascites appeared. Large pleural effusions were also present. Death occurred two days later. During the last few days of life a faint trace of albumin was present in the urine. At autopsy oedema and congestion of the kidneys

were found. Carditis of rheumatic origin was present. The chemistry of the blood and fluid from the pleural cavity on 9.2.34 was:-

	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Blood Pressure % of Normal.
Blood	7.17	3.69	3.48	25.2	53.0	120
Pleural fluid	3.37	1.76	1.61	11.9	43.0	

Case 109, a boy aged 8 years. Eighteen months before admission on 5.1.31 he had rheumatic arthritis. Seventeen months later oedema of the feet was noted. On admission cardiac enlargement to right and left of the middle line was marked and an apical V.S. murmur was audible. The urine was clear. Oedema of the legs was marked and doubtful in the face while ascites was considerable. Occasional vomiting was noted in this patient. Death occurred two months after admission and permission for autopsy was refused.

Blood chemistry. 7.1.31.

Total Protein.....	5.96	gm.%
Albumin.....	3.04	"
Globulin.....	2.92	"
Calculated Oncotic Pressure...	20.8	mm.Hg.
Non-protein Nitrogen.....	28.7	mgm.%

Case 110, a boy aged 4½ years. Six weeks before admission on 21.12.33 he had arthritis followed by chorea. On admission there was evidence of mitral regurgitation without cardiac enlargement. No oedema was present. On 20.1.34 the heart became enlarged to right and left of the middle line and oedema of the face and legs became apparent along with ascites. Some cyanosis was present but no orthopnoea. On treatment with digitalis oedema disappeared and cardiac dulness diminished but did not return to normal. A trace of albumin was present in the urine during the period of decompensation. The child was dismissed without oedema.

Blood chemistry. 23.1.34.

Total Protein.....	7.40	gm.%
Albumin.....	5.21	"
Globulin.....	2.19	"

Calculated Oncotic Pressure..	31.7 mm.Hg.
Non-protein Nitrogen.....	45.8 mgm.%

Case 111, a boy aged 4 years. Three weeks before admission he complained of swelling of the abdomen and of vague pains in the limbs. On admission on 25.12.31 he showed ascites, double pleural effusion and oedema of the legs. Albumin up to 4.0 parts Esbach was present in the urine throughout the illness. No blood was seen. Both borders of the heart were displaced outwards, while the sounds were of very poor quality but no definite murmur was audible. On 13.1.32 he developed chicken-pox and was transferred to a fever hospital where a week later he died. X-ray of the chest showed an abnormally shaped cardiac shadow. From that and lack of evidence of rheumatism a congenital heart lesion with decompensation was diagnosed.

Blood chemistry. 9.1.32.

Total Protein.....	6.71 gm.%
Albumin.....	3.79 "
Globulin.....	2.92 "
Calculated Oncotic Pressure..	24.9 mm.Hg.
Non-protein Nitrogen.....	43.0 mgm.%

Case 112, a girl aged 12½ years. At 9 years she had chorea and at 10 years arthritis, at which time in hospital mitral disease of rheumatic origin was diagnosed. Readmitted on 27.2.34 when aortic and mitral valvular lesions were found. The state of nutrition was very poor. Cardiac decompensation gradually developed and by 2.5.34 orthopnoea, cyanosis, slight albuminuria and oedema of the legs were present. Ascites was marked. At this time also vomiting occurred not infrequently. Death occurred on 4.6.34.

Blood chemistry. 29.5.34.

Total Protein.....	7.82 gm.%
Albumin.....	3.98 "
Globulin.....	3.84 "
Calculated Oncotic Pressure..	27.0 mm.Hg.
Non-protein Nitrogen.....	20.0 mgm.%

Case 113, a girl aged 4 years. In this case the history was of listlessness with occasional vomiting for 6 weeks. Although she was kept in bed, a week before admission on 29.4.34 generalized oedema appeared. In hospital oedema was general with

ascites: there was also double pleural effusion. Cyanosis and orthopnoea were present. The heart condition was diagnosed as a mitral lesion with pericarditis. The nutritional state was good and no vomiting occurred while in hospital. Death occurred on 6.5.34. No autopsy was performed.

Blood chemistry.

Total Protein.....	7.32	gm.%
Albumin.....	3.97	"
Globulin.....	3.35	"
Calculated Oncotic Pressure...	26.5	mm.Hg.
Non-protein Nitrogen.....	29.2	mgm.%

In table 32 is given a summary of the observations on the cardiac cases.

TABLE 32.

The serum proteins in cardiac oedema.

Case	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	Duration of oedema.	Fever.	State of nutrition
105	6.22	5.08	1.14	29.5	5 days	None.	Poor.
106	6.38	4.05	2.33	25.5	4 weeks	Slight.	Poor.
107	6.48	2.41	4.07	18.9	6 weeks	Slight.	Poor.
108	7.17	3.69	3.48	25.2	1 day	None.	Fair.
109	5.96	3.04	2.92	20.8	16 days	None.	Fair.
110	7.40	5.21	2.19	31.7	3 days	None.	Good.
111	6.71	3.79	2.92	24.9	3 weeks	None.	Very poor
112	7.82	3.98	3.84	27.2	4 weeks	None.	Very poor
113	7.32	3.97	3.35	26.5	8 days	None.	Good.

The figures show that serum albumin was twice within normal limits and once below 2.5 gm. per cent.. In the remaining cases slight to moderate reductions were found. Serum

globulin was above normal in 4 cases, in all of which albumin was reduced. The occurrence of oedema with normal protein was found on two occasions. These findings are consistent with those in the literature.

Proteinuria cannot be held responsible for the reduction of serum albumin since in the majority of cases it was present in only small amount. In the case of diphtheritic myocarditis where a fair amount was observed the serum proteins were normal.

Malnutrition in the sense of deficient protein intake or absorption has been held responsible for reduction in serum proteins but as can be seen from table 32 the relationship of serum albumin reduction to the general state of nutrition is a poor one.

Case 108 was actually observed in hospital to be putting on weight on a full diet when cardiac decompensation supervened: one day after the appearance of oedema serum albumin had fallen to 3.69 gm. per cent.

Increased capillary permeability. This view gains some support from the high figures for proteins in the pleural fluid of case 108. It is however difficult to understand why serum globulin was increased in this patient. If permeability is increased from poor nutrition of the capillary walls it is reasonable to suppose that the duration of the oedema would be reflected in the degree of reduction of serum proteins. This correlation,

however, was not found because the serum albumin value was reduced on the day after the appearance of oedema in case 108, and was almost normal in case 106 with oedema of four weeks' duration. But as the protein content of effusions in cardiac oedema is considerably higher than in nephrosis (Peters[5] and van Slyke) increase of capillary permeability cannot be disregarded as a possible cause of the fall of the serum protein.

Infection. In table 32 it has been shown that serum globulin is increased when serum albumin is reduced which finding could not be attributed in these cases to infection. In the diphtheritic case serum globulin was low and in one of the two cases with fever was normal. In the other cases no infection, other than the rheumatic one, was present and as has been said the level of globulin varied inversely with serum albumin. The question of the relation of rise in serum globulin to the presence of an infection will be discussed more fully in a subsequent chapter but it is known that high albumin and low globulin occur in the nephrotic type of nephritis when a febrile infection is not present. In view of these findings it is unlikely that the increase in serum globulin can be attributed to infection in every case.

When present, fall in oncotic pressure is a factor in addition to increase of hydrostatic pressure in the production of oedema. In cases where a reduction of oncotic pressure

exists it is possible that a salt-free diet will be successful in diminishing oedema but in cases with normal serum proteins its use is without object. The cause of the fall in serum protein is still obscure.

Chapter 2.

Nutritional oedema.

A review of the literature on this subject has already been given (p. 11). Oedema without a renal or cardiac basis has been ascribed by numerous workers to reduction of serum oncotic pressure following a deficiency of protein in the diet. Furthermore it has been found that inability to utilise protein as in infections and wasting diseases, may be a cause of serum oncotic pressure reduction and oedema.

The level of serum albumin at which oedema usually appears in this disease is apparently between 2.5 and 3.0 gm. per cent., somewhat higher than in the nephrotic syndrome and definitely higher than in the oedema of plasmapheresis. In the latter condition this finding has been ascribed by Weech (1) et alii to the better physical state and consequently greater elasticity of the tissues.

The following 7 cases showed oedema in the absence of cardiac decompensation or nephritis.

Case 114, a girl aged 16 months. She was admitted to hospital on 24.1.33 with a complaint of swelling of the face and feet of 3 days' duration. From birth she was fed on the breast till 3 months but did not thrive because of insufficiency of milk. After that time till admission the diet consisted of Nestlés' Milk, in half the amount proper for the age, with the addition of bread or pudding once a day. On admission there was pitting oedema of the legs and puffiness of the face. Rickets was marked. The liver and spleen were palpable and a nasal discharge was present. The Wassermann reaction was positive. The urine was normal on admission but on 30.1.33 a pyogenic infection of the urinary tract developed with fever.

Blood chemistry.

Date.	Total Protein gm.%	Albu-min. gm.%	Globu-lin. gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Fever	Oedema	Wt. (kg)	Protein in diet per day. gms.
28.1.33	4.51	2.51	2.00	16.6	29.4	0	+	8.05	46.0
30.1.33	4.08	2.94	1.14	17.8	30.0	+	+	7.5	46.0
13.2.33	6.59	4.09	2.50	25.8	31.0	0	0	6.8	46.0

The diet prior to admission was certainly deficient in protein and a diet containing 6.8 gm. per kilo body weight per day was given following which serum albumin rose and oedema disappeared. The presence of congenital syphilis may have been a contributory factor to the malnutrition.

Case 115, a girl aged 16 months. She was breast-fed entirely and on admission to hospital on 18.9.33 showed oedema of the face, hands and feet. No abnormality was detected on physical examination: urine clear.

It is almost certain that the fall in serum albumin was nutritional in origin since the child was entirely breast-fed at 16 months. Administration of an adequate diet led to gradual rise of serum proteins.

Blood chemistry.

Date.	Total Protein gm.%	Albu-min. gm.%	Globu-ulin. gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%	Fever	Oedema	Wt. (kg)	Remarks.
19.9.33	2.98	1.17	1.81	8.9	18.8	0	+	8.0	Light diet
27.9.33	4.09	2.81	1.28	16.2	20.1	+	∓	7.4	Ileo-colitis Milk.
3.10.33	-	-	-	-	-	0	0	6.8	Light diet
4.10.33	5.15	3.28	1.87	20.7	21.0	0	0	6.5	Light diet
1.6.34	6.80	4.21	2.59	25.9	24.0	0	0	9.5	Light diet

A urea concentration test on this patient gave the following result:-

19.9.33.	Before urea....	1.44	gm.%
	1 hour after...	2.75	"
	2 hours after..	3.88	"

Case 116, a female aged 1 year. She was breast-fed till 10 months; since weaning ceased to thrive and with good reason as the diet was merely whole milk four ounces and sugar one teaspoonful five times a day. On admission on 26.1.34 she was a small child and a typical cretin. Fever was present due to otitis media. On 9.1.34 a pyogenic infection of the urinary tract developed with increase of fever. Sodium bicarbonate, 90 grains daily, was given. On 14.1.34 she began to vomit frequently and the stools became very loose and green. On 17.1.34 owing to dehydration being marked, 240 c.c. of normal saline were given by the intraperitoneal route. By 27.1.34 1.2 Kg. in weight had been gained with appearance of oedema. At this point sodium bicarbonate was omitted and 1.1 Kg. in weight was lost in 10 days with disappearance of oedema. On 7.2.34 broncho-pneumonia developed and the child died three days later. Permission for an autopsy was refused.

Blood chemistry:- 27.1.34.

Total Protein.....	5.64	gm.%
Albumin.....	3.08	"
Globulin.....	2.56	"
Calculated Oncotic Pressure..	20.5	mm.Hg.
Non-protein Nitrogen.....	21.8	mgm.%
Fever.....	+	

Case 117, a girl aged 18 months. She was admitted to hospital with a history of diarrhoea and vomiting of 7 weeks' duration. The child was found to be much wasted and dehydrated. The stools were frequent, loose and green. A pyogenic infection of the urinary tract was found which was treated by hexamine and calcium chloride. Following this treatment cure of the urinary infection occurred but a severe acidosis was induced with exacerbation of diarrhoea and frequent vomiting. Hexamine and calcium chloride were omitted and sodium bicarbonate was given; the acidosis was relieved and vomiting and diarrhoea ceased. At the same time intraperitoneal saline was given daily and in 4 days oedema of the face, hands, and feet appeared.

Blood chemistry. 23.4.34.

Total Protein.....	6.89 gm.%
Albumin.....	2.90 "
Globulin.....	3.99 "
Calculated Oncotic Pressure..	21.5 mm.Hg.
Non-protein Nitrogen.....	23.5 mgm.%
Remarks.....	Oedema disappearing. Fever present.

The fall of serum protein was undoubtedly due to malnutrition caused by the pyogenic infection of the urinary tract causing an acute alimentary upset. This case shows the effect of administration of NaCl, and incidentally of sodium bicarbonate with water to a patient with reduced serum oncotic pressure. Vomiting and diarrhoea associated with calcium chloride poisoning caused dehydration and when the loss of fluid by diarrhoea and vomiting ceased, retention of water and Cl occurred. Oedema gradually disappeared, the infection of the urinary tract was cured and the child began to put on weight.

Case 118, a male aged 9 years. Before admission there had been a period of diarrhoea with the passage of typical large, loose, coeliac motions. On entrance to hospital on 15.6.31 there was oedema of the feet and face. The heart and urine showed no abnormality.

Blood chemistry. 16.6.31.

Total Protein.....	3.76 gm.%
Albumin.....	2.85 "
Globulin.....	0.91 "
Calculated Oncotic Pressure..	16.9 mm.Hg.
Non-protein Nitrogen.....	33.0 mgm.%
Fever.....	0

Within a week oedema disappeared. Marriot[2] noted that oedema was not infrequent in cases of coeliac disease. This is presumably due to reduction of serum protein following non-absorption of nitrogen during the periods of steatorrhoea.

Case 119, a boy aged 17 months. Before admission he was fed chiefly on breast milk with occasional addition of eggs and tea. One month before admission he developed enteritis since when breast milk only had been given. On admission on 20.5.31 oedema of the face and feet was present. No abnormality of the heart or urine was found. The stool was normal but there was some bronchitis with fever.

Blood chemistry. 22.5.31.

Total Protein.....	5.99	gm.%
Albumin.....	2.71	"
Globulin.....	3.28	"
Calculated Oncotic Pressure....	19.5	mm.Hg.
Non-protein Nitrogen.....	33.0	mgm.%
Fever.....	+	

On light diet oedema rapidly disappeared.

Case 120, a female aged 2 years. She presented an indefinite history of vomiting for a fortnight before admission. Two days before admission on 10.10.33 oedema of face and feet was observed. No account of the diet was obtained. On admission generalized oedema was present. No abnormality was present in heart, lungs, abdomen or nervous system. The non-catheter specimen of urine contained neither blood nor casts and insufficient albumin to give more than a trace by Esbach's quantitative method of estimation.

Blood chemistry. 11.10.33.

Total Protein.....	4.58	gm.%
Albumin.....	2.71	"
Globulin.....	1.87	"
Calculated Oncotic Pressure...	17.0	mm.Hg.
Non-protein Nitrogen.....	22.4	mgm.%
Fever.....	0	

The course of events was as follows:-

Date	Oedema	Weight (Kg)	Urine.	Daily intake of protein in gm.
11.10.33	+	10.5	Tr. albumin.	17
18.10.33	+	10.0	Tr. albumin.	50+
23.10.33	+	9.7	Clear (Catheter).	50
27.10.33	±	9.4		50
2.11.33	0	8.0		50

The fact that the urine was clear at least a week before the disappearance of oedema, that neither blood nor casts were seen and that the non-protein nitrogen of the blood was normal are strongly against a diagnosis of nephritis.

In the seven cases described oedema was present without a cardiac lesion. In 3 cases (114, 116, 117, table 33) a pyogenic infection of the urinary tract was found but this is not a recognised cause of oedema and although case 120 showed a trace of albumin in a non-catheter specimen of urine there is no ground for belief that nephritis was present in any of these children. A constant finding was reduction of serum albumin and consequent reduction of oncotic pressure while in cases 114 and 115 a rise of oncotic pressure to a level just below normal was observed to accompany the disappearance of oedema. The state of nutrition, which was poor in all the cases, was not noticeably improved although serum albumin was much increased. This is in accord with the observations of Peters and Eisenman (3) who have pointed out that when an adequate protein intake is provided, return of oncotic pressure to normal precedes improvement in the general condition.

It was also observed that oedema was prone to occur after periods of diarrhoea and/or vomiting when sodium bicarbonate by mouth or sodium chloride parenterally was given. This is similar to what occurs in the nephrotic syndrome where sodium chloride administration in the presence of low serum oncotic pressure is followed by the appearance or aggravation

of the oedema.

There appears to be ample evidence in the literature (p. 11) that a fall in serum albumin may be caused by nitrogen deficiency due either to a diet lacking in protein, as in war oedema, or to inability to utilise protein when offered. In wasting diseases also, when catabolism is increased, low serum albumin has been frequently reported. In nutritional oedema serum globulin is normal or even low in the absence of infection. Table 33 summarises the observations on admission on the cases reported.

TABLE 33.

The serum proteins in nutritional oedema.

Case	Albumin gm.%	Globulin gm.%	Disease or Infection present.	Fever	Percentage of expected weight (oedema free).	Protein intake prior to admission.
114	2.51	2.00	Congenital Syphilis.	-	70	Deficient.
115	1.17	1.81	-	-	67	? deficient - Breast fed.
116	3.08	2.56	Pyuria.	+	63	Deficient.
117	2.90	3.99	Pyuria.	+	51	Adequate.
118	2.85	0.91	Coeliac disease.	-	57	Adequate.
119	2.71	3.28	Bronchitis.	+	54	? deficient. Breast fed.
120	2.71	1.87	-	-	68	Not known.

In four cases protein intake was probably grossly inadequate (cases 114, 115, 116, 119) while in cases 117 and 118

inability to utilise protein because of vomiting or diarrhoea was almost certainly the factor. Consideration of the percentage of expected weight shows that though definitely very low in three cases, in other four it was over 60 but not 70 per cent. of normal. In the series of Peters[3] and Eisenman low serum oncotic pressure was found with oedema in two obese patients and it was suggested that a diet high in calories but poor in protein would allow of the co-existence of reduction in serum proteins and an apparently well-nourished appearance. Although no apparent relation existed between the degree of malnutrition and the serum albumin level in the present series, deficiency of nitrogen seemed to be a factor in its reduction. At least on adequate protein intake oedema disappeared and in two cases serum albumin was observed to return to normal.

Chapter 3.

Other non-renal conditions.

According to Peters[1] and van Slyke the source of the serum proteins with exception of fibrinogen is unknown. The alterations in diseases not cardiac or renal in origin are for the most part reduction in serum albumin while serum globulin may be increased or normal.

Since these changes, which are found in the nephrotic syndrome, are common quite apart from renal disease, Salvesen,[2] Kumpf,[3] Wiener[4] and Wiener and others argue that reduction is not primarily renal but due to alteration in the serum proteins. Salvesen[2] for example found that apart from nephrosis decrease in albumin and increase in globulin were most marked in liver diseases. He also reported fall in albumin but normal globulin in leukaemia and diabetes. Kumpf[3] found low albumin and high globulin in pneumonia, enteric fever, nutritional oedema and cardiac failure with oedema. In all these albuminuria was minimal or absent. He observed that the changes in serum proteins were similar in character though less in degree to those found in glomerulo-nephritis, acute and chronic, lipoid, amyloid and mercuric chloride nephrosis and accordingly concluded that even if albuminuria was present high globulin was still unexplained on the basis of loss in the urine. Wiener[4] and Wiener found that in infections the plasma albumin was reduced and the globulin proportionately increased while in cirrhosis of the liver similar but less marked changes were

present. In cases of jaundice without elevation of temperature plasma proteins were normal or increased owing to elevation of the plasma globulin level. They pointed out that the picture presented by the plasma proteins in acute nephritis was similar to that found in these conditions. In hepatic diseases and infections the increased globulin was perhaps due to greater permeability in the organs which are the sources of the plasma proteins while fall in albumin was caused by increased permeability of the peripheral capillaries. Presumably on this hypothesis increased escape of albumin from the site of production is unable to keep pace with the peripheral loss. If so, it is somewhat difficult to see why the considerable reduction in serum albumin should not be associated with oedema in infections since the oncotic pressure of the serum albumin remaining in the blood would be reduced by the action of the escaped albumin acting against it.

In the presence of infections high globulin has been reported by numerous workers, in tuberculosis and syphilis by Bruckman[5] et alii and in enteric fever and malaria by Lloyd[6] and Paul. Starlinger[7] and Winands in acute infectious diseases found high globulin and not infrequently a well-marked reduction in albumin while Moen[8] and Reimann had similar findings in lobar pneumonia. To find whether rise in globulin was associated merely with fever, or whether infection was essential, Moen[9] et alii subjected one series of dogs to diathermy and in another produced infections. In the former little change

occurred but in the latter a rise in globulin was found. From this they concluded that fever alone was not the etiological factor.

To Peters[10] and Eisenman the changes in serum proteins in conditions neither cardiac nor renal in origin were capable of a more simple explanation than that suggested by Wiener[4] and Wiener, Salvesen[2] and others. Serum albumin reduction they stated was always associated with malnutrition and increase of globulin with infection. Exceptions apparently existed however in liver disease where high globulin was the rule without apparent infection. The decrease in serum albumin was attributed to malnutrition. While in the case of long-drawn-out wasting disease with a marked degree of malnutrition the explanation afforded by Peters[10] and Eisenman seems very reasonable, it is not clear, in acute conditions such as pneumonia or in the acute infections such as diphtheria described by Starlinger[7] and Winands, that malnutrition can be held responsible for reduction in serum albumin.

The position would seem to be that many workers hold that in infections, nephritis and liver diseases some effect is exerted on the production of serum proteins whereby serum albumin is reduced and globulin increased. While an extrinsic cause of serum albumin reduction almost certainly exists in the form of a diet deficient in protein over long periods, there would appear to be some evidence of an intrinsic factor in the upset of serum protein production.

During the course of this work observations were made on a miscellaneous collection of cases with infection. In a number of these the serum proteins were observed to be quite normal, serum globulin tending to be low in some cases (table 34).

TABLE 34.

Normal serum globulin in the presence of infection.

Case.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Disease.	Duration	Fever
121	7.22	5.14	2.08	Lobar pneumonia	5 days	++
122	8.13	5.58	2.55	Broncho-pneumonia	4 days	++
123	6.04	4.83	1.21	Broncho-pneumonia	2 days	++
124	6.43	5.08	1.35	Broncho-pneumonia	8 days	++
126	7.56	4.82	2.74	Tuberculous meningitis.	2 weeks	+
127	7.25	4.97	2.28	Tuberculomata of brain	? 3 mths.	0
129	6.03	4.28	1.75	Tuberculous meningitis	1 week	+

While apparently serum globulin is not invariably high in the presence of infection, increases were observed in the following cases (table 35), some of which were without evidence of infection.

TABLE 35.

Elevation of serum globulin in various conditions.

Case	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Disease	Duration	Fever	Remarks.
102	9.56	5.35	4.21	Idiopathic purpura.	3 days	+	Well-nourished.
103	8.22	5.20	3.02	Idiopathic purpura.	2 days	0	Well-nourished.
104	9.56	5.36	4.20	Idiopathic purpura.	5 days	0	Well-nourished.
125	10.00	6.94	3.06	Catarrhal jaundice.	6 days	+	Well-nourished.
128	7.61	4.47	3.14	Catarrhal jaundice.	11 days	0	Well-nourished.
130	8.75	4.49	4.26	Catarrhal jaundice.	5 days	+	Well-nourished.
131	5.88	2.88	3.00	Hanot's cirrhosis.	6 months ?	0	Well-nourished.
"	9.87	3.62	6.25	"	"	++	"
132	5.31	2.68	2.63	Banti's disease.	2 years	0	Well-nourished.
"	8.28	2.95	5.33	"	"	0	"
133	6.68	2.11	4.57	Lederer's disease.(11)	2 days	+	Well-nourished.

In all save the first observation on case 132 serum globulin was above normal. In the patients with catarrhal jaundice this might be due to the inflammation of the biliary passages and in case 133 Lederer(11) ascribed acute haemolytic anaemia to a streptococcal infection. Reduction of serum albumin was also noted in three cases. In two of these (cases

132 and 131) the illness had lasted over a considerable period but in these, as in the remainder of the group, nutrition was good. Case 133 deserves special consideration. This patient was a boy aged 3 years and 3 months who was in perfect health till one day before admission when he vomited and pallor and jaundice appeared. The urine was observed to be red. On admission on 15.4.31 he was very pale and slightly jaundiced with a moderate degree of fever: liver and spleen not palpable. No purpura. Blood:- Red blood corpuscles 1,280,000 per c.mm.. White blood corpuscles 40,000 per c.mm. Haemoglobin 23 per cent.. Films showed 72 per cent. of polymorphs and some scanty normoblasts. The urine contained much haemoglobin but no red cells. The blood when withdrawn for grouping showed marked lysis. The Wassermann reaction was negative. After two transfusions the child steadily progressed, haemoglobin disappeared from the urine and he was dismissed well. It is highly improbable that the marked alteration produced in the serum albumin, which was reduced to 2.11 gm. per cent. in this case, can be ascribed to malnutrition since the symptoms were of but two days' duration; moreover the child was obviously well nourished. Non-protein nitrogen at the time of the estimation of serum proteins on the day following admission was 130.6 mgm. per cent., probably indicative of a marked degree of tissue breakdown. A similar finding was observed in one of Lederer's three cases. The urine contained, in addition to haemoglobin, a fair amount of albumin which was not quanti-

tatively estimated. While the oncotic pressure was as low as 18.0 mm. Hg., no dropsy was observed. This was due to the fact that prior to admission and for some days thereafter vomiting was frequent so that no fluid was available to form oedema.

SUMMARY.

In a few patients high serum globulin has been observed in conditions with neither a cardiac nor a renal basis and without obvious infection, while low serum albumin has been noted in cases in which no malnutrition was apparent.

Chapter 4.

Acute nephritis.

In a previous chapter it has been shown that fall in serum proteins, involving lowering of oncotic pressure, is of frequent occurrence in acute nephritis and in the following pages will be discussed the possible mechanisms of such a phenomenon.

1. Hydraemia or blood dilution.

The work of the majority of investigators, already summarized, would go to show that hydraemia is not present in acute nephritis and the fall in the ratio of red blood corpuscles to plasma, when found, is to be explained not by dilution but by anaemia. The chief reason given for this conclusion is the unequal reduction of the serum protein fractions so frequently found. Apparent exceptions exist as in the cases reported by Peters and van Slyke.(1) In such, the reduced plasma proteins, low haematocrit level, haemoglobin and red corpuscle counts returned so rapidly to normal on the occurrence of diuresis that blood dilution was considered to be the only possible explanation.

In cases of the nephrotic syndrome, Peters(1) and van Slyke and others have found no evidence of the existence of hydraemia and conclude that the reduction of serum proteins is absolute and not due to dilution.

According to Darrow,(2) Soule and Buckman in children

the normal percentage of red cells to plasma is 36.5 plus 3.0 for shrinkage due to the use of oxalate as an anticoagulant. Peters[1] and van Slyke in the literature find the normal red cell volume to average 44.0 per cent. in adults, irrespective of whether the haematocrit or graduated centrifuge tube be used in its estimation.

On five cases, apparently normal, observations were made on the serum proteins, haematocrit level, haemoglobin and red cell count simultaneously. For the red cell volume the haematocrit method was employed and no allowance was made for shrinkage due to the anticoagulant - potassium oxalate. The results are shown in table 36.

TABLE 36.

Normal cases.

Case	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Haematocrit per cent. R.B.C.	R.B.C. x 10^6 per c.mm.	Hb. per cent.
154	8.02	5.92	2.10	41.0	535	102
155	7.78	5.62	2.16	40.0	539	94
156	8.04	5.25	2.79	40.0	487	90
157	7.03	5.42	1.61	41.0	508	96
158	7.62	5.59	2.03	41.0	509	90
Average	7.69	5.56	2.13	40.6	516	94

In table 37 are shown the results of haematocrit observations on non-renal cases and table 38 those obtained in cases of acute nephritis.

In the non-renal group reduction of serum proteins in conjunction with a fall in haematocrit level was sometimes observed. Normal total protein and albumin also occurred with a low haematocrit level, a finding which was probably due, (cases 182, 183, 184) not to dilution, but to anaemia. The finding in case 114 of a normal haematocrit level with marked fall in serum proteins would suggest an absolute reduction of the latter.

In the examples of acute nephritis (table 38) there would appear to be some evidence of dilution in cases 13, 25, 55 and 93 where rise of serum proteins during diuresis was accompanied by return to normal of the percentage of red cells to plasma, the haemoglobin and the red cell count. It will be observed however that serum total protein was sometimes normal or even above normal in the presence of dilution as indicated by the haematocrit and red cell counts. Serum globulin bore no relation to the degree of dilution: serum albumin, while showing a rather better correlation, occasionally, as in case 25, showed marked variations which were not reflected in the haematocrit level. Cases of the nephrotic type(4,38,99) were usually found to have low serum proteins and normal haematocrit readings.

TABLE 37.

Non-renal cases.

Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Haematocrit per cent. R.B.C.	Hb. per cent.	R.B.C. x 10^6 per c.mm.	Remarks.
105	3.1.34	6.22	5.08	1.14	++	32.0	-	-	Myocarditis.
106	21.1.34	6.38	4.05	2.33	++	30.0	-	-	Rheumatic heart disease.
107	1.2.32	6.48	2.41	4.07	++	42.0	55	470	" " "
108	9.2.34	7.17	3.69	3.48	++	25.0	-	-	" " "
110	23.1.34	7.40	5.21	2.19	++	40.0	75	490	" " "
111	9.1.32	6.71	3.79	2.92	++	32.0	-	-	Congenital heart disease.
113	1.5.34	7.32	3.97	3.35	++	33.0	66	400	Rheumatic heart disease.
114	28.1.33	4.51	2.51	2.00	+	38.0	-	-	Nutritional oedema.
"	30.1.33	4.08	2.94	1.14	+	40.0	-	-	" "
"	13.2.33	6.59	4.09	2.50	0	38.0	-	-	" "
116	27.1.33	5.64	3.08	2.56	++	22.0	50	268	" "
120	11.10.33	4.58	2.71	1.87	++	31.0	42	470	" "
182	7.4.33	6.41	4.20	2.21	0	14.0	30	150	Haemophilia.
183	5.3.32	6.38	5.04	1.34	0	25.0	60	280	Nutritional anaemia.
184	7.4.34	6.56	4.16	2.40	0	33.0	85	429	Rheumatism.

TABLE 38.

Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Haematocrit per cent. R.B.C.	Hb. per cent.	R.B.C. x 10^6 per c.mm.
2	9.10.33	5.27	3.78	1.49	∓	29.0	74	475
4*	29.9.33	4.36	1.92	2.44	21.5 (Kg.)	45.0	92	520
"	6.10.33	5.61	1.72	3.89	22.2	42.0	84	461
"	18.10.33	5.04	3.20	1.84	21.6	34.0	92	487
"	21.11.33	6.46	2.40	4.06	18.8	36.0	-	-
"	1.12.33	7.80	2.67	5.13	18.8	36.0	-	-
"	6.2.34	3.84	2.14	1.70	25.0	43.0	100	530
"	7.2.34	4.56	1.46	3.10	24.8	40.0	-	-
"	13.2.34	4.49	2.34	2.15	25.4	43.0	-	-
"	14.2.34	4.03	2.76	1.27	25.3	41.0	104	529
"	20.2.34	5.47	2.17	3.30	25.2	39.0	85	500
"	21.2.34	5.08	2.78	2.30	23.8	39.0	-	-
"	28.2.34	4.67	1.85	2.82	20.0	36.0	-	-
"	1.3.34	3.79	2.89	0.90	20.0	33.0	-	-
"	5.3.34	5.07	1.41	3.66	22.0	35.0	90	450
"	6.3.34	3.68	2.48	1.20	22.8	34.0	85	431
"	14.3.34	3.87	1.12	2.75	25.0	32.0	92	481
"	28.3.34	3.90	1.08	2.82	28.6	30.0	75	390
"	18.4.34	7.62	2.54	5.08	21.5	27.0	66	381
"	22.5.34	5.21	1.50	3.71	23.7	24.0	-	-
5	15.12.33	7.38	5.00	2.38	++	32.0	73	413
"	18.12.33	7.69	5.52	2.17	∓	36.8	74	429
13	14.3.34	6.71	3.54	3.17	++	37.1	85	462
"	16.3.34	6.37	3.58	2.79	+	38.0	90	488
"	19.3.34	8.01	4.16	3.85	∓	40.0	90	491
"	23.3.34	8.06	4.59	3.45	0	40.0	96	525
21	21.2.33	6.67	4.37	2.30	+	32.0	-	-

* Oedema present throughout.

TABLE 38 (contd).

Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Haematocrit per cent. R.B.C.	Hb. per cent.	R.B.C $\times 10^6$ per c.mm.
25	12.12.33	6.17	4.19	1.98	++	32.0	72	366
"	15.12.33	8.71	5.60	3.11	+	36.0	84	423
"	18.12.33	8.56	3.57	4.99	0	42.0	85	512
"	27.12.33	6.87	4.72	2.15	0	40.0	90	525
32	24.3.34	8.19	4.17	4.02	+	38.0	89	453
"	27.3.34	8.06	5.07	2.99	0	40.0	-	-
35	12.10.33	7.94	5.48	2.46	+	36.0	78	393
38*	28.12.32	5.08	1.71	3.37	28.8 (Kg.)	38.0	-	-
	3.1.33	4.84	2.11	2.73	24.8	39.0	-	-
	11.1.33	4.63	2.41	2.22	24.2	37.0	-	-
	19.1.33	4.08	2.43	1.65	24.6	42.0	-	-
	22.1.33	4.91	2.12	2.79	26.7	34.0	-	-
	30.1.33	3.35	1.74	1.61	29.6	36.0	-	-
	13.2.33	4.39	1.94	2.45	29.5	41.0	-	-
	27.2.33	5.67	3.29	2.38	28.2	41.0	-	540
	7.3.33	5.19	2.64	2.55	27.7	40.0	-	-
	13.3.33	4.42	2.31	2.11	27.5	34.0	-	-
41	8.1.34	8.36	3.51	4.85	+	32.0	70	410
47	24.3.34	7.32	4.56	2.76	∓	40.0	96	525
"	27.3.34	8.16	5.23	2.93	0	37.0	-	-
48	3.10.33	5.25	1.56	3.69	++	34.0	70	354
	18.11.33	4.24	1.30	2.94	++	18.0	-	-
	1.12.33	7.49	1.73	5.76	++	18.0	-	-
55	1.1.33	6.37	4.16	2.21	∓	27.0	-	-
"	14.1.33	7.99	4.67	3.32	0	38.0	-	-
57	14.2.34	6.57	3.29	3.28	++	39.0	-	-

* Oedema present throughout.

TABLE 38 (contd).

Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Haematocrit per cent. R.B.C.	Hb. per cent.	R.B.C. x 10^6 per c.mm.
62*	21.4.34	3.96	2.03	1.93	18.7 (Kg.)	32.0	76	390
"	24.4.34	5.97	1.94	4.03	18.2	34.0	80	454
"	23.5.34	4.01	2.22	1.79	20.0	35.0	-	-
"	6.6.34	5.70	1.19	4.51	20.9	36.0	-	-
75	11.10.33	6.84	4.07	2.77	++	32.0	73	378
76	10.10.33	6.58	2.72	3.86	++	38.0	75	396
81	30.10.32	8.30	4.04	4.26	+	30.0	-	-
"	3.11.32	6.71	4.32	2.39	+	24.0	-	-
"	7.11.32	5.79	3.47	2.32	∓	26.0	-	-
"	11.11.32	7.31	3.87	3.44	0	32.0	-	-
"	29.11.32	7.81	6.29	1.52	0	26.0	-	-
91	10.2.33	6.32	4.44	1.88	+	40.0	-	-
93	27.3.34	5.86	3.07	2.79	++	35.0	-	-
"	3.4.34	7.84	4.97	2.87	0	43.0	-	-
94	17.10.33	7.25	3.91	3.34	+	40.0	85	471
96	17.10.33	8.66	4.92	3.74	0	39.0	88	483
98	18.10.33	4.89	1.79	3.10	++	35.0	78	434
"	18.4.34	6.88	2.48	4.40	+	33.0	68	398
99*	12.1.34	6.86	2.47	4.39	17.6 (Kg.)	40.0	-	-
"	23.2.34	4.09	1.84	2.25	20.4	36.0	-	-
"	2.3.34	6.42	1.89	4.53	20.2	39.0	-	-
"	20.3.34	5.81	1.81	4.00	20.4	40.0	-	-
100	15.7.33	10.10	3.98	6.08	0	31.0	-	-

* Oedema present throughout.

TABLE 38 (contd).

Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Haematocrit per cent. R.B.C.	Hb. per cent.	R.B.C. x 10^6 per c.mm.
185	24.12.32	7.47	-	-	++	28.0	-	-
"	27.12.32	6.72	-	-	++	30.0	-	-
"	12.1.33	7.73	4.66	3.07	0	25.0	-	-
"	19.1.33	6.23	3.87	2.36	0	35.0	-	-
"	30.1.33	6.19	3.53	2.66	0	31.0	-	-
"	1.3.33	7.34	4.66	2.68	0	35.0	72	345
188	6.2.33	4.84	1.60	3.24	++	31.0	65	462
193*	19.2.33	3.67	1.80	1.87	10.5 (Kg.)	41.0	75	510
"	27.2.33	4.24	1.80	2.44	10.7	40.0	-	-
"	13.3.33	3.92	2.38	1.54	10.7	42.0	-	-
195	6.4.34	4.32	2.46	1.86	++	38.0	50	493
"	11.4.34	4.91	2.52	2.39	++	34.0	55	450
"	1.5.34	4.27	1.39	2.88	++	25.5	45	370

* Oedema present throughout.

In case 38, when salt was added to the diet, oedema became much more marked and a temporary fall in the haematocrit level occurred. This is suggestive of dilution but subsequent observations showed that a fall in red cell percentage again occurred on 13.3.33 while oedema remained unchanged on a "salt-free" diet. A similar fall in the haematocrit level was observed in case 99 which was associated with a well-marked fall in serum proteins. In this patient the diet was "salt-free" throughout. In case 4, coincident with the administration of large doses of alkali, the percentage of red cells to plasma showed a marked drop which was attributed to shrinkage[3] of the red corpuscles. In this patient serum albumin increased and oedema diminished with fall in the haematocrit level while later when the haematocrit level returned to normal serum proteins fell. Fall in the haematocrit level on 28.2.34 and thereafter was attributed to anaemia induced by protein shock therapy.

It is thus impossible to form any conclusions on the results obtained in this series. It seems, however, justifiable to conclude that if dilution does occur the diluting fluid must contain protein, globulin frequently and in large amount and occasionally albumin also. On no other hypothesis is it possible to explain the high levels of total protein, globulin and occasionally albumin in the serum when the percentage of red cells, the haemoglobin, and the red cell count are low.

2. Increased capillary permeability.

This question has already been discussed (p. 37) and only a brief recapitulation is now given, summing up the evidence against the presence of such a factor as the cause of serum protein reduction in acute nephritis.

(1) There is no evidence as far as children are concerned that the capillary walls are damaged. Haemorrhages in the fundi or elsewhere are of extreme rarity.

(2) It is commonly allowed that in nephrosis the capillary wall is normal; nevertheless oedema fluids from that condition contain but little less protein than the same fluids in acute nephritis.

(3) The fractions of the serum proteins are not equally reduced. Albumin having a smaller molecule might escape more easily than globulin and absolute increase of the latter might be explained by increase produced by an associated infection. Such a rise in globulin is not invariable however in nephritis complicated by infection and moreover is very frequently seen in nephrotic cases where there is no demonstrable infection.

(4) Where clinical capillary damage is at a maximum, as in idiopathic purpura, it might be anticipated that the changes postulated in serum proteins by the upholders of the

capillary damage hypothesis might be found in high degree. This however is not the case: a considerable increase in serum globulin was the only change found in the present series.

(5) If oedema is associated with increased capillary permeability and escape of serum proteins into the tissues, it is very difficult to explain the presence of dropsy in 12 per cent. of cases of this series when no alteration in the serum proteins whatever was observed.

(3) The relation of malnutrition to low serum proteins and oedema.

It has already been shown that nitrogen starvation is responsible for reduction of serum proteins and development of dropsy in the condition known as nutritional oedema. A similar cause is said by some authors to account for the state of affairs in acute nephritis.

Peters[4] et alii found in patients suffering from the nephrotic syndrome that a very definite degree of malnutrition was present. They observed that in patients with low serum albumin, administration of a high protein diet was accompanied by a rise in serum albumin in spite of persistent albuminuria. With regard to oedema in acute nephritis, Peters[5] and his collaborators state that serum protein reduction, when it occurs, is also due in part to protein starvation. In the series of cases they presented, serum albumin fell only in association with digestive disturbances such as anorexia and

vomiting or following restriction of diet.

The most cogent argument against this view is the marked reduction which has been observed to take place in serum albumin at a very early stage in the disease in children showing no obvious evidence of malnutrition. (Table 39).

TABLE 39.

Marked reduction of serum albumin early in acute nephritis.

Case.	Serum Albumin. gm.%.	Day of illness.
29	2.39	10
48	1.66	4
49	2.50	6
56	2.91	4
69	2.78	11
70	2.82	4
71	2.45	2
76	2.72	5
87	2.63	3

Digestive disturbances were not a feature of the cases and vomiting was infrequent or absent save in cases complicated by the presence of uraemia where serum protein reduction was gross in only one of the twelve examples (case 29). Again, in the nephrotic type of case, the onset

was frequently insidious and several of the patients were ambulant on admission to hospital without gastro-intestinal symptoms. It was in cases of this type that the most marked and protracted fall in serum albumin was observed.

A further test of the existence of a relation between malnutrition and serum albumin level was made by constructing a graph, correlating the percentage of expected weight (oedema-free) and the serum albumin. (The oedema-free weight was obtained during the convalescent stage). Figure 43 shows that in 52 per cent. of cases the body weight was between 70 and 80 per cent. of normal, in 35 per cent. above 80 per cent. of normal and in 13 per cent. below 70 per cent.. It is clear that there is no relation between the serum albumin level and the percentage of body weight.

In the course of the investigation it was observed that serum albumin, unless reduced below oedema level, invariably returned to normal in a few days. No difference in the rate of regeneration of serum albumin was observed with varying amounts of protein in the diet. The following table illustrates these points (table 40).

It can be seen that the protein intake had no apparent influence. Case 38 of the nephrotic type received 4.0 gm. of protein per Kg. of body weight daily over a considerable period without appreciable effect on the serum albumin level.

Fig. 43.

Graph Showing Absence of Relationship between Percentage of Expected Body Weight in Acute Nephritis and Serum Albumin Level.

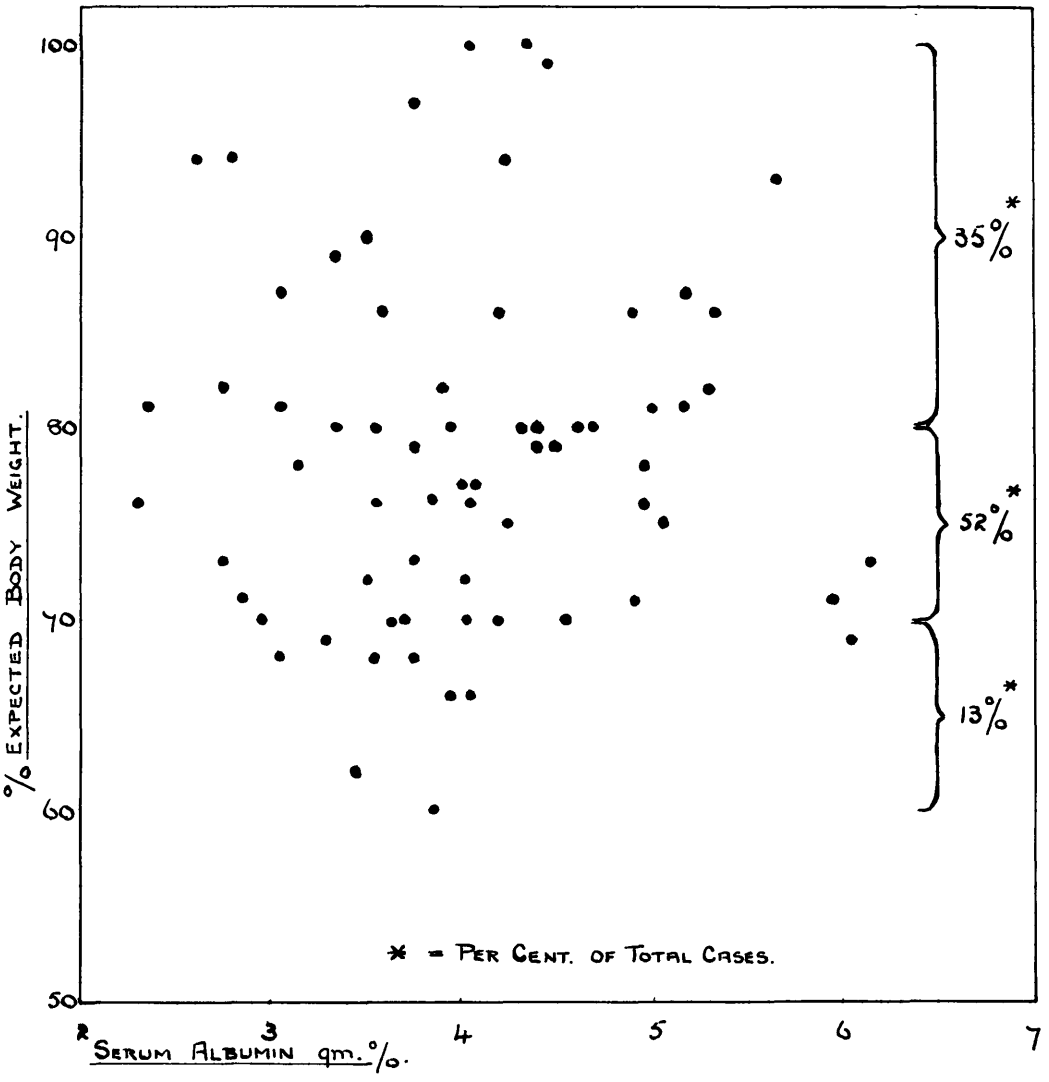


TABLE 40.

The absence of influence of the protein intake on the serum albumin level.

Case	Day of illness.	Serum Albumin. gm.%	Protein in diet.	
			Grams per day.	Grams per kilo body weight.
8	9	3.18	22	1.2
"	18	5.23	"	"
29	11	2.39	40.0	1.8
"	16	3.44	"	"
"	19	3.69	"	"
"	27	3.96	"	"
"	33	3.57	"	"
38	15	1.71	24.0	1.0
"	32	2.41	40.0	1.7
"	40	2.43	63.0	2.6
"	65	1.94	95.0	4.0
"	113	2.31	"	"
48	4	1.66	22.0	1.2
"	12	2.86	"	"
70	4	2.82	22.0	1.5
"	23	4.22	"	"
74	7	3.30	51.0	3.5
"	13	5.17	"	"

4. Proteinuria.

To most workers fall in serum albumin is adequately explained by loss in the urine through damage to the kidney and it has been generally observed that protracted oedema is associated with massive albuminuria. While Linder[6] et alii found a fair degree of correlation between the plasma albumin level and proteinuria, Peters[4] and his associates were unable to account entirely for its reduction by the amount of albumin

in the urine. In certain cases they observed a high degree of proteinuria over long periods without alteration in plasma albumin. In his monograph on nephrosis, Leiter[7] states that the evidence is in favour of a causal relationship between serum albumin deficit and proteinuria.

Shaw Dunn[8,9] points out with Christian,[10] Gainsborough,[11] Bell[12] and others that glomerular lesions are always to be found in so-called nephrosis. The damage however is so slight that it is difficult to believe that massive and long-continued proteinuria can be adequately explained by it. He suggests that the amount of protein in the glomerular filtrate is slight and great concentration occurs through excessive reabsorption of fluid by the tubules. In this connection the work of Hiller[13] et alii is of interest. These workers pointed out that the albumin : globulin ratio in the urine is generally above 10 in nephrosis, 5 to 10 in acute nephritis and below 5 in chronic interstitial nephritis. In amyloid disease however it is very low, about 1. While serum albumin, which has a smaller molecule than serum globulin, presumably escapes more easily through the kidney, it is reasonable to suppose that with increasing severity of kidney damage the albumin : globulin ratio in the urine falls. In amyloid disease, as reported by Peters[14] and his co-workers, however, serum albumin is reduced while serum globulin remains normal or is slightly increased. This appears to be difficult of explanation by any theory of increased permeability of the

kidney vessels.

In the present study of nephritis in childhood some difficulty has been experienced in obtaining complete 24 hour specimens of urine, more particularly in young patients who were acutely ill and many of whom received magnesium sulphate. Where possible the total loss of protein in 24 hours was calculated from the urinary output of that period.

The following table (41) shows that a rough relationship existed between the serum albumin level and the degree of albuminuria.

TABLE 41.

The relationship between albuminuria and serum albumin level.

Type of nephritis.	Albuminuria.	Serum Albumin. gm.%.
Hyperpietic	Variable.	> 4.45
Nephrotic	++	< 2.5
Mixed Type A	++	< 2.5
Mixed Type B	Variable.	2.5-4.45

These results, admittedly far from conclusive, because of inability to obtain a sufficient number of cases in which albuminuria could be measured accurately, do indicate some degree of relationship between proteinuria and serum albumin level. In patients where a reduction of serum albumin was marked and protracted, albuminuria was always found to be

heavy. Reference to table 45 however shows that a well-marked reduction of serum albumin (below 3.0 gm. per cent.) was not infrequent: in some of these cases (27, 71, 76) proteinuria was comparatively slight. Further inconsistency is exemplified by case 65 in which serum albumin was 4.45 gm. per cent. on admission. Albuminuria, 1-4 parts Esbach, was incessant but three months later serum albumin was still normal - 4.50 gm. per cent.. These few observations indicate that it is not possible to form an exact correlation between the degree of albuminuria and the serum albumin level.

4. Disturbance of Metabolism.

To Epstein[15] nephrosis is not a disease of the kidney. Through some metabolic upset serum proteins are altered and owing to some change in their physico-chemical character are excreted in the urine. He suggests that the lowered basal metabolic rate and high blood cholesterol are evidence in favour of his view. It has however been observed by Peters[4] and others that although tolerance to thyroid is greatly increased its use in nephrotic states is not followed by appreciable benefit, while by the same authors and by others it has been shown that reduction of the basal metabolic rate is not confined to so-called nephrosis but is frequent in the other forms of oedema.

For Epstein's[15] contention however some support is to be found in the literature. Kumpf,[16] because he found re-

duction of serum albumin and increase of globulin in many diseases besides nephritis, attributed the alterations to infection: Salvesen[17] and Wiener[18] and Wiener made observations of a similar nature (p.175). These authors apparently believe that changes in serum proteins are not specific and that altered production or destruction occurs in other states besides nephritis. To find evidence of difference between the protein of blood and urine in nephrotic cases many attempts have been made with most conflicting results. According to Thomas[19] and his co-workers and Schenck[20] and Schlüter urinary proteins in nephritis differ from those of the blood and therefore if the urinary protein is derived from that of the blood it undergoes some change presumably before excretion. Hewitt[21] however found no evidence of change and Cavett[22] and Gibson found the proteins in blood, urine and oedema fluid to be identical in structure. In 1931 Leiter[7] in his comprehensive view of nephrosis concluded that definite proof was lacking that urinary protein differed from that of the blood. Recently Hayman[23] and Bender injected blood from nephrotic cases into normal subjects intravenously without the appearance of proteinuria. On the whole the evidence would appear to be against the presence of any difference between the protein of the blood and of the urine but this has been countered by some with the statement that the changes may not be detectable with the methods employed.

Certain observations in blood chemistry now fall to be considered relative to the view that reduction in serum proteins may be due to a metabolic disturbance.

(1) Serum fat.

In children Harrison[24] and Wyllie found that blood cholesterol was high in parenchymatous but not in acute nephritis. Chamberlain[25] found that cholesterol as a rule varied directly with the degree of oedema but since exceptions did occur the relationship could not be a causal one. Calvin and Goldberg[26] found a fairly constant inverse relation between serum albumin and cholesterol. The high cholesterol they attributed to an upset of metabolism but since the relationship was not exact they considered that high cholesterol could not be ascribed to an attempt to make good the diminution in serum protein osmotic pressure. Gardner[27] and Gainsborough found that globulin possessed a special affinity for cholesterol and Chamberlain made the interesting suggestion that blood cholesterol increased because of increase of globulin. While he reported that the increase in cholesterol in acute nephritis was roughly proportionate to oedema, Fleming[28] found no such relationship. Neither Chamberlain,[25] Fleming[28] nor Maxwell[29] observed any rise in cholesterol in cardiac oedema.

From metabolic experiments Hiller[30] and his co-workers found no disorder of fat metabolism in nephrotic cases. Peters[1] and van Slyke believe that the mobilization of fat

even in nephrotic conditions is due to malnutrition and since hypercholesterolaemia occurs in starvation there is some ground for this hypothesis. On the other hand the high cholesterol level reported by Barker[31] and Kirk after plasmapheresis seems rather to be against the view of Peters[1] and van Slyke. To Maxwell[29] renal oedema and hypercholesterolaemia were both due to a toxic effect on the reticulo-endothelial system.

According to Peters and van Slyke[1] in nephritis of the nephrotic type, fat, fatty acid, and cholesterol of the blood are all increased. In this work consideration has been given to total serum fat only. McQuarrie[32] et alii recently reported the following figures in normal children.

	Mean in gm. per cent.
Cholesterol	0.167
Total fatty acid	0.312

During the course of this investigation a number of observations were made on serum fat in acute nephritis. A few observations were also made on cases of cardiac and nutritional oedema and on other conditions. Table 42 shows the results in nephritis.

(Table 42).

TABLE 42.

Case	Date	Serum Fat gm.%	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Type of Nephritis.
2	10.10.33	1.0	5.27	3.78	1.49	++	Mixed Type B
11	4.10.33	0.2	8.29	6.51	1.78	0	"
19	29.6.33	0.8	5.84	2.96	2.88	+	"
30	27.9.33	0.2	6.90	4.27	2.63	0	"
53	16.3.34	0.6	5.06	3.04	2.02	+	"
70	7.9.33	0.6	6.69	2.82	3.87	++	"
73	25.9.33	0.4	6.05	3.32	2.73	+	"
75	11.10.33	0.2	6.84	4.07	2.77	++	"
76	10.10.33	0.9	6.58	2.72	3.86	++	"
74	17.10.33	0.9	7.35	3.92	3.42	+	"
35	12.10.33	0.2	7.94	5.48	2.46	+	Hyperpietic.
29	8.9.33	1.0	7.62	2.39	5.23	++	Mixed Type A
"	16.9.33	1.4	7.61	3.69	3.92	++	"
"	28.9.33	0.9	6.27	3.96	2.31	0	"
48	13.9.33	0.9	3.87	1.49	2.38	++	"
"	13.10.33	1.1	5.25	1.56	3.69	++	"
"	18.11.33	2.4	4.24	1.30	2.94	++	"
49	29.6.33	2.4	5.84	2.54	3.30	++	"
"	11.7.33	1.6	5.06	2.19	2.87	++	"
62	21.4.34	1.0	3.96	2.03	1.93	++	"
"	24.4.34	2.8	5.97	1.94	4.03	++	"
4	6.10.33	3.28	5.61	1.72	3.89	++	Nephrotic Type
"	18.10.33	2.84	5.04	3.20	1.84	+	"
"	13.2.34	3.08	4.49	2.34	2.15	++	"
"	14.2.34	3.00	4.03	2.76	1.27	++	"
"	20.2.34	2.64	5.47	2.17	3.30	++	"
"	21.2.34	2.48	5.08	2.78	2.30	++	"
38	12.10.33	1.30	5.97	2.61	3.36	++	"
"	19.3.34	1.02	5.81	1.81	4.00	+	"

TABLE 42 (contd).

Case	Date.	Serum Fat gm.%	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Type of Nephritis.
98	30.8.33	2.10	-	-	-	++	Nephrotic Type
"	19.9.33	3.64	4.56	1.64	2.92	++	"
"	28.9.33	2.96	6.29	2.42	3.87	++	"
"	18.10.33	3.24	4.89	1.79	3.10	++	"
99	23.2.34	2.04	4.09	1.84	2.25	++	"
"	12.3.34	2.13	4.90	1.86	3.04	++	"
181	8.5.34	0.98	7.97	2.17	5.80	0	"
195	6.4.34	1.76	4.32	2.46	1.86	++	Infant.
"	11.4.34	2.64	4.91	2.52	2.39	++	"
"	1.5.34	4.84	4.27	1.39	2.88	++	"
196*	28.6.33	2.28	2.99	1.76	1.23	++	Nephrotic Type

* Adult aged 22 years.

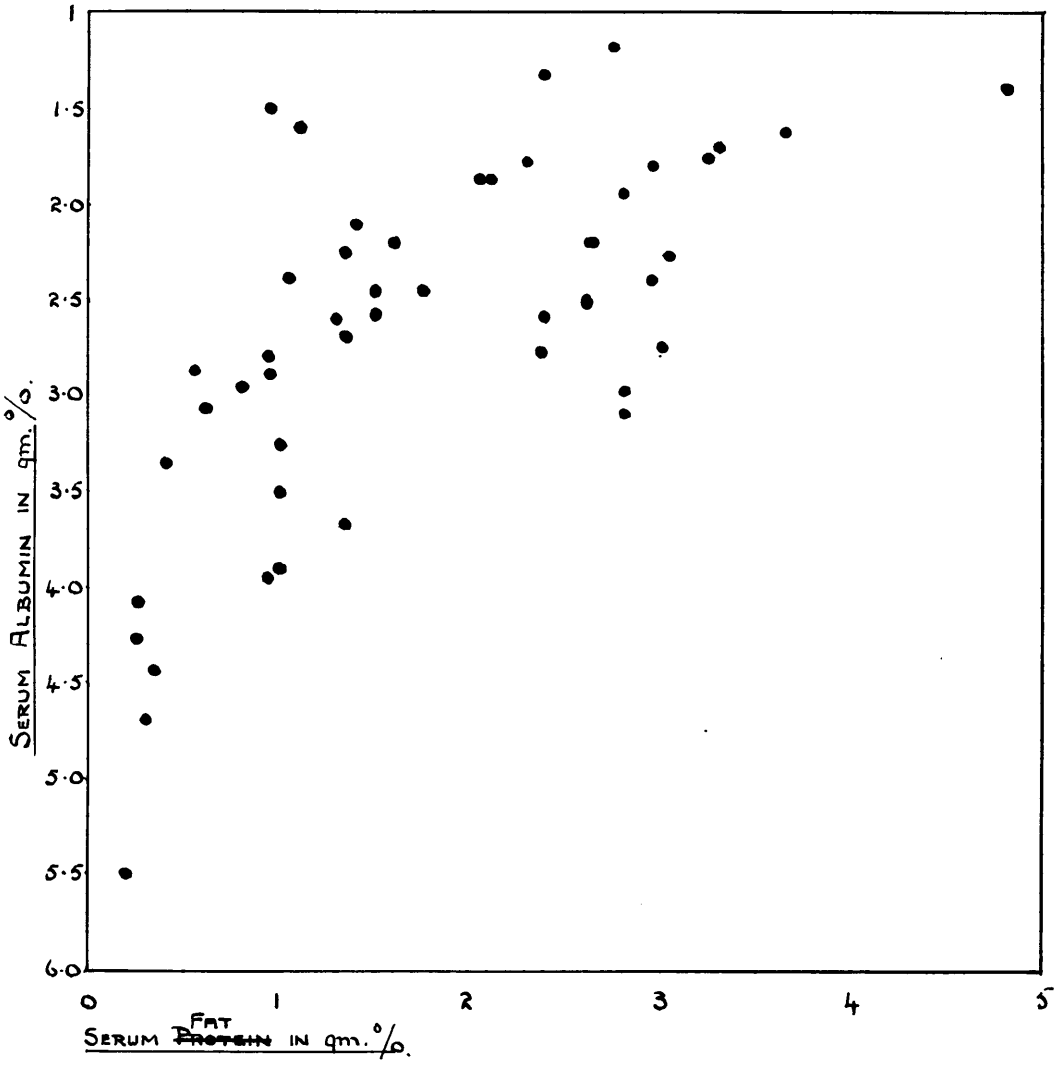
From these figures the following conclusions may be drawn.

(1) The presence of oedema does not necessarily entail an increase of blood fat while in all but two instances (cases 29 and 181) oedema was present when hyperlipaemia existed. In these two patients serum albumin was reduced. It will be noted that normal or but slightly elevated fat levels were found in the hyperpietic and mixed type B groups of nephritis where serum proteins were normal or but slightly reduced. This would suggest that a relation between serum fat and oedema exists only when the dropsy is associated with marked reduction of serum proteins,

(2) Figure 44 shows that a fairly well-marked relation exists

Fig. 44 .

The Relation Between Serum Albumin and Serum Fat.



between serum albumin and fat. In only two instances is serum fat over 1.0 gm. per cent. without serum albumin being below 3.0 gm. per cent.. Figure 45 shows a complete absence of relation between serum globulin and fat thus rendering very unlikely the suggestion of Chamberlain[25] that high cholesterol is to be attributed to increase of serum globulin.

(3) Table 43, which shows the results of observations on a small number of non-renal conditions, demonstrates that irrespective of the presence of oedema serum fat was only above normal where serum albumin was reduced, although in one case (108) serum albumin was reduced to 3.69 gm. per cent. without a concomitant rise in serum fat.

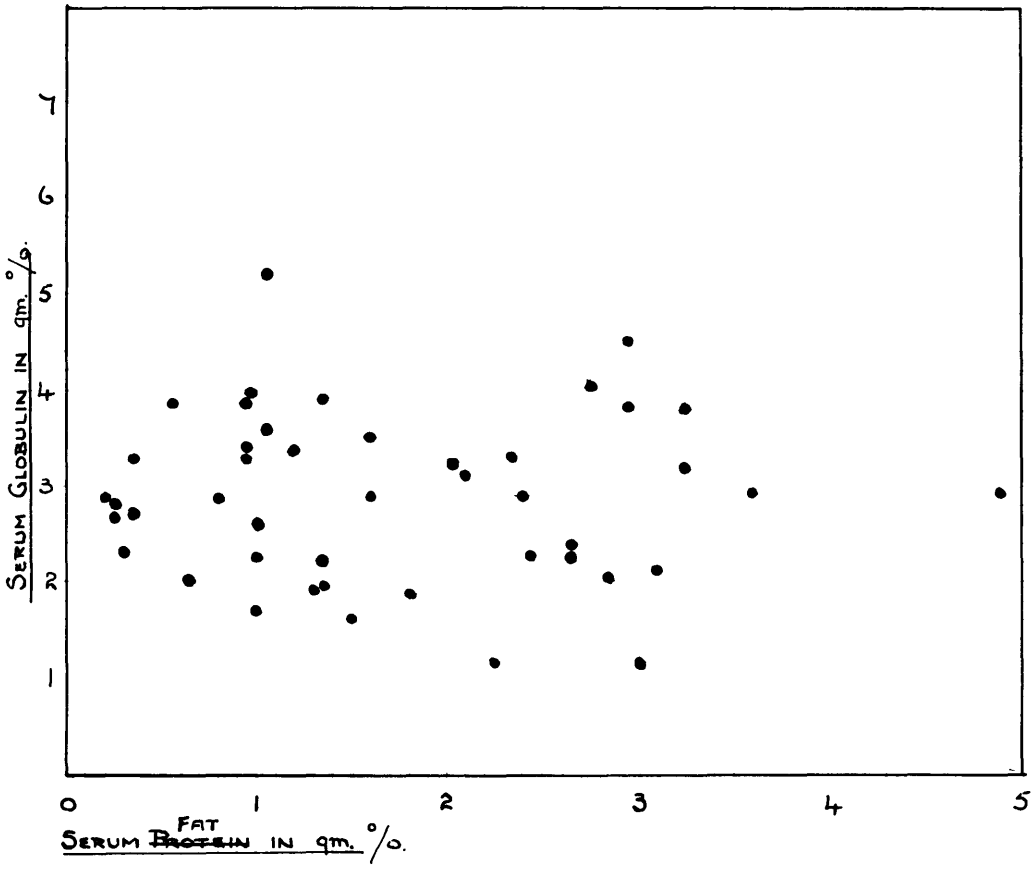
TABLE 43.

Serum fat in non-renal cases.

Case	Date	Serum Fat gm.%	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Oedema	Disease.
101	13.10.33	0.36	9.11	6.17	2.94	0	Purpura.
106	21.1.34	0.4	6.38	4.05	2.33	++	Cardiac oedema.
108	9.2.34	0.4	7.17	3.69	3.48	++	" "
110	23.1.34	0.48	7.40	5.21	2.19	++	" "
115	19.9.33	1.8	2.98	1.17	1.81	++	Nutritional oedema.
"	10.10.33	1.0	5.15	3.28	1.87	+	" "
116	26.2.34	0.91	5.64	3.08	2.56	+	" "
120	11.10.33	0.96	4.58	2.71	1.87	++	" "
157	25.9.33	0.27	6.99	4.14	2.85	0	Convalescent rheumatism.
158	4.10.33	0.24	7.44	5.06	2.38	0	" "

Fig. 45 .

The Absence of Relationship Between Serum Globulin and Serum Fat.



While these findings shed no fresh light on the existence of a metabolic disturbance causing fall in serum proteins they at least indicate that serum albumin and fat vary inversely.

2. Alteration in the concentration of the fractions of the serum proteins.

Serum globulin in the majority of reports on both acute nephritis and the nephrotic syndrome is usually above normal. The interpretations of this phenomenon do not however agree. The simplest explanation is that of Peters[4,5,14] and his co-workers who suggest that all cases of the nephrotic syndrome and of acute nephritis, in which globulin is elevated, show the presence of an infection most frequently of pyogenic nature: by this school, increase of globulin in any diseased state, is always associated with the presence of infection. They admit however that there is no apparent infection to explain the hyperglobulinaemia present in some diseases of the liver.

Such a straightforward explanation is not accepted by numerous other workers. Epstein[15] in considering nephrosis, held that the high globulin level indicated tissue breakdown. Wiener[18] and Wiener found high serum globulin and low albumin in nephritis, infections and liver diseases, and considered that this evidence favoured some disorder of serum protein production. On the ground that precisely the same changes in serum proteins were found in many conditions, irrespective of

the presence of albuminuria, Salvesen[17] also came to the conclusion that the changes in nephrosis were attributable to an upset in the production of serum proteins. Against the infective origin of high serum globulin in the nephrotic type of nephritis is the very thoroughly investigated case of Mackay[33] and Johnstone. In 15 observations over a period of a year serum globulin was over 3.0 gm. per cent. on all but three occasions.

In table 44 are shown cases of nephritis which bring out the following points:-

(1) The first group consists of cases in which were present various types of infection. The serum globulin was above normal. It is worth noting that in case 29, which had the highest and most persistent elevation of serum globulin, the infection was not of an acute nature consisting of otorrhoea of 18 months' duration.

(2) The second group consists of cases in which, although an acute infection was present, the serum globulin showed little alteration from normal.

(3) In the third group no infection could be demonstrated, yet serum globulin was found to be above normal.

In the nephrotic cases (4, 38, 58, 98, 99) high serum globulin was a common finding in the absence of infection. Fever <u>per se</u> was not associated with rise in serum globulin.

TABLE 44.

	Case	Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Infection.	Fever.
1.	66	14.7.31	6.46	3.11	3.35	Lobar pneumonia.	+
	24	31.3.33	8.52	3.79	4.73	"	+
	63	29.5.33	7.26	3.44	3.82	"	++
	64	27.5.31	8.90	4.25	4.65	Pneumococcal Meningitis.	+
	51	3.5.33	7.66	4.27	3.39	Tonsillitis.	-
	71	23.3.32	6.34	2.45	3.89	Bronchiectasis.	-
	29	8.9.33	7.62	2.39	5.23	Otitis media	-
2.	90	21.9.31	6.99	4.90	2.09	Lobar pneumonia.	++
	92	18.4.31	6.58	4.77	1.81	"	++
	67	3.2.31	4.82	3.74	1.08	"	++
	10	23.1.31	6.25	3.75	2.50	Erysipelas	+
	2	10.10.33	5.27	3.78	1.49	Diphtheria.	+
	19	29.6.33	5.84	2.96	2.88	Scarlet Fever.	-
3.	49	25.4.33	6.25	2.50	3.75	None.	-
	56	17.3.32	6.31	2.91	3.40	"	+
	20	29.4.31	8.12	3.02	5.10	"	-
	81	30.10.32	8.30	4.04	4.26	"	+
	50	3.5.33	8.02	4.22	3.80	"	-
	62	23.5.34	5.70	1.19	4.51	"	-

In 7 cases in the table serum globulin was high in the presence of a normal temperature and in 5 low when fever was present. Most workers attribute the elevation of serum globulin to infection. It has just been shown however that the behaviour of serum globulin in the presence of infection shows no consistency and that an increase is found apart from an infective process. Accordingly one cannot accept the view that the increase in serum globulin, or its maintenance at a normal level while albumin is reduced, can be even in the majority of cases attributed to infection. Furthermore since the highest and most persistent elevation of globulin is found when serum albumin is most reduced there would appear to be some support for the contention of Epstein (15) that a metabolic upset is present.

The behaviour of the protein fractions in other diseases and of serum globulin in acute nephritis suggests that there may be a disturbance of the mechanism of production of serum proteins. In table 45 are shown cases in which marked fall in serum albumin was observed within a short period of the appearance of oedema. The feature of all the cases in table 45 is the great reduction in the serum albumin found a comparatively short time after the development of oedema. In spite of marked reduction in serum albumin comparatively little albuminuria was noted in cases 27, 71 and 76. In the other cases the initial albuminuria was marked. It would appear therefore that in

TABLE 45.

Case	Duration of oedema in days.	Serum Albumin. gm.%	Remarks.
27	3	2.81	Esbach 1.5 for 2 days. Thereafter albumin a trace.
29	7	2.39	Esbach 2.0 or more for weeks.
48	3	1.66	Esbach 20.0-0.5 in a week. For 9 weeks albuminuria slight then heavy till death 14 weeks later.
49	5	2.50	Esbach 16.0-1.75 till death 2 months later.
70	3	2.82	Esbach 11.0-1.0 for first week. 0.5 thereafter for 2 weeks.
71	2	2.45	In hospital suffering from bronchiectasis. Esbach 1.0-0.25 for a week. Thereafter trace of albumin in urine.
76	4	2.72	Esbach 1.0 for 3 days. Trace of albumin thereafter. Haematocrit 38 per cent. R.B.C.
87	3	2.63	Esbach 12.0-0.75 in first week. Thereafter a trace of albumin only.

some instances the rapidity of the fall in serum albumin may be such that it cannot be explained by the loss of protein in the urine. It must be frankly admitted, however, that there is no proof at present.

While it seems well established that a reduction of serum albumin is of frequent occurrence in acute nephritis

there is as yet no proof as to whether the diminution is relative or absolute. Of the former there would appear to exist some evidence from determination of the haematocrit level but the inconsistencies which have been demonstrated leave much unexplained. Absolute diminution of serum proteins might result from insufficiency of nitrogen for their synthesis: it has been shown that this is not a factor.
Of loss of protein into the tissues by increase of capillary permeability there is no evidence. While proteinuria is always gross when the reduction of serum albumin is protracted, leakage through the kidney does not explain the marked and rapid fall in serum albumin in certain cases: moreover an equally marked degree of proteinuria has been observed to exist without reduction of serum albumin.
No direct evidence of a failure in synthesis of serum proteins in acute nephritis has been offered but it remains a possibility. In conclusion no single factor was found which could explain the reduction of serum albumin in every case.

PART V.

GENERAL SUMMARY.

In a survey of the literature in part I concerning the pathogenesis of oedema in nephritis it has been set forth that dropsy can be explained on the basis of Starling's hypothesis as originally applied by Epstein. One of the arguments, among others which have been quoted, against the adoption of this theory, lies in the fact that it fails to explain the oedema of acute nephritis. This conclusion has been reached, apparently by all investigators, in view of the fact that the oncotic pressure of the serum, even when reduced, falls but seldom below the level associated with oedema in the chronic form of the disease.

Part II is concerned with the serum protein levels in apparently normal children between 2 and 11 years of age and in infants under 2 years.

In part III, prior to a discussion on the serum proteins in acute nephritis and their relation to oedema, some general observations are made. No evidence existed to show that an increase of capillary permeability was present. With regard to increased hydrostatic pressure, only 2 per cent. of cases showed cardiac dilatation and therefore back pressure could not be a factor in the production of oedema in acute nephritis. Elevation of blood pressure, however, was a frequent finding and oedema was

always present in some degree when the level was higher than 140 per cent. of normal for the age. In a large number of cases a reduction of serum proteins was found to exist but in only 10 per cent. was this below the critical level for oedema and the existence of another factor was evident. While a relation between the serum protein level and the degree of oedema was found to be present, this was not an exact one. In chapter 5 it has been shown that two causal factors operate - fall of oncotic and rise of blood pressure - in the majority of cases of acute nephritis. In chapter 6 the important secondary rôle of sodium chloride has been indicated: that it was a factor only when oncotic pressure is much reduced indicates that the effect is not due to the kidney. In a small number of cases of the nephrotic type various forms of treatment have been tried: in all the cases which showed improvement however the result was apparently spontaneous and not due to treatment. With regard to prognosis the importance of the serum albumin level is indicated. When this was found to be below 2.5 gm. per cent. early in the illness, the prognosis was poor. Chapter 9 deals with acute nephritis in infancy. At this age period oedema was massive and always associated with a serum albumin level below 3.0 gm. per cent.. In the final chapter 12 cases showing cerebral manifestations of acute nephritis are discussed.

In part IV consideration has been given to the pathogenesis of the fall in serum proteins. Before acute nephritis

is dealt with it is shown in chapters 1 and 2 that reduction of serum albumin occurred, not infrequently in cardiac oedema, invariably in nutritional oedema. The cause in the former remains obscure while in the latter it would seem to be insufficiency of nitrogen either in the diet or through failure to assimilate. Alteration in the serum protein was found in a few cases of non-renal or cardiac origin, in some of which a disorder of metabolism may have been the cause. As far as acute nephritis is concerned, concerning the pathogenesis of the fall in serum protein, no definite conclusion was arrived at.

ANALYTICAL METHODS.

Serum proteins: Howe's[1] method modified by Hawk[2] and Bergeim.

Non-protein nitrogen: Folin[3] and Wu.

Calcium: Kramer[4] and Tisdall.

Phosphorus: Tisdall.[5]

Blood fat: Rückert.[6]

Congo-red Test: Matthew[7] and Cameron.

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STUDIES IN ACUTE NEPHRITIS IN INFANCY AND CHILDHOOD.

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VOLUME II.

From the University Department of Paediatrics and the Biochemical Laboratory, Royal Hospital for Sick Children, Glasgow.

TABLE OF CONTENTS.

VOLUME II.

CASE 1. A girl aged 9 years. Two days before admission swelling of the face and hands was noted and the urine was red in colour.

6.9.33. On admission there was oedema of the face and body. Ascites was also present. In the urine, blood and albumin were present, and the systolic blood pressure was 140 mm. Hg.. Ophthalmoscopic examination was negative.

7.9.33. Blood chemistry:- Total protein 6.64, albumin 3.54, globulin 3.10 gm. per cent.. Calculated oncotic pressure 23.8 mm. Hg.. Non-protein nitrogen 36.3 mgm. per cent.. The systolic blood pressure was 138 mm. Hg..

9.9.33. Urea concentration test:- Before urea 2.80, one hour after 2.86, two hours after 2.97 gm. per cent.. Gross haematuria ceased.

15.9.33. No oedema.

8.10.33. Systolic blood pressure 110 mm. Hg..

15.10.33. The urine was clear.

CASE 2. A girl aged 5½ years. Three days before admission she developed a sore throat and the glands of the neck became swollen. Two days later the urine became dark in colour.

9.10.33. On admission slight oedema of the face was present and the urine contained blood and albumin. The systolic blood pressure was 115 mm. Hg.. The fundi showed no abnormality. Some membrane was present on right tonsil and the cervical glands were swollen.

10.10.33. Systolic blood pressure 112 mm. Hg.. The blood chemistry was:- Total protein 5.27, albumin 3.78, globulin 1.49 gm. per cent.. Calculated oncotic pressure 22.9 mm. Hg.. Non-protein nitrogen 87.0 mgm. per cent..

11.10.33. Since the throat swab was positive for b. diphtheriæ the child was transferred to a fever hospital.

CASE 3. A boy aged 7 years. He complained of headache and began to vomit 3 days before admission. Some swelling of the face was observed.

7.6.32. On admission to hospital some oedema of the face was noted and blood and albumin were present in the urine. The systolic blood pressure was 140 mm. Hg.. Examination of the fundi revealed no abnormality. Blood chemistry:- Total protein 7.70, albumin 6.15, globulin 1.55 gm. per cent.. Calculated oncotic pressure 35.9 mm. Hg.. Non-protein nitrogen 42.8 mgm. per cent.. Urea concentration test:- Before urea 2.12 per cent.. 1 hour after 2.96 per cent.. 2 hours after 3.45 gm. per cent..

11.6.32. Oedema was noted to be gone.

16.6.32. Systolic blood pressure 70 mm. Hg..

9.8.32. Urine clear.

CASE 4. A boy aged 7 years. Four weeks before admission the ankles became swollen. He made no complaints and was not confined to bed.

4.8.33. On admission oedema was general and ascites present. Heart and fundi normal. The systolic blood pressure was 120 per cent. of normal. In the urine there was a great deal of albumin, scanty red cells and casts. The Wassermann reaction and the congo red test were negative. Blood non-protein nitrogen 18.0 mgm. per cent.. Fluids (salt-free) were given and in a week 2.0 Kg. in weight were lost but oedema was still present. Albuminuria at this time was less marked. On a salt-containing diet being permitted oedema rapidly increased, 4.0 Kg. being gained. Albumin became again more marked.

29.9.33. Systolic blood pressure 110 mm. Hg..

3.10.33. Guaiac reaction in the urine positive.

14.10.33. Sodium bicarbonate grains 40 every 4 hours was
5.11.33. begun and increased. No gross haematuria present.

21.11.33. Now getting 960 grains of sodium bicarbonate. Oedema unchanged. No red cells seen in the urine.

Oedema less.

13.12.33. Oedema tended to increase.

23.12.33. Alkali administration ceased, the dose having been gradually decreased. Oedema still rather less than on 14.10.33 but tending to increase. Macroscopic haematuria was present for three days. Full diet allowed.

6.2.34. Oedema increasing steadily.
25 millions T.A.B. vaccine intravenously. No febrile reaction followed and oedema was unaltered.

13.2.34. Oedema rather worse. 50 millions T.A.B. vaccine intravenously. Temperature 101°F. for a few hours following this.

20.2.34. 100 million T.A.B. vaccine intravenously - no reaction.

28.2.34. Oedema very much less - 6.0 Kg. in weight lost. 150 million T.A.B. vaccine intravenously - no reaction.

5.3.34. Gained 3.0 Kg. Oedema worse. 200 million T.A.B. vaccine intravenously - no reaction. Systolic blood pressure 100 mm. Hg.. Fundi normal.

14.3.34. Oedema back at degree seen before vaccine therapy.

28.3.34. Oedema at its maximum point so far in the illness. Systolic blood pressure 98 mm. Hg.. Salyrgan, given intravenously, 0.5 c.c.

30.3.34. Cellulitis of thigh with slight fever. Salyrgan 1 c.c.

2.4.34. Salyrgan 2 c.c.

4.4.34. Salyrgan 2 c.c. Vomited twice after injection. Cellulitis gone.

6.4.34. Salyrgan 1 c.c. Oedema less.

9.4.34. Salyrgan 1 c.c. Oedema still diminishing.

12.4.34. Salyrgan 1 c.c. Still less oedema - 7.0 Kg. lost since 28.3.34.

14.4.34. Weight rising again. Salyrgan 2 c.c.

18.4.34. Ammonium chloride grains 120 daily. Oedema less.

1.5.34. Weight unchanged. Salyrgan 1 c.c.

5.5.34. Weight unchanged. Salyrgan 1 c.c.

9.5.34. Ammonium chloride omitted.

17.5.34. Oedema slightly increased. Systolic blood pressure 100 mm. Hg..

22.5.34. Oedema unchanged. Guaiac reaction positive in the urine. Calcium gluconate 10 c.c. intramuscularly.

26.5.34. Calcium gluconate 10 c.c. No gross haematuria.

28.5.34. Calcium gluconate 10 c.c. Red cells absent from the urine.

30.5.34. Oedema rather less. Calcium gluconate 10 c.c.

1.6.34. Calcium gluconate 10 c.c. Oedema increased.

3.6.34. Calcium gluconate 10 c.c.

5.6.34. Calcium gluconate 10 c.c. No change in oedema from 22.5.34.

14.6.34. Oedema increased. Thyroid was now given in a dose increased gradually from 1 grain daily to 16½ grains daily. The weight increased from 26.4 to 28.0 Kg. in that period. No increase in pulse-rate was noted.

29.6.34. Stools loose. Vomited twice. Thyroid omitted.

4.7.34. Lost 2.0 Kg. in weight. Diarrhoea still present.

5.7.34. Diarrhoea ceased. Guaiac reaction positive in the urine.

10.7.34. Oedema increased. No gross haematuria.

17.7.34. Oedema still increasing. No red cells seen in the urine.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin. Gm.%	Globulin. Gm.%	Calculated oncotic pressure. mm. Hg.	N.P.N. mgm.%
29.9.33	4.36	1.92	2.44	13.9	36.7
6.10.33	5.61	1.72	3.89	14.9	24.0
18.10.33	5.04	3.20	1.84	20.2	25.1
21.11.33	6.46	2.40	4.06	18.9	17.4
1.12.33	7.80	2.67	5.13	21.8	27.2
6. 2.34	3.84	2.14	1.70	14.3	33.6
7. 2.34	4.56	1.46	3.10	12.2	39.9
13. 2.34	4.49	2.34	2.15	15.7	37.1
14. 2.34	4.03	2.76	1.27	16.8	24.0
20. 2.34	5.47	2.17	3.30	16.5	25.0
21. 2.34	5.08	2.78	2.30	18.5	19.0
28. 2.34	4.67	1.85	2.82	14.1	24.0
1. 3.34	3.79	2.89	0.90	17.9	24.4
5. 3.34	5.07	1.41	3.66	12.9	25.0
6. 3.34	3.68	2.48	1.20	15.3	23.0
14. 3.34	3.87	1.12	2.75	11.0	26.0
28. 3.34	3.90	1.08	2.82	9.9	21.0
18. 4.34	7.62	2.54	5.08	20.1	25.4
22. 5.34	5.21	1.50	3.71	13.5	16.0
6. 6.34	4.84	1.93	2.81	14.5	21.0

Urea Concentration Tests.

Date	Before Urea.	1 hour after.	2 hours after.
10.8.33	1.24 gm. %	1.75 gm. %	3.32 gm. %
12.3.34	1.51 " "	1.97 " "	2.82 " "

CASE 5. A boy aged 7 years in whom oedema of the face was observed a week before admission, and of the legs 5 days later.

14.12.33 On admission he showed very marked oedema of face and extremities. Ascites was also present. Ophthalmoscopic examination was negative. The systolic blood pressure was 170 mm. Hg.. A moderate amount of blood and albumin was present in the urine.

15.12.33 Systolic blood pressure 166 mm. Hg.. Oedema slightly less.

18.12.33 Systolic blood pressure 150 mm. Hg.. Oedema less.

20.12.33 Systolic blood pressure 118 mm. Hg.. Oedema less.

17. 1.34 No oedema. A trace of albumin was still present in the urine. Systolic blood pressure 90 mm. Hg.. Urea concentration test:- Before urea 1.1 per cent., 1 hour after 2.78 per cent., 2 hours after 4.96 gm. per cent..

5. 3.34 Urine clear.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
15.12.33	7.38	5.00	2.38	30.9	35.5
18.12.33	7.69	5.52	2.17	33.4	45.4
17. 1.34	-	-	-	-	23.3

CASE 6. A boy aged 8 years. A week before admission oedema of the face appeared and two days later both ears began to discharge.

30.10.31 On admission oedema of the face and extremities was present and the urine contained blood and albumin. The fundi showed no abnormality. The systolic blood pressure was 110 mm. Hg.. Blood chemistry:- total protein 6.23, albumin 3.73, globulin 2.50 gm. per cent.. Calculated oncotic pressure 24.0 mm. Hg.. Non-protein nitrogen 52.0 mgm. per cent.. Urea Concentration test:- Before urea 0.80, one hour after 1.34, two hours after 1.31 gm. per cent..

5.11.31 No oedema.

9.11.31 Non-protein nitrogen of the blood 31.2 mgm. per cent..

17.11.31 Systolic blood pressure 95 mm. Hg..

17.12.31 Gross haematuria persisted till this date.

24.2.32 Urine clear.

7.5.34 A faint trace of albumin was present in the urine.

CASE 7. A boy aged 10 years. Six days before admission oedema of the hands and face appeared and four days later he complained of headache and began to vomit frequently. On the same night he began to take frequent convulsions.

6.5.33 On admission he was comatose and showed oedema of the face. The urine contained blood and albumin and the systolic blood pressure was 140 mm. Hg.. Ophthalmoscopic examination revealed dilatation of the retinal veins. Lumbar puncture was performed and 50 c.c. of clear fluid under increased pressure were withdrawn. 50 c.c. of blood were also removed. Blood chemistry:- Total protein 6.84, albumin 4.41, globulin 2.43 gm. per cent.. Calculated oncotic pressure 27.6 mm. Hg.. Non-protein nitrogen 23.2 mgm. per cent..

7.5.33 No further fits occurred and the boy was much more alert.

8.5.33 Systolic blood pressure 114 mm. Hg.. No oedema. Blood chemistry:- Total protein 6.71, albumin 5.04, globulin 1.67 gm. per cent.. Calculated oncotic pressure 30.1 mm. Hg.. Non-protein nitrogen 51.7 mgm. per cent.. Urea Concentration test:- Before urea 3.45, one hour after 4.12, two hours after 4.52 gm. per cent..

17.5.33 Gross haematuria ceased.

26.5.33 Tonsillectomy.

27.5.33 Slight macroscopic haematuria again present.

1.6.33 Dismissed. A trace of blood and of albumin was still present in the urine.

CASE 8. A girl aged 6 years. One week before admission the face and legs became swollen and the urine red in colour.

14.5.32 On admission oedema was general and ascites was present. The urine contained blood and albumin. The fundi were not examined. A diet of half milk was given containing 22.0 gm. of protein per day.

15.5.32 The systolic blood pressure was 130 mm. Hg.. Oedema was unchanged from admission. Urea Concentration test:- Before urea 1.64, 1 hour after 1.50, 2 hours after 1.79 gm. per cent.. Blood chemistry:- Total protein 5.79, albumin 3.18, globulin 2.61 gm. per cent.. Calculated oncotic pressure 21.4 mm. Hg.. Non-protein nitrogen 47.7 mgm. per cent..

21.5.32 Systolic blood pressure 120 mm. Hg..

24.5.32 There was no oedema. Blood chemistry:- Total protein 7.68, albumin 5.23, globulin 2.45 gm. per cent.. Calculated oncotic pressure 32.2 mm. Hg. Non-protein nitrogen 45.5 mgm. per cent..

24.8.32 A positive guaiac reaction in the urine was obtained daily until this date.

9.9.32 A trace of albumin was still present in the urine on dismissal.

21.5.34 Urine clear.

CASE 9. A boy aged 4 years. Eight days before admission he vomited and complained of headache. Six days later the face became puffy and the urine dark in colour.

28.5.32 On admission oedema was general and ascites was present. The urine contained blood and albumin. The blood pressure was not taken and the fundi were not examined. Blood chemistry:- Total protein 4.44, albumin 3.01, globulin 1.43 gm. per cent.. Calculated oncotic pressure 18.5 mm. Hg.. Non-protein nitrogen 20.7 mgm. per cent..

4.6.32 No gross haematuria was observed after this date.

6.6.32 No oedema.

9.6.32 Dismissed from hospital with mumps.

1.7.32 A trace of albumin was still present in the urine.

23.3.33 Readmitted with a right apical pneumonia from which he made a good recovery. The urine was clear during this admission.

15.1.34 Urine clear.

CASE 10. A girl aged 6 years. Four days before admission the urine was observed to be dark and three days later the face became swollen.

23.1.31 On admission oedema of the face and legs was present and the urine contained blood and albumin. The systolic blood pressure was 125 mm. Hg.. The fundi were not examined. Blood chemistry:- Total protein 6.25, albumin 3.75, globulin 2.50 gm. per cent.. Calculated oncotic pressure 24.1 mm. Hg.. Non-protein nitrogen 49.5 mgm. per cent..

24.1.31 High fever. Erysipelas was diagnosed and the child was transferred to a fever hospital.

CASE 11. A boy aged 5 years. Two weeks before admission his face was observed to be puffy and his urine dark.

19.9.33. On admission oedema of the face only was present. The urine contained blood and albumin and the systolic blood pressure was 115 mm. Hg.. The fundi showed no abnormality. Blood chemistry:- Total protein 6.91, albumin 3.94, globulin 2.97 gm. per cent.. Calculated oncotic pressure 25.8 mm. Hg.. Non-protein nitrogen 19.1 mgm. per cent..

21.9.33. No further gross haematuria occurred after this date. No oedema was present.

4.10.33. The systolic blood pressure was 90 mm. Hg.. Blood chemistry:- Total protein 8.29, albumin 6.51, globulin 1.78 gm. per cent.. Calculated oncotic pressure 38.3 mm. Hg.. Non-protein Nitrogen 23.7 mgm. per cent.. Urea concentration test:- Before urea 1.75, one hour after 2.55, two hours after 3.54 gm. per cent..

25.10.33. The urine was clear on dismissal.

7.5.34. Urine clear.

CASE 12. A boy aged 8 years. Five days before admission he developed sore throat with cervical adenitis. Two days later swelling of the face and oedema of extremities appeared. The urine was reported to be red and on the day of admission vomiting was frequent.

30.1.31. On admission he was found to be very drowsy; oedema was general and in addition ascites was present. Much blood and albumin were present in the urine. No observation of the blood pressure was made. The fundi showed no abnormality. Shortly after admission generalized convulsions occurred. Lumbar puncture was performed and 25 c.c. of fluidwere removed under increase of pressure. 200 c.c. of blood were withdrawn by venipuncture. Blood Chemistry:- Total protein 5.60, albumin 3.60, globulin 2.00 gm. per cent.. Calculated oncotic pressure 22.6 mm. Hg.. Non-protein nitrogen 40.6 mgm. per cent.. Immediate improvement followed this treatment but for two days he complained of blindness.

2.2.31. The systolic blood pressure 100 mm. Hg.. No oedema was made out.

22.2.31. No gross haematuria was observed after this date.

2.4.31. The urine was free from albumin.

26.6.33. The patient was readmitted to hospital. On the previous day the urine was observed to be red in colour but no oedema was observed. On examination blood and albumin were found in the urine but there was no oedema. Ophthalmoscopic examination revealed no abnormality.

27.6.33. The systolic blood pressure was 104 mm. Hg.. Blood chemistry:- Total protein 7.34, albumin 5.37, globulin 1.97 gm. per cent.. Calculated oncotic pressure 32.3 mm. Hg.. Non-protein nitrogen 25.8 mgm. per cent..

18.7.33. Urine was clear.

27.7.33. Urea concentration test:- Before urea 2.30, 1 hour after 1.70, 2 hours after 3.54 gm. per cent..

22.1.34. Urine clear. The systolic blood pressure was 110 mm. Hg..

CASE 13. A boy aged 3 years. Four days before admission oedema of the face and extremities was observed.

13.3.34. On admission he was found to have very marked oedema of the face and extremities. Ascites was also present. Albumin and blood were present in the urine. The systolic blood pressure was 138 mm. Hg.. Ophthalmoscopic examination revealed no abnormality.

14.3.34. The systolic blood pressure was still 130 mm. Hg. and oedema was unchanged.

16.3.34. Systolic blood pressure was 126 mm. Hg.. Oedema was less as indicated by a loss of 1.2 Kg. since admission.

19.3.34. Systolic blood pressure 98 mm. Hg.. Some oedema present.

23.3.34. A further fall in blood pressure to 84 mm. Hg. was observed. No oedema was present, 2.9 Kg. in weight having been lost since admission. Urea concentration test:- Before urea 0.19, 1 hour after 0.48, 2 hours after 1.21 gm. per cent..

1.5.34. Urine was reported to have been clear for a week.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
14.3.34	6.71	3.54	3.17	23.9	35.7
16.3.34	6.37	3.58	2.79	23.6	31.0
19.3.34	8.01	4.16	3.85	28.3	30.4
23.3.34	8.06	4.59	3.45	30.1	31.4

CASE 14. A girl aged 8 years. On the day before admission the urine was observed to be red and she felt off colour.

6.11.32. On admission slight puffiness of the face was present and the urine contained blood and albumin. The systolic blood pressure was 120 mm. Hg.. The fundi showed no abnormality. Blood chemistry:- Total protein 7.36, albumin 3.92, globulin 3.44 gm. per cent.. Calculated oncotic pressure 26.4 mm. Hg.. Non-protein nitrogen 22.7 mgm. per cent..

14.11.32. No oedema. Gross haematuria ceased.

1.12.32. Gross blood again present in the urine. Oedema however did not reappear.

17.12.32. Macroscopic haematuria again ceased. Slight albuminuria was still present.

12.1.33. Tonsillectomy.

14.1.33. Much gross blood was again present in the urine, again without the appearance of oedema.

22.1.33. No gross haematuria. Search for a tuberculous focus in the urinary tract was unsuccessful and there was no evidence of calculus.

16.2.33. Dismissed with a trace of albumin in the urine.

18.6.34. A faint trace of albumin was present in the non-catheter specimen of urine.

CASE 15. A girl aged 4½ years. Seven days before admission oedema of the face and legs appeared. Five days later cough became severe and she seemed to be acutely ill.

14.1.31. On admission oedema was general with ascites. Much râle was audible at both bases and considerable cyanosis was present. Very drowsy. The urine contained much albumin and blood. Prominence of the retinal veins was found on ophthalmoscopic examination.

15.1.31. Drowsiness and cyanosis were much more marked. The systolic blood pressure was 144 mm. Hg.. Lumbar puncture was performed and 40 c.c. of clear fluid under moderate pressure were removed and 80 c.c. of blood were withdrawn by venipuncture. Death, which occurred twelve hours later, was preceded by some twitching of the limbs. Blood chemistry:- Total protein 6.02, albumin 3.71, globulin 2.31 gm. per cent.. Calculated oncotic pressure 23.5 mm. Hg.. Non-protein nitrogen 56.1 mgm. per cent.. Autopsy showed acute nephritis and marked pulmonary oedema to be present.

CASE 16. A girl aged 3½ years. Four weeks before investigation she had a sore throat and a rash. Two weeks later cervical adenitis appeared for which she was admitted to a surgical ward where the urine was found to contain blood and albumin.

14.5.31. On transfer to a medical ward there was no oedema. Blood and albumin were present in the urine. The systolic blood pressure was 92 mm. Hg.. The fundi were not examined. Blood chemistry:- Total protein 9.00, albumin 5.30, globulin 3.70 gm. per cent.. Calculated oncotic pressure 33.8 mm. Hg.. Non-protein nitrogen 34.5 mgm. per cent.. Urea concentration test:- Before urea 1.25, one hour after 2.32, two hours after 2.55 gm. per cent..

19.5.31. No gross haematuria present.

1.6.31. Urine clear.

16.10.33. Urine clear.

CASE 17. A girl aged 7 years. Four days before admission some puffiness of the face was observed and the urine was dark in colour.

10.4.31. On admission oedema of the face was present and the urine contained blood and albumin. The systolic blood pressure was 120 mm. Hg.. No abnormality was detected in the fundi. Blood chemistry:- Total protein 8.46, albumin 3.34, globulin 5.12 gm. per cent.. Calculated oncotic pressure 26.6 mm. Hg.. Non-protein nitrogen 61.2 mgm. per cent..

17.4.31. No oedema.

23.4.31. No gross haematuria was observed after this date.

20.5.31. Urine clear.

18.6.34. Urine clear.

CASE 18. A boy aged 8 years. Six days before admission the face was noted to be puffy and he complained of headache. Five days later the legs became swollen and he vomited once.

3.9.32. On admission oedema of the face and extremities was present and the systolic blood pressure was 140 mm. Hg.. The urine contained blood and albumin. The fundi were not examined.

5.9.32. Oedema clinically was unaltered but by weight 0.7 Kg. was lost. The systolic blood pressure was 132 mm. Hg.. Blood chemistry:- Total protein 6.32, albumin 4.12, globulin 2.20 gm. per cent.. Calculated oncotic pressure 25.7 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent..
No gross haematuria was now present.

13.9.32. No oedema was now present. Blood chemistry:- Total protein 7.25, albumin 4.70, globulin 2.55 gm. per cent.. Calculated oncotic pressure 32.4 mm. Hg. Non-protein nitrogen 32.1 mgm. per cent..

16.9.32. Dismissed from hospital irregularly. Albuminuria was still present.

9.4.34. Urine clear.

CASE 19. A girl aged 3 years. 15 days before admission she developed a generalized rash and 5 days later complained of headache and developed swelling of the face.

28.6.33. On admission oedema of the face and extremities was present. In the urine blood and albumin were present. A soft basal V.S. murmur was audible but no cardiac enlargement was made out. The fundi were not examined. Desquamation of the palms and soles was well marked. Systolic blood pressure 128 mm. Hg..

27.6.33. Blood chemistry:- Total protein 5.84, albumin 2.96, globulin 2.88 gm. per cent.. Calculated oncotic pressure 20.3 mm. Hg.. Non-protein nitrogen 176.5 mgm. per cent.. The systolic blood pressure had now fallen to 98 mm. Hg.. No further observations were made owing to the transfer of the patient to a fever hospital.

CASE 20. A boy aged 4 8/12 years. Two weeks before admission developed headache and swelling of the face. He vomited several times and the urine was noted to be dark in colour.

28.4.31. On admission oedema of the face was observed but none elsewhere. No abnormality of the fundi was observed. The urine contained blood and albumin. The systolic blood pressure was 114 mm. Hg..

29.4.31. Blood chemistry:- Total protein 8.12, albumin 3.02, globulin 5.10 gm. per cent.. Calculated oncotic pressure 23.7 mm. Hg.. Non-protein nitrogen 35.1 mgm. per cent.. Systolic blood pressure 110 mm. Hg.. Urea concentration test:- Before urea 1.73, 1 hour after 2.41, 2 hours after 2.43 gm. per cent..

1.5.31. Systolic blood pressure 80 mm. Hg.. No oedema.

29.5.31. Blood chemistry:- Total protein 8.94, albumin 4.77, globulin 4.17 gm. per cent.. Calculated oncotic pressure 32.1 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent..

24.6.31. Dismissed from hospital. Urine clear.

16.3.34. Urine clear.

CASE 21. A boy aged 4 years. Three weeks before admission he lost appetite and developed a right-sided otorrhoea. Seventeen days later the face was swollen and the urine was dark. Occasional vomiting occurred.

21.2.33. On admission oedema of the face and legs was present and the urine contained blood and albumin. The fundi were not examined. At the base of the heart a short V.S. murmur was audible but dulness was not increased. The systolic blood pressure was 150 mm. Hg.. Blood chemistry:- Total protein 6.67, albumin 4.37, globulin 2.30 gm. per cent.. Calculated oncotic pressure 27.2 mm. Hg.. Non-protein nitrogen 43.0 mgm. per cent.. Urea concentration test:- Before urea 1.40, one hour after 1.69, two hours after 1.85 gm. per cent..

2.3.33. ? if any oedema. On this date a pneumonia of the left lower lobe appeared. High fever - 106°F. Temperature fell by crisis on the 8th day.

21.3.33. Gross haematuria ceased.

8.4.33. Urine clear.

CASE 22. A boy aged 8 years. One month before admission he had a sore throat but no rash. Three weeks later oedema of the face and ankles appeared. The urine was dark in colour.

12.6.33. On admission oedema of the face and ankles was present. The systolic blood pressure was 135 mm. Hg.. The fundi showed no abnormality. No desquamation. Much blood and albumin were present in the urine.

16.6.33. Oedema was now limited to some fulness of the face, 3.0 Kg. in weight having been lost. The systolic blood pressure was 125 mm. Hg.. Blood Chemistry:- Total protein 8.70, albumin 5.79, globulin 2.91 gm. per cent.. Calculated oncotic pressure 35.9 mm. Hg.. Non-protein nitrogen 47.6 mgm. per cent..

22.6.33. No oedema. Gross haematuria ceased.

26.6.33. Non-protein nitrogen of the blood 40.8 mgm. per cent.. Urea concentration test:- Before urea 1.16, one hour after 2.01, two hours after 4.01 gm. per cent.

15.8.33. The urine was clear of albumin on dismissal.

CASE 23. A boy aged 3½ years. A week before admission the urine was observed to be red and a few days later swelling of the face became obvious.

21.2.32. On admission to hospital oedema of the face was present but none elsewhere. The urine contained blood and albumin. No opthalmoscopic examination was made and blood pressure was not estimated.

23.2.32. Systolic blood pressure 116 mm. Hg.. Blood chemistry:- Total protein 6.34, albumin 4.62, globulin 1.72 gm. per cent.. Calculated oncotic pressure 27.9 mm. Hg.. Non-protein nitrogen 34.7 mgm per cent..

25.2.32. Fundi normal. No oedema was present. Urea concentration test:- Before urea 2.53, 1 hour after 2.69, 2 hours after 2.93 gm. per cent..

5.3.32. No gross haematuria was observed after this date.

15.3.32. Urea concentration test:- Before urea 0.94, 1 hour after 1.84, 2 hours after 4.10 gm. per cent..

6.5.32. The patient still showed a trace of albumin in the urine.

20.11.33. Urine clear.

CASE 24. A boy aged 6 years. On 22.3.33 he developed cough and fever and 6 days later blood was found in the urine.

31.3.33. On admission oedema was very marked and ascites was present. The urine contained blood and albumin. Ophthalmoscopic examination revealed no abnormality. A pneumonia involving the right upper lobe was present, and the temperature was 102°F. No observation on the blood pressure was made. Blood chemistry was:- Total protein 8.52, albumin 3.79, globulin 4.73 gm. per cent.. Calculated oncotic pressure 27.6 mm. Hg.. Non-protein nitrogen 136.0 mgm. per cent..

10.4.33. No oedema was apparent. The systolic blood pressure was 90 mm. Hg.. The temperature was now normal.

17.5.33. Gross haematuria ceased.

9.6.33. A trace of albumin was still present in the urine.

30.4.34. Urine clear.

CASE 25. A boy aged 12 years. Four days before admission swelling of the face noted and a red colouration of the urine.

11.12.33. On admission oedema was general. Ascites was present. A slight degree of bronchitis with moderate fever was present. In the urine there were blood and albumin: the fundi were normal; the systolic blood pressure was 140 mm. Hg..

12.12.33. The systolic blood pressure was 148 mm. Hg. and the condition was unchanged.

15.12.33. The blood pressure was still 150 mm. Hg. but oedema was considerably less.

18.12.33. The blood pressure was now 90 mm. Hg. and oedema was absent.

17. 1.34 Systolic blood pressure 90 mm. Hg.. Congo red test negative. Urea concentration test:- Before urea 1.18, one hour after 1.50, two hours after 3.40 gm. per cent..

1.2.34. A faint trace of albumin was present in the urine on dismissal.

7.5.34. Urine clear.

Blood chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
12.12.33	6.17	4.19	1.98	25.8	48.7
15.12.33	8.71	5.60	3.11	35.1	32.2
18.12.33	8.56	3.57	4.99	26.6	32.4
27.12.33	6.87	4.72	2.15	28.9	34.4

CASE 26. A boy aged 2 years. Twelve days before admission he vomited and complained of sore throat. Next day the face seemed puffy.

7.1.31. On admission oedema of the face was present. The urine contained blood and albumin and the systolic blood pressure was 110 mm. Hg.. The fundi showed no abnormality. Blood chemistry:- Total protein 6.14, albumin 3.48, globulin 2.66 gm. per cent.. Calculated oncotic pressure 22.9 mm. Hg.. Non-protein nitrogen 60.3 mgm. per cent..

12.1.31. No oedema present.

22.1.31. Gross haematuria ceased.

20.2.31. A trace of albumin was still present in the urine on dismissal.

CASE 27. A boy aged 7 years and 6 months. A week before admission he developed a cough and a herpes appeared on his upper lip. Three days later he began to vomit and next day the face was swollen and the urine was red in colour.

2.5.31. On admission the child was found to be sharply ill with a left sided lobar pneumonia. The heart was not enlarged but a V.S. murmur was audible at the base. Oedema was general and ascites was present. The urine contained blood and albumin. Ophthalmoscopic examination revealed no abnormality. The systolic blood pressure was 118 mm. Hg..

3.5.31. Blood pressure was unchanged and the blood chemistry was:- Total protein 4.61, albumin 2.81, globulin 1.80 gm. per cent.. Calculated oncotic pressure 18.2 mm. Hg.. Non-protein nitrogen 18.2 mgm per cent..

6.5.31. The temperature fell by lysis and reached normal on this date. Systolic blood pressure 94 mm. Hg..

3.6.31. The guaiac reaction became negative on this date when the systolic blood pressure was 90 mm. Hg.. Blood chemistry:- Total protein 8.17, albumin 5.05, globulin 3.12 gm. per cent.. Calculated oncotic pressure 32.1 mm. Hg.. Non-protein nitrogen 27.2 mgm. per cent..

24.6.31. Urine clear.

18.3.34. Urine clear. Systolic blood pressure 90 mm. Hg..

CASE 28. A boy aged 5 years and 10 months. For a week before admission the face and extremities were observed to be swollen.

9.2.33. On admission oedema of the face and extremities was present and blood and albumin were found in the urine. The systolic blood pressure was 128 mm. Hg.. The fundi were not examined. A V.S. murmur was audible at the base of the heart but no increase of dulness was detected.

10.2.33. Blood chemistry:- Total protein 6.72, albumin 3.75, globulin 2.97 gm. per cent.. Calculated oncotic pressure 24.9 mm. Hg.. Non-protein nitrogen 50.0. Urea concentration test:- Before urea 0.73, 1 hour after 0.71, 2 hours after 0.31 gm. per cent.. Systolic blood pressure 125 mm. Hg..

13.2.33. Systolic blood pressure 130 mm. Hg.. Oedema was unchanged.

17.2.33. No oedema present.

13.4.33. No gross haematuria was observed after this date.

20.4.33. Urine clear.

29.1.34. Urine clear.

CASE 29. A boy aged 10 years. Ten days before admission he became listless and began to vomit. Four days later the face became puffy and the urine was observed to be dark. On the day before admission twitching of the arms and legs was observed.

7.9.33. On admission oedema was general with ascites. A basal V.S. murmur was audible but cardiac dulness was not increased. Drowsiness was marked. The urine contained blood and albumin and the systolic blood pressure was 148 mm. Hg.. Retinoscopy revealed no abnormality. Diet - milk containing 40 gm. of protein per day.

8.9.33. No twitching was observed. The systolic blood pressure was 140 mm. Hg.. Oedema unchanged.

13.9.33. The systolic blood pressure had fallen to 132 mm. Hg. and oedema was less, 2.0 Kg. in weight having been lost.

15.9.33. Slight loss of weight continued. The blood pressure was unchanged.

16.9.33. The condition was now much worse though loss of weight continued. Vomiting was frequent and he was very drowsy and cyanosed. The systolic blood pressure had risen to 164 mm. Hg.. Lumbar puncture was performed and 25 c.c. of clear fluid under increased pressure withdrawn. 100 c.c. of blood removed. Following the operation the systolic blood pressure was found to be 134 mm. Hg.. Blood CO_2 56.8 vols. per cent..

17.9.33. The drowsiness was less and the colour improved. No further vomiting. The systolic blood pressure was 144 mm. Hg..

18.9.33. Mental condition normal.

28.9.33. Oedema still present. The systolic blood pressure was 146 mm. Hg..

4.10.33. Systolic blood pressure 120 mm. Hg.. No oedema.

7.10.33. Milk increased to give 53.0 gm. of protein daily.

18.10.33. No oedema. Systolic blood pressure 120 mm. Hg..

10.11.33. Systolic blood pressure 98 mm. Hg.. Urea concentration test:- Before urea 0.66, one hour after 1.63, two hours after 2.5 gm. per cent. Macroscopic haematuria was still present.

28.11.33. Systolic blood pressure 120 mm. Hg.. Light diet permitted and full diet one month later.

17.2.34. Gross haematuria ceased.

16.3.34. Systolic blood pressure 115 mm. Hg..

19.3.34. Urea concentration test:- Before urea 1.63, one hour after 1.93, two hours after1.95 gm. per cent.

23.3.34. Systolic blood pressure 110 mm. Hg.. On dismissal a trace of albumin was present in the urine but no blood on dismissal on this date.

7.5.34. Systolic blood pressure 116 mm. Hg.. A trace of albumin was still present in the urine.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
8.9.33	7.62	2.39	5.23	20.5	280.0
13.9.33	7.52	3.44	4.08	24.6	222.0
16.9.33	7.61	3.69	3.92	25.8	133.0
28.9.33	6.27	3.96	2.31	25.0	30.4
4.10.33	7.36	3.57	3.79	24.9	23.0
18.10.33	-	-	-	-	31.8
19.3.34	8.31	5.39	2.92	33.7	20.0

Urea Concentration Tests.

Date.	Before Urea.	1 hour after.	2 hours after.
13.11.33	0.66 gm. %	1.63 gm. %	2.50 gm. %
23. 3.33	1.63 gm. %	1.93 gm. %	1.95 gm. %

CASE 30. A boy aged 5 years. Seven days before admission swelling of the face was observed.

22.9.33. On admission oedema was confined to the face. The urine contained albumin but no gross blood. The fundi were not examined. A short V.S. murmur was audible at the base of the heart but dulness was not increased.

27.9.33. The systolic blood pressure was 88 mm. Hg.. Oedema was now absent. Blood chemistry:- Total protein 6.90, albumin 4.27, globulin 2.63 gm. per cent.. Calculated oncotic pressure 27.1 mm. Hg.. Non-protein nitrogen 20.6 mgm. per cent.. Serum fat - 0.2 gm. per cent..

3.10.33. Systolic blood pressure 90 mm. Hg.. Urea concentration test:- Before urea, 1.06, 1 hour after 3.30, 2 hours after 3.78 gm. per cent.. Non-protein nitrogen of the blood 24.5 mgm. per cent..

31.10.33. The urine was quite normal.

22.1.34. The urine contained a faint trace of albumin.

CASE 31. A boy aged 3 years who developed swelling of the feet six days before admission. For four days prior to this he was out of sorts and the urine was red in colour.

28.10.32. On admission he was found to have oedema of the extremities. The urine contained blood and albumin. The systolic blood pressure was 120 mm. Hg.. No ophthalmoscopic examination was made.

29.10.32. Blood chemistry:- Total protein 7.40, albumin 4.93, globulin 2.47 gm. per cent.. Calculated oncotic pressure 30.5 mm. Hg.. Non-protein nitrogen 43.9 mgm. per cent.. Urea concentration test:- Before urea 1.86 per cent.. 1 hour after 2.24 per cent.. 2 hours after 3.17 gm. per cent..

4.11.32. No oedema was present.

8.11.32. Systolic blood pressure 70 mm. Hg.. Urine clear.

9.1.33. Urine clear.

CASE 32. A girl aged 4 years. Three days before admission the face and legs became swollen and the urine was noted to be red.

23.3.34. On admission oedema was general. No ascites was detected. There was blood and albumin in the urine and the systolic blood pressure was 144 mm. Hg.. The fundi were not examined.

24.3.34. The systolic blood pressure was 134 mm. Hg. and no oedema was found save of the face. Blood chemistry:- Total protein 8.19, albumin 4.17, globulin 4.02 gm. per cent.. Calculated oncotic pressure 28.5 mm. Hg.. Non-protein nitrogen 28.4 mgm. per cent.

27.3.34. No oedema. The systolic blood pressure was 88 mm. Hg.. Blood chemistry:- Total protein 8.06, albumin 5.07, globulin 2.99 gm. per cent.. Calculated oncotic pressure 33.1 mm. Hg.. Non-protein nitrogen 61.1 mgm. per cent.

29.3.34. Urea concentration test:- Before urea 3.93, one hour after 2.78, two hours after 3.13 gm. per cent..

3.4.34. Gross haematuria ceased.

11.4.34. Urine clear.

CASE 33. A boy aged 3 years. Four days before admission swelling of face and legs was observed.

31.5.31. On admission oedema was general and marked. Ascites was present. Blood and albumin were present in the urine.

1.6.31. Ophthalmoscopic examination revealed no abnormality. The systolic blood pressure was 120 mm. Hg.. Blood chemistry:- Total protein 6.03, albumin 3.36, globulin 2.67 gm. per cent.. Calculated oncotic pressure 22.2 mm. Hg.. Non-protein nitrogen 24.8 mgm. per cent..

3.6.31. Systolic blood pressure 126 mm. Hg. Oedema was unchanged.

10.6.31. Systolic blood pressure 90 mm. Hg. No oedema.

14.6.31. No gross haematuria was seen from now on.

13.7.31. Urine clear.

CASE 34. A boy aged 10 years and 9 months. Three weeks before admission he complained of sore throat and joint pains and a few days later right otorrhoea developed. Five days before admission the face became swollen, followed by generalized oedema.

28.4.31. On admission generalized oedema was present. The urine contained blood and albumin. The systolic blood pressure was 160 mm. Hg.. Ophthalmoscopic examination showed physiological cupping only.

29.4.31. Oedema was unaltered and systolic blood pressure was 152 mm. Hg.. Blood chemistry:- Total protein 6.04, albumin 3.57, globulin 2.47 gm. per cent.. Calculated oncotic pressure 22.5 mm. Hg.. Non-protein nitrogen 46.3 mgm. per cent..

1.5.31. Systolic blood pressure 170 mm. Hg..

7.5.31. Oedema was much less. Systolic blood pressure 120 mm. Hg..

11.5.31. Systolic blood pressure 110 mm. Hg.. No oedema was present.

28.5.31. Gross blood was still present in the urine. Blood chemistry:- Total protein 7.34, albumin 4.59, globulin 2.75 gm. per cent.. Calculated oncotic pressure 29.1 mm. Hg.. Non-protein nitrogen 43.3 mgm. per cent..

4.7.31. No gross blood was observed in the urine after this date.

30.7.31. Dismissed from hospital. The urine still contained a trace of albumin.

27.11.33. Urine clear.

CASE 35. A boy aged 11 years who 3 weeks before admission was in bed for 1 week with a sore throat. Two days before admission swelling of face was noted.

11.10.33. On admission to hospital he was found to have oedema of the face. The urine contained blood and albumin and the systolic blood pressure was 138 mm. Hg.. Ophthalmoscopic examination revealed no abnormality.

12.10.33. Blood chemistry:- Total protein 7.94, albumin 5.48, globulin 2.46 gm. per cent.. Calculated oncotic pressure 33.6 mm. Hg.. Non-protein nitrogen 42.0 mgm. per cent. Serum fat 0.2 gm. per cent..

21.1.34. Till this date a positive guaiac reaction was obtained in the urine. Albuminuria was not marked.

31.1.34. Trace of albumin only.

24.7.34. Urine clear.

CASE 36. A boy aged 8 years. Six days before admission swelling of face and legs was observed.

13.3.33. On admission oedema of face and extremities was present and the urine contained blood and albumin. The fundi were not examined.

14.3.33. The systolic blood pressure was 148 mm. Hg.. Blood chemistry:- Total protein 5.97, albumin 4.67, globulin 1.30 gm. per cent.. Calculated oncotic pressure 28.2 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent.. Urea concentration test:- Before urea 2.54, 1 hour after 2.77, 2 hours after 2.75 gm. per cent..

22.3.33. There was no oedema apparent and the guaiac reaction in the urine was negative.

5.4.33. Systolic blood pressure 105 mm. Hg..

9.4.33. Urine clear.

CASE 37. A boy aged 10 years who developed fever, cough and oedema of the face 10 days before admission. Four hours before entering hospital he took a series of generalized convulsions.

28.1.32. On admission he was very drowsy and showed oedema of the face and legs. The urine contained much blood and albumin. Blood pressure was 150 mm. Hg. systolic. Ophthalmoscopic examination revealed no abnormality. Cardiac dulness was increased to right and left of the middle line and a V.S. murmur was audible at the base. Under chloroform anaesthesia lumbar puncture was performed and 50 c.c. of cerebro-spinal fluid removed under increased pressure, 80 c.c. of blood were also withdrawn. Right ear discharging.

29.1.32. Child was no longer comatose. Blood pressure 150 mm. Hg. systolic.

30.1.32. Cardiac dulness was within normal limits although the blood pressure was still 150 mm. Hg. systolic. Oedema was much less.

9.2.32. Child was free from oedema. Blood pressure had fallen to 110 mm. Hg. systolic.

10.2.32. Salt containing diet allowed.

13.2.32. Guaiac test for blood in the urine negative from this date.

25.2.32. Blood pressure was 110 mm. Hg. systolic and the only apparent abnormality remaining was a trace of albumin in the urine.

24.3.32. Dismissed from hospital still with slight albuminuria.

12.12.32. The boy appeared to be well a year after the illness but a trace of albumin was still present in the urine. Systolic blood pressure 100 mm. Hg..

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
28.1.32.	6.38	4.17	2.21	26.0	29.8
2.2.32.	7.99	5.60	2.39	34.1	72.0
9.2.32.	6.62	4.10	2.52	26.0	58.8
25.2.32.	6.30	4.16	2.14	25.9	45.4
12.12.32.	7.01	4.62	2.39	28.3	20.0

Urea Concentration Tests.

Date.	Before Urea.	1 hour after.	2 hours after.
2.2.32.	1.23 gm. %	1.87 gm. %	0.3 gm. %
10.2.32.	1.65 gm. %	2.41 gm. %	2.75 gm. %

CASE 38. A girl aged 11 years. Two weeks before admission she took a cold, lost her appetite and complained of headache. The face was observed to be swollen. Since then the oedema became much worse and extended to the legs. This patient walked up to the out-patient department and was not acutely ill.

28.12.32. On admission there was very great generalized oedema and ascites was also present. The heart and fundi presented no abnormality and the systolic blood pressure was 90 mm. Hg.. The urine contained much albumin, some casts and red blood cells. There was some bronchitis but no fever. Wassermann reaction negative. A diet of half milk was given containing 240 gm. of protein per day.

3.1.33. As a result of diuresis the weight had fallen from 28.7 to 24.0 Kg. and oedema was almost gone. No haematuria even microscopic observed after this date.

11.1.33. Oedema unaltered. Diet altered to whole milk giving a protein intake of 40.0 gm. per day.

19.1.33. Given full diet with the usual quantity of salt.

20.1.33. The patient was not weighed but oedema was definitely more noticeable.

21.1.33. Oedema still worse, 2.0 Kg. in weight gained since 19.1.32. Full diet without salt given. Oedema increased for several days and then tended to diminish somewhat.

16.2.33. No change was noted in the condition. A high protein and salt-poor diet containing 95 gm. of protein per day was commenced.

14.3.33. Oedema rather less.

29.3.33. Oedema rather more marked. Full diet salt free.

10.4.33. Oedema again increased.

21.4.33. Gum acacia intravenously, 24 gm. in 340 c.c. normal saline, was followed by cyanosis, vomiting and fever.

22.4.33. Oedema was rather more marked. Systolic blood pressure 100 mm. Hg..

23.5.33. Condition unchanged, oedema still present. Allowed up.

2.6.33. Salt permitted in the diet.

4.6.33. A gain of 1.0 Kg. in body weight since 2.6.34 was observed.

15.6.33. Tonsillectomy performed. Systolic blood pressure 118 mm. Hg..

21.6.33. Dismissed from hospital.

27.6.33. Oedema very marked.

11.9.33. Oedema unchanged. The child seemed fairly well and was not confined to bed. Systolic blood pressure 110 mm. Hg..

Readmitted to hospital for further observation. A diet poor in salt and containing 95 gm. of protein per day was started.

26.9.33. Oedema unchanged. Full diet "salt-free."

9.11.33. Dismissed from hospital. The oedema was unaltered and the urine still contained much albumin. Dismissed on ordinary full diet.

15.1.34. No oedema. Systolic blood pressure 98 mm. Hg.. Congo red test negative. Albuminuria unaltered.

20.2.34. Oedema present.

5.3.34. No oedema. Albuminuria seemed rather less.

19.3.34. Relapse had occurred and oedema and albuminuria were both marked once more.

10.4.34. Oedema seemed rather less.

7.6.34. No oedema present. Albuminuria slight. Systolic blood pressure 94 mm. Hg..

Blood chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
28.12.32	5.08	1.71	3.37	14.1	33.3
3.1.33	4.84	2.11	2.73	15.4	28.8
11.1.33	4.63	2.41	2.22	16.3	31.2
19.1.33	4.08	2.43	1.65	15.7	29.0
21.1.33	4.91	2.12	2.79	15.6	30.9
30.1.33	3.35	1.74	1.61	11.2	19.1
13.2.33	4.39	1.94	2.45	14.1	32.0
27.2.33	5.67	3.29	2.38	21.4	30.0
7.3.33	5.19	2.64	2.55	18.5	31.5
13.3.33	4.42	2.31	2.11	15.6	35.5
23.3.33	4.61	2.39	2.22	16.2	35.0
31.3.33	4.23	1.91	2.32	13.3	33.0
10.4.33	4.41	1.90	2.51	13.9	44.4
17.4.33	4.27	1.95	2.32	14.1	28.1
21.4.33	3.48	1.78	1.70	12.2	20.4
22.4.33	3.84	1.65	2.19	12.1	37.5
1.5.33	5.04	2.34	2.70	16.1	25.0
12.5.33	4.19	2.65	1.54	16.7	34.3
29.5.33	5.02	3.35	1.67	20.7	20.7
1.6.33	4.69	2.19	2.50	15.5	22.8
20.6.33	4.58	2.00	2.58	14.6	24.0
25.9.33	5.09	2.07	3.02	15.6	25.8
12.10.33	5.97	2.61	3.36	19.0	24.0
15.1.34	7.87	2.98	4.89	23.2	29.1
20.2.34	5.81	3.29	2.52	21.6	30.7
5.3.34	6.87	3.49	3.38	23.9	21.5
19.3.34	5.81	1.81	4.00	15.5	29.7
10.4.34	5.74	2.97	2.77	20.2	23.4
7.6.34	7.82	5.39	2.43	34.0	23.2

Urea concentration tests.

Date.	Before Urea.	1 hour after.	2 hours after.
30.12.32	0.76 gm. %	3.10 gm. %	2.90 gm. %
3.1.33	2.35 " "	3.51 " "	3.72 " "
11.1.33	2.0 " "	3.55 " "	3.90 " "
30.1.33	1.85 " "	3.58 " "	3.76 " "
13.2.33	1.30 " "	1.95 " "	2.60 " "
13.3.33	3.02 " "	3.85 " "	3.90 " "
23.3.33	4.25 " "	3.91 " "	4.41 " "
31.3.33	2.38 " "	3.50 " "	4.46 " "
10.4.33	2.16 " "	3.62 " "	3.20 " "
29.5.33	1.75 " "	3.95 " "	4.26 " "
12.10.33	2.28 " "	2.87 " "	4.14 " "

CASE 39. A boy aged 11 years. Two days before admission the urine was observed to be dark in colour. No oedema was observed.

28.6.33. On admission there was no oedema. The urine contained blood, albumin and casts. The systolic blood pressure was 100 mm. Hg.. No abnormality was detected in the fundi. Blood chemistry:- Total protein 7.35, albumin 5.93, globulin 1.42 gm. per cent.. Calculated oncotic pressure 34.6 mm. Hg.. Non-protein nitrogen 25.0 mgm. per cent..

3.7.33. Weight unchanged from admission. Gross haematuria ceased.

27.7.33. Urea concentration test:- Before urea 1.60, one hour after 1.84, two hours after 2.64 gm. per cent.. Non-protein nitrogen of the blood 29.2 mgm. per cent.. Urine clear of albumin.

CASE 40. A boy aged 8 years. Five days before admission he complained of headache and began to vomit. Next day there was oedema of the face and twelve hours before admission generalized convulsions began.

17.5.33. On admission he was very drowsy and complained of headache. Oedema of the face was present and there was blood and albumin in the urine. Retinoscopy revealed some fulness of the retinal veins. The systolic blood pressure was 150 mm. Hg.. Lumbar puncture was performed and 25 c.c. of clear fluid under increased pressure withdrawn. 60 c.c. of blood were removed. As a result of this the blood pressure fell to 128 mm. Hg.. Blood chemistry:- Total protein 8.86, albumin 3.67, globulin 5.19 gm. per cent.. Calculated oncotic pressure 27.4 mm. Hg.. Non-protein nitrogen 82.2 mgm. per cent..

18.5.33. Vomiting continued and there seemed to be little change in his condition.

19.5.33. The systolic blood pressure was again 150 mm. Hg. Convulsions recurred and following these a right hemiplegia appeared. Blindness was complained of. Lumbar puncture was repeated and 80 c.c. of blood were withdrawn. Following this operation the systolic blood pressure fell to 117 mm. Hg.. Blood chemistry:- Total protein 11.14, albumin 4.36, globulin 6.78 gm. per cent.. Calculated oncotic pressure 33.5 mm. Hg.. Non-protein nitrogen 92.3 mgm. per cent..

20.5.33. No further convulsions but still drowsy. Hemiplegia and blindness still present. Systolic blood pressure 136 mm. Hg..

21.5.33. Systolic blood pressure 128 mm. Hg.. No oedema.

22.5.33. There was no evidence of uraemia but paresis of the right arm and leg was still present. Vision was improved and he was able to count fingers 18" from his face.

29.5.33. Urea concentration test:- Before urea 1.13, one hour after 1.17, two hours after 1.30 gm. per cent.. Non-portein nitrogen of the blood 49.0 mgm. per cent..

6.6.33. Systolic blood pressure 95 mm. Hg.. No macroscopic haematuria. Vision normal. Non-protein nitrogen of the blood 34.2 mgm. per cent.. Wassermann reaction in blood and cerebro-spinal fuid negative.

12.6.33. Urea concentration test:- Before urea 1.37, one hour after 1.40, two hours after 1.60 gm. per cent..

5.7.33. Urea concentration test:- Before urea 1.40, one hour after 1.75, two hours after 1.78 gm. per cent..

10.7.33. Right arm and leg still rather weak.

23.8.33. No evidence of hemiplegia. A trace of albumin was still present in the urine.

26.3.34. A trace of albumin was still present in the urine.

CASE 41. A boy aged 9 years. Three weeks before admission the right ear began to discharge and some days later he became rather drowsy. On the day before entrance to hospital he complained of headache, vomited, and took a convulsion. Previous to admission he was lumbar punctured. The fluid was normal.

8.1.34. On admission he was comatose. Oedema of the face and slight pitting of the legs was present. The urine contained blood and albumin. The systolic blood pressure was 120 mm. Hg.. Retinoscopy revealed no abnormality. The right knee jerk was exaggerated and clonus was present, while the plantar response was flexor. Venipuncture was performed and 100 c.c. of blood removed. Blood chemistry:- Total protein 8.36, albumin 3.51, globulin 4.85 gm. per cent.. Calculated oncotic pressure 26.1 mm. Hg.. Non-protein nitrogen 88.2 mgm. per cent..

9.1.34. Although no further convulsions occurred he was still very drowsy and vomiting was frequent. Lumbar puncture was repeated and a further 100 c.c. of blood were withdrawn.

10.1.34. The condition was unchanged though vomiting had ceased.

11.1.34. Brighter. Systolic blood pressure 96 mm. Hg.. No oedema. No evidence of a lesion of the pyramidal tract.

14.1.34. Mental condition normal.

10.3.34. Gross haematuria ceased on this date. Non-protein nitrogen of the blood 31.2 mgm. per cent.. Urea concentration test:- Before urea 1.4, one hour after 2.12, two hours after 2.28 gm. per cent..

24.3.34. A trace of albumin was still present in the urine on dismissal.

24.6.34. The urine still contained a trace of albumin.

CASE 42. A girl aged 6 years and 2 months. Three days before admission she was observed to be swollen about the face and to be passing red urine.

1.5.33. On admission oedema was absent. The urine contained blood and albumin. Systolic blood pressure 108 mm. Hg.. The fundi were not examined. A short V.S. murmur was audible at the base of the heart but dulness was not increased.

2.5.33. Blood chemistry:- Total protein 7.11, albumin 4.54, globulin 2.57 gm. per cent.. Calculated oncotic pressure 28.6 mm. Hg.. Non-protein nitrogen 65.0 mgm. per cent.. Systolic blood pressure 108 mm. Hg.. No oedema.

4.5.33. Urea concentration test:- Before urea 2.64, 1 hour after 1.09, 2 hours after 0.57 gm. per cent..

9.5.33. Blood chemistry:- Total protein 7.24, albumin 5.27, globulin 1.97 gm. per cent.. Calculated oncotic pressure 31.7 mm. Hg.. Non-protein nitrogen 40.8 mgm. per cent..

13.5.33. No gross haematuria was observed from now on.

31.5.33. Dismissed from hospital. Urine clear.

CASE 43. A girl aged 2 years 6 months. Five days before admission the face and feet became swollen and the urine red. Vomiting occurred once.

22.10.32. On admission oedema was general but there was no ascites. The urine contained blood and albumin and the systolic blood pressure was 120 mm. Hg.. The fundi were not examined.

24.10.32. Oedema unchanged. (0.4 Kg. in weight lost.) Blood chemistry:- Total protein 7.25, albumin 3.92, globulin 3.33 gm. per cent.. Calculated oncotic pressure 26.2 mm. Hg.. Non-protein nitrogen 38.0 mgm. per cent..

30.10.32. No oedema.

8.11.32. Systolic blood pressure 80 mm. Hg..

30.12.32. No gross haematuria observed after this date.

17.1.33. The urine was clear on dismissal.

26.6.34. Urine clear.

CASE 44. A boy aged 7 years. Five days before admission he developed a sore throat with abdominal pain and vomiting. Two days later he developed headache and swelling of the face.

6.7.31. On admission oedema of the face was present and the urine contained blood and albumin. The systolic blood pressure was 130 mm. Hg.. The fundi showed no abnormality.

7.7.31. Oedema unchanged. The systolic blood pressure was 120 mm. Hg.. Blood chemistry:- Total protein 6.77, albumin 3.81, globulin 2.96 gm. per cent.. Calculated oncotic pressure 25.1 mm. Hg.. Non-protein nitrogen 26.2 mgm. per cent.. Urea concentration test:- Before urea 0.91, one hour after 1.08, two hours after 1.90 gm. per cent..

10.7.31. No oedema. No gross haematuria was observed after this date. The systolic blood pressure was 88 mm. Hg..

12.7.31. Blood chemistry:- Total protein 6.98, albumin 3.87, globulin 3.11 gm. per cent.. Calculated oncotic pressure 25.6 mm. Hg.. Non-protein nitrogen 30.1 mgm. per cent..

23.7.31. Blood chemistry:- Total protein 8.24, albumin 4.96, globulin 3.28 gm. per cent.. Calculated oncotic pressure 31.9 mm. Hg.. Non-protein nitrogen 31.5 mgm. per cent..

29.7.31. Urine clear on dismissal from hospital.

24.12.32. Urine clear.

CASE 45. A boy aged 11 years. Ten days before admission to hospital oedema of the face and legs was noted. The urine was seen to be dark in colour.

24.3.31. On admission oedema of face and extremities was present and the urine contained blood and albumin. The fundi showed no abnormality. The area of cardiac dulness was increased to right and slightly to the left of the middle line. A V.S. murmur was audible all over the praecordium.

25.3.31. Blood chemistry:- Total protein 5.93, albumin 4.31, globulin 1.62 gm. per cent.. Calculated oncotic pressure 25.9 mm. Hg.. Non-protein nitrogen 35.5 mgm. per cent.. Urea concentration test:- Before urea 1.44, one hour after 1.71, two hours after 2.15 gm. per cent.. The systolic blood pressure was 156 mm. Hg..

26.2.31. Cardiac dulness now within normal limits. Murmur still audible at the base.

28.2.31. Systolic blood pressure 130 mm. Hg.. Oedema diminishing.

3.3.31. Systolic blood pressure 110 mm. Hg.. There was no oedema and gross haematuria ceased on this date.

16.3.31. Urea concentration test:- Before urea 1.39, one hour after 0.91, two hours after 2.06 gm. per cent.. Urine clear.

8.5.33. Urine clear. Systolic blood pressure 104 mm. Hg..

CASE 46. A girl aged 7 years. Three days before admission oedema of face and feet was observed.

21.6.31. On admission oedema was general and ascites was present. The urine contained blood and albumin. The blood pressure was not estimated. In the fundi no abnormality was detected. Blood chemistry:- Total protein 5.95, albumin 3.48, globulin 2.47 gm. per cent.. Calculated oncotic pressure 22.5 mm. Hg.. Non-protein nitrogen 23.4 mgm. per cent..

23.6.31. The systolic blood pressure was 118 mm. Hg.. Since admission oedema had become less (2.0 Kg. in weight lost). No gross haematuria was observed after this date.

1.7.31. No oedema.

12.7.31. No albumin was present in the urine.

3.9.31. Urine quite clear.

CASE 47. A boy aged 2 years. Two weeks before admission the face became swollen and the urine dark in colour.

23.3.34. On admission oedema of the face was present and there was blood and albumin in the urine. The systolic blood pressure was 118 mm. Hg.. The fundi were not examined.

24.3.34. Systolic blood pressure 133 mm. Hg.. Blood chemistry:- Total protein 7.32, albumin 4.56, globulin 2.76 gm. per cent.. Calculated oncotic pressure 28.9 mm. Hg.. Non-protein nitrogen 35.3 mgm. per cent..

27.3.34. No oedema. Systolic blood pressure 90 mm. Hg.. Blood chemistry:- Total protein 8.16, albumin 5.23, globulin 2.93 gm. per cent.. Calculated oncotic pressure, 32.9 mm. Hg.. Non-protein nitrogen 45.0 mgm. per cent.. Urea concentration test:- Before urea 1.40, one hour after 1.10, two hours after 0.78 gm. per cent..

1.6.34. Slight macroscopic haematuria was still present.

5.6.34. No gross haematuria.

9.7.34. Urine clear.

CASE 48. A girl aged 6 years. Two days before admission swelling of the legs and face was noted.

15.6.33. On admission anasarca with marked ascites was present. The urine contained much blood and albumin and the systolic blood pressure was 128 mm. Hg.. The heart and fundi showed no abnormality. Fever was present and the throat was acutely inflamed. A diet of milk supplying 22.0 gm. of protein daily was given.

16.6.33. Oedema unchanged. Protein intake increased to 44.0 gm. daily.

24.6.33. No oedema. No gross haematuria. Very little albumin was now present in the urine.

29.6.33. Salt-containing full diet permitted - about 60 gm. of protein daily.

13.7.33. Oedema was still absent. Systolic blood pressure 116 mm. Hg.. Microscopic haematuria still present.

29.7.33. Slight pitting of the shins was noticed.

21.8.33. No oedema was observed during the past fortnight.

27.8.33. Oedema began to increase markedly and the amount of albumin in the urine became much more from this time.

30.8.33. Diet reduced to milk - protein 44.0 gm. daily.

2.9.33. Oedema still increasing. Systolic blood pressure 130 mm. Hg..

13.9.33. After reaching a maximum on 5.9.33. oedema became somewhat less but was still very marked. Systolic blood pressure 115 mm. Hg.. On 79.33 gross blood reappeared in the urine.

27.9.33. Oedema was unchanged and the systolic blood pressure was 133 mm. Hg..

3.10.33. Oedema unchanged. Systolic blood pressure 127 mm. Hg.. A diet containing 64 gm. of protein per day was given.

11.10.33. No change in oedema was noted. Full diet, "salt-free" given (60 gm. of protein).

25.10.33. Oedema began to increase further.

3.11.33. Oedema still increasing.

20.11.34. Gross haematuria and albuminuria continued and oedema continued to increase.

25.11.34. The child was cyanosed and almost unconscious but complained of epigastric pain. Some râle was audible at the bases of the lungs. There was high fever and much distension of the abdomen.

1.12.34. Died. Permission for autopsy was refused.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic Pressure.	N.P.N. mgm.%
16.6.33.	4.27	1.66	2.61	12.8	74.6
24.6.33.	8.25	2.86	5.39	23.3	30.9
13.7.33.	8.26	5.92	2.34	35.8	28.3
2.9.33.	5.97	2.00	3.97	16.5	65.2
13.9.33.	3.87	1.49	2.38	11.5	40.5
27.9.33.	3.39	1.57	1.82	11.4	27.0
3.10.33.	5.25	1.56	3.69	13.7	47.6
18.11.33.	4.24	1.30	2.94	11.8	33.1
1.12.33.	7.49	1.73	5.76	17.6	76.0

Urea Concentration Tests.

Date.	Before Urea.	1 hour after.	2 hours after
16.6.33.	3.83 gm. %	3.83 gm. %	3.45 gm. %
3.10.33.	1.57 gm. %	-	2.18 gm. %

CASE 49. A boy aged 8 years. On 23.3.33 he complained of joint pains and subsequently developed a rash. Next day he attended the out-patient department of the hospital. A well marked purpuric rash was present on the trunk, legs and scrotum. Some extravasation of blood was also present. The spleen was not palpable. The urine contained neither blood nor albumin. The capillary resistance test was negative. On 6.4.33 he reported and the rash was found to be fading. No fresh spots were present. On 19.4.33 he felt cold and next day the face and legs were swollen and the urine was dark in colour.

24.4.33. On admission oedema was general and ascites was present. The urine contained blood and albumin and the systolic blood pressure was not observed. The fundi showed no abnormality. Neither purpura, arthritis nor splenic enlargement was present. Diet-milk supplying 33.0 gm. of protein daily.

25.4.33. Systolic blood pressure 118 mm. Hg..

28.4.33. Systolic blood pressure 102 mm. Hg..

2.5.33. Systolic blood pressure 110 mm. Hg..

6.5.33. At 5 a.m. he complained of severe colicky pain in the umbilical region and vomited. To the right of the umbilicus a mass was palpable. At the subsequent operation an enteric intussusception was found and a foot of gangrenous small bowel removed.

12.5.33. From the operation the child made an uninterrupted recovery. Oedema seemed to be less. Diet throughout unchanged.

8.6.33. Systolic blood pressure 112 mm. Hg..

15.6.33. High protein diet (salt free) - 60 gm. of protein daily - started.

29.6.33. Systolic blood pressure 138 mm. Hg.. High protein diet stopped: milk given (33 gm. protein daily).

6.7.33. Systolic blood pressure 138 mm. Hg..

11.7.33. Systolic blood pressure 130 mm. Hg..

14.7.33. From now till death vomiting occurred several times daily.

20.7.33. Rather drowsy. Systolic blood pressure 127 mm. Hg.. Ophthalmoscopic examination showed no abnormality.

24.7.33. Unconscious, breathing deep and rapid. At the bases of both lungs some râle was audible. Since very great abdominal distension was present paracentesis was performed with a Southey's tube but only some 20 c.c. of fluid was obtained. Examination of this showed only scanty cells and no organisms. The culture was sterile. Some eleven hours later, following a convulsion, the child died. Permission for autopsy was refused.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	mm.Hg. Calculated Oncotic Pressure.	N.P.N. mgm.%
25.4.33	6.25	2.50	3.75	19.0	50.0
28.4.33	6.07	2.28	3.79	17.8	77.9
2.5.33	6.01	2.06	3.95	16.9	88.2
6.5.33	Intussusception.		operation	-	-
12.5.33	4.44	2.14	2.30	15.0	76.0
8.6.33	6.98	2.25	4.73	18.9	72.2
14.6.33	5.09	2.25	2.84	16.4	85.0
29.6.33	5.84	2.54	3.30	18.6	69.0
11.7.33	5.06	2.19	2.87	16.0	90.0
20.7.33	5.26	2.65	2.61	18.2	133.3

Chemistry of ascitic fluid.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	N.P.N. mgm.%
6.5.33	0.98	0.61	0.37	57.9

Urea Concentration Test.

Date.	Before Urea.	1 hour after.	2 hours after.
8.6.33	1.08 gm. %	1.33 gm. %	1.75 gm. %

CASE 50. A girl aged 5 years 6 months. Two weeks before admission the urine was observed to be red and some swelling of the face and extremities was noted.

27.4.33. On admission no oedema was observed. Blood and albumin were present in the urine. No ophthalmoscopic examination was made. The Systolic blood pressure was 99 mm. Hg.. Blood chemistry:- Total protein 8.02, albumin 4.22, globulin 3.80 gm. per cent.. Calculated oncotic pressure 28.5 mm. Hg.. Non-protein nitrogen 65.0 mgm. per cent..

3.5.33. The patient developed chickenpox and was dismissed from hospital.

29.1.34. Urine clear.

CASE 51. A boy aged 3 years. Two weeks before admission oedema of the face was noted and the urine was said to be red in colour.

28.4.33. On admission to hospital some puffiness of the face was found but there was no oedema elsewhere. Blood and albumin were present in the urine. No examination of the fundi was made and the blood pressure was not estimated.

3.5.33. Since admission 2.0 Kg. in weight were lost and oedema was absent. Blood chemistry:- Total protein 7.66, albumin 4.27, globulin 3.39 gm. per cent.. Calculated oncotic pressure 28.2 mm. Hg.. Non-protein nitrogen 28.2 mgm. per cent..

22.5.33. Chickenpox developed and the child was dismissed from hospital. The urine still contained gross blood and a moderate amount of albumin.

19.6.33. The child appeared to be well: the urine contained merely a trace of albumin.

CASE 52. A boy aged 3 years and 6 months. Three days before admission the urine was observed to be bright red in colour. There was no oedema observed.

26.5.33. On admission there was slight generalized oedema and puffiness of the face. The urine contained blood and albumin and the systolic blood pressure was 115 mm. Hg.. The fundi were not examined. A short V.S. murmur was audible at the base of the heart which was not enlarged. Blood chemistry:- Total protein 5.86, albumin 4.06, globulin 1.80 gm. per cent.. Calculated oncotic pressure 24.8 mm. Hg.. Non-protein nitrogen 37.5 mgm. per cent..

27.5.33. A profuse discharge appeared from the left ear.

20.6.34. No gross haematuria was observed after this date.

14.7.34. The urine was clear of albumin on dismissal.

CASE 53. A girl aged 5 years. Five weeks before admission she had a purpuric rash lasting two weeks. A week later she complained of joint pains, the rash reappeared and the urine was noted to be red in colour.

9.2.34. On admission a well marked purpuric eruption over the legs, arms and neck was found. Oedema of the face was present and the urine contained blood, casts, and albumin (12 gm. per litre). The systolic blood pressure was 108 mm. Hg.. Examination of the fundi revealed no abnormality. The spleen was not palpable and the platelet count, bleeding time and clotting time were normal. No petechial eruption was provoked by the capillary resistance test. The Wassermann reaction was negative.

12.2.34. Systolic blood pressure 110 mm. Hg..

18.2.34. Systolic blood pressure 120 mm. Hg.. Pitting oedema was now present.

23.2.34. A fresh crop of petechiae appeared. Oedema was still present.

4.3.34. A further profuse crop of petechiae appeared. Fundi normal. Spleen not felt. The systolic blood pressure was 114 mm. Hg.. Profuse albuminuria and haematuria continued.

15.3.34. A basal V.S. was now audible but no increase in cardiac dulness was present. Oedema still unchanged.

4.4.34. Systolic blood pressure 128 mm. Hg.. Albuminuria was now rather less, 1-5 gm. per litre, while haematuria was unabated.

22.5.34. No oedema.

12.6.34. Dismissed from hospital. Blood was still present in large amount in the urine while albumin was 0.5-3 gm. per litre. No oedema.

Blood chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
12.2.34.	5.02	3.06	1.96	19.6	21.8
23.2.34.	6.56	3.88	2.68	25.1	29.0
16.3.34.	5.06	3.04	2.02	19.5	24.0
4.4.34.	6.22	3.81	2.41	24.3	31.2
29.5.34.	-	-	-	-	26.4

Urea Concentration Tests.

Date.	Before urea.	1 hour after.	2 hours after.
12.2.34.	1.60 gm. %	1.70 gm. %	1.90 gm. %
4.4.34.	0.75 gm. %	1.23 gm. %	1.86 gm. %
29.5.34.	2.45 gm. %	2.51 gm. %	2.66 gm. %

CASE 54. A girl aged 2 years. Two weeks ago the urine was observed to be red and the child was feverish and irritable.

25.9.31. On admission oedema of the face was present and the urine contained blood and albumin. The systolic blood pressure was 100 mm. Hg.. The fundi were not examined. Blood chemistry:- Total protein 8.19, albumin 4.17, globulin 4.02 gm. per cent.. Calculated oncotic pressure 28.7 mm. Hg.. Non-protein nitrogen 45.4 mgm. per cent..

28.9.31. ? if any oedema. Cough, rhinitis and fever present. No gross haematuria.

5.10.31. Measles. The patient was transferred to a fever hospital still with a trace of albumin in the urine.

31.10.32. Urine clear.

CASE 55. A boy aged 12 years who developed severe headache four days before admission. Three days later oedema appeared. Next day he could not see.

1.1.33. On admission he was a well-nourished boy. Puffiness of the face was present but no oedema elsewhere; wild delirium present. Ophthalmoscopic examination revealed two small haemorrhages in the right fundus. The blood pressure was 184 mm. Hg. systolic. The urine contained blood and albumin. 150 c.c. of blood were withdrawn and 20 c.c. of cerebro-spinal fluid which was under increased pressure. After these procedures blood pressure was found to be 146 mm. Hg. systolic and he was much quieter.

2.1.33. Although the systolic blood pressure had risen to 158 mm. Hg. improvement was maintained. He was, however, unable to distinguish light from darkness.

5.1.33. Systolic blood was 120 mm. Hg.; there was no headache and he was able to see perfectly. No oedema apparent.

14.1.33. A trace of albumin was still present in the urine and a few red cells. The guaiac test was negative. Systolic blood pressure 110 mm. Hg.

3.2.33. Urea concentration test:- Before urea 1.55 per cent., 1 hour after 2.48 per cent.. 2 hours after 2.31 gm. per cent.. The urine was clear.

Blood chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
1.1.33.	6.37	4.16	2.21	26.1	30.0
5.1.33.	6.84	4.45	2.39	27.8	31.1
14.1.33.	7.99	4.67	3.32	30.3	42.3
3.2.33.	7.02	4.76	2.26	29.5	27.2

CASE 56. A boy aged 7 years. A month before admission the neck was swollen and fever was present. Three days before admission the face and ankles became oedematous.

17.3.32. On admission generalized oedema was marked and ascites was present. Blood and albumin were present in the urine and the systolic blood pressure was 140 mm. Hg.. A V.S. murmur was audible at the base of the heart which was not enlarged. The fundi showed no abnormality. Blood chemistry:- Total protein 6.31, albumin 2.91, globulin 3.40 gm. per cent.. Calculated oncotic pressure 20.9 mm. Hg.. Non-protein nitrogen 39.6 mgm. per cent..

22.3.32. The systolic blood pressure was still 140 mm. Hg. but oedema was less, 2.0 Kg. in weight having been lost.

25.3.32. No oedema was present. The systolic blood pressure was 104 mm. Hg.. Urea concentration test:- Before urea 1.89, one hour after 2.13, two hours after 2.30 gm. per cent..

14.4.32. No gross haematuria present.

23.4.32. A trace of albumin was still present on dismissal.

CASE 57. A boy aged 6 years. Two weeks before admission the face and legs became swollen.

16.2.34. On admission there was oedema of the face and extremities and slight ascites. The urine contained albumin but no gross blood. Microscopically red cells were present. The fundi showed no abnormality. The systolic blood pressure was 160 mm. Hg..

19.2.34. Oedema was rather less, 1.0 Kg. in weight having been lost. The systolic blood pressure was 125 mm. Hg.. Blood chemistry:- Total protein 6.57, albumin 3.29, globulin 3.28 gm. per cent.. Calculated oncotic pressure 23.7 mm. Hg.. Non-protein nitrogen 49.0 mgm. per cent.. Urea concentration test:- Before urea 1.15, one hour after 1.00, two hours after 2.97 gm. per cent..

24.2.34. No oedema. The systolic blood pressure was 94 mm. Hg..

2.3.34. Blood chemistry:- Total protein 8.23, albumin 5.29, globulin 2.94 gm. per cent.. Calculated oncotic pressure 33.2 mm. Hg.. Non-protein nitrogen 34.9 mgm. per cent..

11.3.34. A trace of albumin was present in the urine on dismissal.

CASE 58. A girl aged 9 years. One week before admission swelling of the legs appeared but she did not seem ill and the appetite was unimpaired.

13.3.33. On admission oedema was general and ascites was present. The heart and fundi presented no abnormality and the systolic blood pressure was 110 per cent. of normal. The urine contained much albumin and some casts, but no blood even microscopic. The non-protein nitrogen of the blood was 20.0 mgm. per cent.. The Wassermann reaction was negative. Diet - milk.

23.3.33. Discharged from hospital as a measles contact.

10.4.33. Readmitted: Condition unchanged, oedema being still very marked. Diet - whole milk giving a protein intake of 32 gm. per day. Systolic blood pressure 110 mm. Hg..

17.4.33. 2.0 Kg. in weight lost and oedema less. High protein, "salt-free" diet giving an intake of protein of 95 gm. per day.

24.4.33. Oedema unaltered. Diet changed to whole milk giving a daily protein intake of 27.6 gm..

11.5.33. Ordinary diet with salt. Protein 63 gm. daily. Systolic blood pressure 100 mm. Hg..

13.5.33. Oedema more marked, 1.8 Kg. in weight gained since 10.5.33.

17.5.33. Oedema still more marked, ordinary diet "salt-free."

2.6.33. Lost 3.0 Kg.. Full diet with salt.

21.6.33. Gained 1.0 Kg.. Fluids only.

26.6.33. Lost 1.0 Kg. Full diet with salt.

Dismissed from hospital.

18.12.33. Seen in the out-patient department. According to the mother swelling of the ankles and puffiness of the face with prominence of the abdomen had been present from time to time since dismissal. On examination pitting over the sacrum and tibiae was present. Ascites could not be definitely made out. The systolic blood pressure was 115 mm. Hg.. The urine contained much albumin. No casts or red cells were seen.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
11.4.33	4.92	2.06	2.86	15.3	31.3
17.4.33	5.09	2.18	2.91	16.1	21.0
24.4.33	5.46	2.52	2.94	17.9	30.0
10.5.33	4.54	2.22	2.32	15.4	21.0
17.5.33	4.31	2.46	1.85	16.1	38.0
29.5.33	4.76	2.31	2.45	16.1	25.2
20.6.33	5.49	2.30	3.19	17.1	22.2
18.12.33	5.06	3.21	1.85	20.2	40.0

Urea Concentration tests:

Date.	Before urea.	One hour after.	Two hours after.
11.4.33	2.45 gm. %	3.03 gm. %	3.27 gm. %
17.5.33	1.53 gm. %	2.95 gm. %	2.58 gm. %
30.5.33	1.07 gm. %	1.85 gm. %	2.45 gm. %

CASE 59. A boy aged 4 years. Two days before admission the urine was observed to be red.

25.7.33. On admission slight puffiness of the face was found and the urine contained blood and albumin. No observations were made of the fundi or on the blood pressure level on this date.

27.7.33. The face was still slightly puffy and the blood pressure was 115 mm. Hg. systolic. Blood chemistry:- Total protein 6.75, albumin 4.36, globulin 2.39 gm. per cent.. Calculated oncotic pressure 27.3 mm. Hg.. Non-protein nitrogen 44.8 mgm. per cent.. Urea concentration test:- Before urea 2.95, 1 hour after 2.32, 2 hours after 2.89 gm. per cent..

11.9.33. There was a faint trace of albumin present but no blood.

CASE 60. A boy aged 12 years. Two days before admission the face and legs became swollen.

17.9.31. On admission oedema was general but there was no ascites. The urine contained blood and albumin and the systolic blood pressure was 130 mm. Hg.. The fundi showed no abnormality. Blood chemistry:- Total protein 6.34, albumin 3.87, globulin 2.47 gm. per cent.. Calculated oncotic pressure 24.7 mm. Hg.. Non-protein nitrogen 35.5 mgm. per cent..

25.9.31. Gross haematuria absent for two days. The systolic blood pressure was 98 mm. Hg.. No oedema. Blood chemistry:- Total protein 8.13, albumin 5.04, globulin 3.09 gm. per cent.. Calculated oncotic pressure 32.0 mm. Hg.. Non protein nitrogen 33.3 mgm. per cent..

6.10.31. Urine clear.

CASE 61. A boy aged 7 years. Four days before admission the face was observed to be puffy and the urine red.

22.6.33. On admission moderate oedema of the face and extremities was present and the urine contained blood and albumin. The fundi showed no abnormality. Systolic blood pressure was 120 mm. Hg.. Blood chemistry:- Total protein 8.27, albumin 3.55, globulin 4.72 gm. per cent.. Calculated oncotic pressure 25.5. mm. Hg.. Non-protein nitrogen 26.6 mgm. per cent..

24.6.33. The temperature, which was 102°F. on admission but had fallen to normal, rose to 104°-102°F. for three days. This was ascribed to tonsillitis.

27.6.33. No oedema.

5.7.33. No gross haematuria was observed after this date.

26.7.33. Non-protein nitrogen of the blood:- 31.2 mgm. per cent.. Urea concentration test:- Before urea 0.53, one hour after 0.97, two hours after 2.57 gm. per cent..

2.8.33. The urine was clear of albumin on dismissal.

11.9.33. Urine clear.

CASE 62. A boy aged 4 years. Two weeks before admission oedema of the face and body was observed.

20.4.34. On admission there was generalized oedema and ascites. The heart and fundi showed no abnormality. In the urine there was much albumin and some blood. The systolic blood pressure was 110 mm. Hg.. The diet was milk supplying 34.0 gm. of protein daily.

22.4.34. Gross blood was now absent from the urine.

20.5.34. Condition unaltered. Systolic blood pressure 98 mm. Hg..

23.5.34. Calcium gluconate 10 c.c. intramuscularly. Systolic blood pressure 102 mm. Hg..

25.5.34. Calcium gluconate 10 c.c.

27.5.34. Calcium gluconate 10 c.c.

29.5.34. Calcium gluconate 10 c.c.

31.5.34. Calcium gluconate 10 c.c. Much gross blood was present again in the urine.

2.6.34. Calcium gluconate 10 c.c. Systolic blood pressure 110 mm. Hg..

4.6.34. Calcium gluconate 10 c.c.

6.6.34. Calcium gluconate 10 c.c. At the end of this treatment oedema was quite unaltered.

15.6.34. Oedema was slightly increased. Ammonium chloride grains 90 per day.

19.6.34. Vomiting frequent. Ammonium chloride omitted.

25.6.34. The patient was dismissed against medical advice, still with albuminuria, haematuria and marked oedema.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
21.4.34.	3.96	2.03	1.93	13.8	45.7
24.4.34.	5.97	1.94	4.03	16.3	19.0
23.5.34.	4.01	2.22	1.79	14.6	53.6
6.6.34.	5.70	1.19	4.51	12.8	60.1

Urea Concentration test.

Date.	Before urea.	1 hour after.	2 hours after.
23.4.34.	1.24 gm. %	1.40 gm. %	2.02 gm. %

CASE 63. A boy aged 13 years. Nine days before admission legs and face became swollen but a week later oedema of the legs disappeared.

28.5.33. On admission oedema of the face only was present. The urine contained blood and albumin and the systolic blood pressure was 140 mm. Hg.. The fundi were not examined. A right basal consolidation was present with moderate fever.

29.5.33. The systolic blood pressure was 130 mm. Hg.. Oedema of the face was still present but 0.5 Kg. in weight had been lost. Blood chemistry:- Total protein 7.26, albumin 3.44, globulin 3.82 gm. per cent.. Calculated oncotic pressure 24.0 mm. Hg.. Non-protein nitrogen 113.0 mgm. per cent.. Urea concentration test:- Before urea 1.01, one hour after 1.08, two hours after 1.40 gm. per cent..

6.7.33. No oedema. No fever. Child much improved.

11.7.33. Gross haematuria ceased.

26.7.33. Urine clear.

9.10.33. The urine contains a faint trace of albumin.

CASE 64. A boy aged 3 years and six months. Two weeks before admission he became drowsy and vomited his food occasionally. For a week the left ear discharged.

26.5.31. On admission he showed a moderate degree of oedema of the face. The urine contained blood and albumin. In the fundi no abnormality was observed. The boy did not seem acutely ill.

27.5.31. The systolic blood pressure was 112 mm. Hg. and the blood chemistry was:- Total protein 8.90, albumin 4.25, globulin 4.65 gm. per cent.. Calculated oncotic pressure 29.9 mm. Hg.. Non-protein nitrogen 76.0 mgm. per cent..

2.6.31. For the past two days vomiting was frequent and there was a high, swinging temperature. The puffiness of the face was unchanged. Child was very drowsy. Lumbar puncture indicated the presence of pneumococcal meningitis of which he died four days later.

At autopsy acute nephritis was present and in addition pneumococcal meningitis.

CASE 65. A boy aged 5 years. Save for whooping cough at $2\frac{1}{2}$ years was well till 2 weeks before admission when he was out of sorts. 11 days later the face became swollen.

26.12.33. On admission he was found to be fairly well nourished but showing a marked degree of oedema with ascites. The heart showed no lesion and the blood pressure was 210 per cent. of normal for the age. No desquamation. The urine contained albumin, 7.0 parts Esbach, gave a faint reaction to guaiac and showed numerous casts. Diet 1,470 c.c. of milk daily. Fluids unrestricted. Electric cage twice daily.

27.12.33. Condition unchanged. Blood pressure 190 per cent. of normal. Blood chemistry:- Total serum protein 6.98, albumin 4.45, globulin 2.53 gm. per cent.. Non-protein nitrogen 120.0 mgm. per cent.. Oncotic pressure 28 mm.Hg..

7.1.34. Weight at lowest level. No oedema. Blood pressure 110 per cent. of normal. Excretion of albumin still 4-8 parts Esbach. Guaiac reaction still positive.

14.1.34. Condition unchanged. Electric cage stopped.

15.1.34. Phenolsulphonephthalein excretion 59.2 per cent. in two hours.

16.1.34. Non-protein nitrogen 36.2 mgm. per cent. Urea concentration test:- Before urea 1.85 per cent., 1 hour after 2.05 per cent., 2 hours after 1.62 gm. per cent..

5.2.34. Pudding permitted. Proteinuria unaltered. No haematuria.

7.2.34. Blood pressure 130 per cent. of normal. Full diet.

4.3.34. Condition unaltered. Phenolsulphonephthalein excretion 47.1 per cent. in two hours.

5.3.34. Urea concentration test:- Before urea 2.27 per cent., 1 hour after 1.58 per cent., 2 hours after 1.78 gm. per cent..

16.3.34. Blood pressure 135 per cent. of normal. Proteinuria unchanged. Blood chemistry:- Total serum protein 6.50, albumin 4.55, globulin 1.95 gm. per cent.. Non-protein nitrogen 35.0 mgm. per cent..

23.3.34. Condition unchanged. Urea concentration test:- Before urea 1.30 per cent., 1 hour after 1.80 per cent., 2 hours after 1.84 gm. per cent..

29.3.34. Allowed up. Proteinuria unabated. Blood pressure still 130 per cent. of normal.

3.4.34. Phenolsulphonephthalein excretion 51.7 per cent. in two hours.

4.4.34. Urea concentration test:- Before urea 1.20 per cent., 1 hour after 1.51 per cent., 2 hours after 1.75 gm. per cent..

Dismissed home excreting up to 5.0 parts Esbach of albumin in the urine in 24 hours.

9.7.34. Albumin still ++ in the urine but no blood present. Face looks puffy.

CASE 66. A boy aged 4 years 6 months. Three days before admission he became feverish and the face was observed to be puffy. Two days later breathing became rapid and the urine contained blood.

12.7.31. On admission oedema was general and marked, with ascites. The urine contained blood and albumin and the systolic blood pressure was 120 mm. Hg.. The fundi were not examined. A left lobar pneumonia (lower lobe) was present with a moderate degree of fever, 102°F.

14.7.31. Oedema unchanged. (0.5 Kg. in weight lost) Blood chemistry:- Total protein 6.46, albumin 3.11, globulin 3.35 gm. per cent.. Calculated oncotic pressure 21.8 mm. Hg.. Non-protein nitrogen 17.0 mgm. per cent.. Systolic blood pressure was 115 mm. Hg..

19.7.31. Temperature normal, having fallen by lysis.

20.7.31. No oedema. Systolic blood pressure 95 mm. Hg..

10.8.31. The guaiac reaction in the urine ceased to be positive.

9.9.31. The urine on dismissal was clear.

15.10.33. A faint trace of albumin was present. Systolic blood pressure 90 mm. Hg..

CASE 67. A boy aged 6 years 6 months. Five days before admission the face and ankles became swollen and the urine red. Cough, headache and vomiting were present.

3.2.31. On admission there was moderate oedema of the face and extremities and the urine contained blood and albumin. The blood pressure was not estimated and the fundi were not examined. Pneumonia involving the right upper lobe was present and the temperature was 103°F. Blood chemistry:- Total protein 4.82, albumin 3.74, globulin 1.08. Calculated oncotic pressure 22.0 mm. Hg.. Non-protein nitrogen 22.4 mgm. per cent..

6.2.31. The temperature reached normal by lysis.

9.2.31. Oedema was now absent and no gross blood was observed in the urine after this date. Urea concentration test:- Before urea 2.10, one hour after 2.64, two hours after 2.40 gm. per cent.. Non-protein nitrogen of the blood 44.1 mgm. per cent..

27.2.31. A slight trace of albumin was present in the urine on dismissal.

18.6.34. Urine clear. Systolic blood pressure 88 mm. Hg..

CASE 68. A girl aged 7 years. Four days before admission she developed headache and swelling of the face.

11.9.33. On admission oedema of the face was present and the urine contained blood and albumin. The systolic blood pressure was 140 mm. Hg.. No examination of the fundi was made.

14.9.33. Oedema was slightly less. The systolic blood pressure was 125 mm. Hg.. Blood chemistry:- Total protein 6.72, albumin 3.76, globulin 2.96. Calculated oncotic pressure 24.8 mm. Hg.. Non-protein nitrogen 48.7 mgm. per cent.. Urea concentration test:- Before urea 1.53, 1 hour after 0.77, 2 hours after 1.58 gm. per cent..

27.9.33. No oedema was present. No gross haematuria was observed after this date.

16.10.33. Urine clear.

CASE 69. A girl aged 3 years. Ten days before admission swelling of the hands was noticed which became general 3 days later. Nine days later there was some vomiting.

1.5.31. Anasarca general with ascites. The urine contained blood and albumin. No observations were made on the blood pressure or the condition of the fundi. Blood Chemistry:- Total protein 5.40, albumin 2.78, globulin 2.62 gm. per cent.. Calculated oncotic pressure 18.9 mm. Hg.. Non-protein nitrogen 43.1 mgm. per cent..

4.5.31. Urea concentration test:- Before urea 1.61, one hour after 1.53, two hours after 1.81 gm. per cent.. Severe cough was present.

6.5.31. Oedema much less. No gross haematuria was observed after this date.

18.5.31. The child was transferred to a fever hospital with whooping cough: there was still a considerable degree of albuminuria.

25.9.33. Urine clear.

CASE 70. A girl aged 4 years. Two days before admission oliguria and oedema of the face were noted. Next day oedema was general.

6.9.33. On admission oedema was present in the face and extremities. The urine contained much albumin and blood. The systolic blood pressure was 125 mm. Hg.. Ophthalmoscopic examination revealed no abnormality. The diet contained 22 gm. of protein daily (half milk).

7.9.33. Blood chemistry:- Total protein 6.69, albumin 2.82, globulin 3.87 gm. per cent.. Calculated oncotic pressure 20.9 mm. Hg.. Non-protein nitrogen 133.0 mgm. per cent..

8.9.33. Weight unchanged. Non-protein nitrogen 104.0 mgm. per cent..

9.9.33. Urea concentration test:- Before urea 2.30, 1 hour after 1.50, 2 hours after 1.84 gm. per cent..

21.9.33. No oedema was observed after this date.

26.9.33. Blood chemistry:- Total protein 6.90, albumin 4.23, globulin 2.67 gm. per cent.. Calculated oncotic pressure 27.0 mm. Hg.. Non-protein nitrogen 21.9 mgm. per cent.. The systolic blood pressure was 110 mm. Hg..

5.10.33. Blood chemistry:- Total protein 6.81, albumin 4.54, globulin 2.27 gm. per cent.. Calculated oncotic pressure 28.1 mm. Hg.. Non-protein nitrogen 28.6 mgm. per cent..

21.11.33. In association with the development of diphtheria gross haematuria reappeared in the urine.

She was transferred to a fever hospital.

23.4.34. Urine clear.

CASE 71. A boy aged 6 years. Prior to the development of nephritis this child was in a Country Home suffering from bronchiectasis. He was afebrile and on full diet. On 12.2.32. examination of the urine had revealed no abnormal constituents.

19.3.32. Face puffy. Blood and albumin were found in the urine.

20.3.32. Marked oedema was now present.

21.3.32. Oedema more marked. Ascites was present and much fluid in the scrotal sac. A murmur was audible at the base of the heart but no enlargement was made out. The systolic blood pressure was 118 mm. Hg.. Blood and a moderate amount of albumin were present in the urine. Blood chemistry:- Total protein 6.34, albumin 2.45, globulin 3.89 gm. per cent.. Calculated oncotic pressure 18.9 mm. Hg.. Non-protein nitrogen 35.3 mgm. per cent.. Diet milk only. Protein intake 47 gm. daily.

31.3.32. No oedema present. A guaiac reaction was not obtained in the urine after this date.

7.4.32. Full diet.

11.5.32. A faint trace of albumin was still present in the urine on dismissal.

CASE 72. A boy aged 6 years. Four days before admission he became feverish and vomited. Next day there was cough and breathlessness and the urine was observed to be dark.

13.6.33. On admission there was no oedema. The urine contained blood and albumin and the systolic blood pressure was 108 mm. Hg.. Consolidation was present at the left base and moderate fever was present. The fundi were not examined.

16.6.33. Weight unchanged. Blood chemistry:- Total protein 7.84, albumin 5.14, globulin 2.70 gm. per cent.. Calculated oncotic pressure 32.0 mm. Hg.. Non-protein nitrogen 96.0 mgm. per cent.. Urea concentration test:- Before urea 2.57, one hour after 2.47, two hours after 2.73 gm. per cent..

24.6.33. Gross haematuria ceased.

6.7.33. Tonsillectomy.

7.7.33. Haematuria again gross.

14.8.33. Urine clear.

2.7.34. Urine clear.

CASE 73. A boy aged 7 years. Eight days before admission generalized oedema appeared and 5 days later it was noticed that the urine contained blood.

24.9.33. On admission oedema of the face and extremities was present and the urine contained albumin and blood.

25.9.33. The systolic blood pressure was 150 mm. Hg.. Blood chemistry:- Total protein 6.05, albumin 3.32, globulin 2.73 gm. per cent.. Calculated oncotic pressure 22.9 mm. Hg. Non-protein nitrogen 25.1 mgm. per cent..

3.10.33. Full diet with salt permitted. No oedema present clinically.

4.10.33. Blood chemistry:- Total protein 6.85, albumin 4.85, globulin 2.00 gm. per cent.. Calculated oncotic pressure 29.5 mm. Hg.. Non-protein nitrogen 24.0 mgm. per cent..

15.10.33. Gross haematuria ceased.

25.10.33. Urea concentration test:- Before urea 2.22, one hour after 2.50, two hours after 2.67 gm. per cent..

7.11.33. Urine clear.

2.7.34. Urine clear.

CASE 74. A boy aged 5 years 6 months. Five days before admission the face became swollen and he vomited once. The urine was noted to be dark in colour and he was very short of breath on the day before admission.

2.5.33. On admission oedema of the face and extremities was present. Blood and albumin were present in the urine and the systolic blood pressure was 120 mm. Hg.. The fundi were not examined. A left upper lobe pneumonia was present with high fever. Diet allowed 51 gm. protein daily (whole milk).

3.5.33. Blood pressure and oedema unchanged. Blood chemistry:- Total protein 5.72, albumin 3.30, globulin 2.42 gm. per cent.. Calculated oncotic pressure 21.7 mm. Hg.. Non-protein nitrogen 60.0 mgm. per cent.. Urea concentration test:- Before urea 1.75, one hour after 1.83, two hours after 1.75 gm. per cent..

7.5.33. The temperature fell by crisis.

9.5.33. No oedema. Blood chemistry:- Total protein 6.79, albumin 5.17, globulin 1.62 gm. per cent.. Calculated oncotic pressure 30.7 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent.. Urea concentration test:- Before urea 1.97, one hour after 1.97, two hours after 2.10 gm. per cent.. Systolic blood pressure 90 mm. Hg..

30.5.33. No gross haematuria observed after this date.

19.6.33. Systolic blood pressure 98 mm. Hg..

28.6.33. Urine clear on dismissal.

5.2.34. Trace of albumin present in the urine.

CASE 75. A boy aged 20 months. Two days before admission the face and body generally became swollen.

11.10.33. On admission oedema was general with ascites. The urine contained blood and albumin. The systolic blood pressure was 104 mm. Hg. (?) No abnormality of the fundi was detected. A loud V.S. murmur was audible at the base, of maximum intensity at the pulmonic area. The heart was not enlarged. Blood chemistry:- Total protein 6.84, albumin 4.07, globulin 2.77 gm. per cent.. Calculated oncotic pressure 26.2 mm. Hg.. Non-protein nitrogen 44.7 mgm. per cent..

21.10.33. No oedema.

11.11.33. No gross haematuria observed after this date.

22.11.33. Non-protein nitrogen of the blood 28.7 mgm. per cent..

5.12.33. Urine clear on dismissal.

CASE 76. A boy aged 4 years 6 months. For one week was off colour and in the 3 days previous to admission swelling of the face was observed.

9.10.33. On admission he was found to have very marked oedema. Ascites was present. Systolic blood pressure 106 mm. Hg.. No examination of the fundi was made. Blood and albumin were abundant in the urine.

10.10.33. Urea concentration test:- Before urea 2.07, 1 hour after 2.80, 2 hours after 2.73 gm. per cent.. Blood chemistry:- Total protein 6.58, albumin 2.72, globulin 3.86 gm. per cent.. Calculated oncotic pressure 20.4 mm. Hg.. Non-protein nitrogen 34.8 mgm. per cent.. Oedema was unchanged.

18.10.33. No oedema was present. Blood pressure not again estimated.

30.11.33. No gross haematuria was noted after this date.

10.12.33. Urine clear.

CASE 77. A girl aged 7 years. Six days before admission she seemed out of sorts. On the day before admission the face was observed to be swollen, headache developed and vomiting became frequent. Little urine was passed and cough was troublesome.

16.12.33. On admission to hospital oedema was marked and ascites was present. There was no fever but some bronchitis was found. The heart and fundi were normal and blood pressure was 188 per cent. of normal for the age. The urine contained albumin, only sufficient to give a reading of 0.25 Esbach, gross blood and numerous casts.

17.12.33. Condition unchanged. Blood pressure 178 per cent. of normal. Blood chemistry:- Total serum protein 7.65, albumin 5.19, globulin 2.46 gm. per cent.. Calculated oncotic pressure 31.9 mm. Hg.. N.P.N. 52.0 mgm. %.

23.12.33. Blood pressure 120 per cent. of normal for the age. No oedema now present, 3.0 kilos in weight having been lost since admission. Right ear discharging pus. Only microscopic blood present in the urine.

30.12.33. Systolic blood pressure 100 mm. Hg..

10.1.34. Tonsillitis. Slight fever. No change in urine. Fluid diet.

17.1.34. N.P.N. 25.0 mgm. % Urea concentration test:- Before urea 1.28 per cent., 1 hour after 2.29 per cent., 2 hours after 3.58 per cent..

23.1.34. Congo red intravenously - no dye in urine in 24 hours.

30.1.34. Dismissed on full diet. Faint trace of albumin still present.

21.5.34. In the non-catheter specimen of urine a faint trace of albumin was present.

CASE 78. A girl aged 7 years. Four days before admission swelling of the face was noticed and the urine was red in colour.

14.9.33. On admission oedema was confined to the face. The urine contained blood and albumin and the systolic blood pressure was 138 mm. Hg.. The fundi were not examined.

19.9.33. Some puffiness of the face was still present. Blood chemistry:- Total protein 6.62, albumin 4.11, globulin 2.51 gm. per cent.. Calculated oncotic pressure 26.1 mm. Hg.. Non-protein nitrogen 66.0 mgm. per cent.. Urea concentration test:- Before urea 1.29, one hour after 0.51, two hours after 1.02 gm. per cent..

24.9.33. No oedema.

9.11.33. No gross haematuria after this observation.

19.1.34. A trace of albumin was still present in the urine on dismissal.

18.6.34. A faint trace of albumin was still present in the non-catheter specimen of urine.

CASE 79. A boy aged 10 years. Seven days before admission swelling of the face was observed and 4 days later oedema of the extremities.

22.9.32. On admission he was found to be a well-nourished child with oedema of the face only. The urine contained blood and albumin. Ophthalmoscopic examination revealed no abnormality. Systolic blood pressure 148 mm. Hg.. Blood chemistry:- Total protein 8.63, albumin 6.12, globulin 2.51 gm. per cent.. Calculated oncotic pressure 37.1 mm. Hg.. Non-protein nitrogen 44.1 mgm. per cent..

27.9.32. Systolic blood pressure 115 mm. Hg..

20.11.32. Guaiac reaction negative for first time.

10.12.32. No haematuria. Albumin still a trace.

6.1.32. Patient was dismissed still with slight albuminuria.

Urea Concentration Tests.

Date.	Before Urea.	1 hour after.	2 hours after.
23.9.32.	1.14 Gm. %	2.25 Gm. %	2.62 Gm. %
13.10.32.	1.81 Gm. %	1.37 Gm. %	0.60 Gm. %
29.11.32.	1.29 Gm. %	2.75 Gm. %	4.06 Gm. %
4.1.33.	1.51 Gm. %	2.50 Gm. %	3.19 Gm. %

CASE 80. A boy aged 3 years who developed oedema of face and extremities 3 days before admission.

11.10.32. On admission he was found to be free of oedema save for some puffiness of the face. The systolic blood pressure was 100 mm. Hg.. No examination of the fundi was made. The urine contained blood and albumin.

12.10.32. Blood chemistry of the serum:- Total protein 7.02, albumin 5.31, globulin 1.71 gm. per cent.. Calculated oncotic pressure 31.8 mm. Hg.. Non-protein nitrogen 77.0 mgm. per cent.. Urea concentration test:- Before urea 0.98 per cent.. 1 hour after 0.35 per cent.. 2 hours after 0.98 per cent..

19.10.32. No oedema was detected. Non-protein nitrogen of the blood 33.5 mgm. per cent.. No gross haematuria was noted after this date.

27.11.32. Urine clear.

CASE 81. A boy aged 8 years. Four days before admission oedema of the face and legs developed and two days later he became very drowsy and vomited frequently.

30.10.32. On admission oedema of the face and legs was present and he was very drowsy. Four hours later a convulsion took place. The systolic blood pressure was 150 mm. Hg. and the urine contained blood and albumin. The fundi were normal. Lumbar puncture was performed and 25 c.c. of clear fluid under increased pressure removed. 80 c.c. of blood were withdrawn. As a result of this operation the blood pressure fell to 115 mm. Hg..

1.11.32. No further convulsions took place and he was much brighter.

3.11.32. Mental condition normal. Systolic blood pressure 118 mm. Hg..

7.11.32. Systolic blood pressure 100 mm. Hg..

13.11.32. No oedema. Systolic blood pressure 90 mm. Hg..

15.11.32. Gross haematuria ceased.

29.11.32. Urea concentration test:- Before urea 0.92, one hour after 1.86, two hours after 2.55 gm. per cent.. Systolic blood pressure 98 mm. Hg..

8.12.32. Slight macroscopic haematuria appeared for 13 days without obvious cause.

4.1.33. Urea concentration test:- Before urea 1.06, one hour after 2.14, two hours after 3.67 gm. per cent..

10.1.33. Urine clear.

Blood Chemistry.

Date.	Total Protein Gm. %	Albumin Gm. %	Globulin Gm. %	mm. Hg. Calculated oncotic pressure	N.P.N. mgm. %
30.10.32	8.30	4.04	4.26	28.1	96.7
3.11.32	6.71	4.32	2.39	27.1	51.7
7.11.32	5.79	3.47	2.32	22.3	49.1
11.11.32	7.31	3.87	3.44	26.1	30.5
29.11.32	7.81	6.29	1.52	36.7	25.0

Urea Concentration tests.

Date.	Before Urea.	One hour after.	Two hours after.
29.11.32.	0.92 Gm. %	1.86 Gm. %	2.55 Gm. %
4.1.33.	1.06 Gm. %	2.14 Gm. %	3.67 Gm. %

CASE 82. A boy aged 9 years. Three days before admission the face became swollen and next the feet. Urine was reported to be dark in colour and in the last 24 hours vomiting occurred three times.

27.1.31. On admission oedema of the face, extremities and lumbar region was present. The urine contained blood and albumin and the systolic blood pressure was 124 mm. Hg.. The fundi were not examined.

28.1.31. Blood chemistry:- Total protein 5.02, albumin 3.75, globulin 1.27 gm. per cent.. Calculated oncotic pressure 22.4 mm. Hg.. Non-protein nitrogen 96.3 mgm. per cent.. Systolic blood pressure 120 mm. Hg..

1.2.31. Oedema was much less.

6.2.31. No oedema. Systolic blood pressure 104 mm. Hg..

9.2.31. Non-protein nitrogen of the blood 68.7 mgm. per cent.. Urea concentration test:- Before urea 2.10, 1 hour after 2.64, 2 hours after 2.40 gm. per cent..

26.2.31. Non-protein nitrogen of the blood 28.6 mgm. per cent.. Urea concentration test:- Before urea 1.92, 1 hour after 2.80, 2 hours after 2.76 gm. per cent..

2.3.31. Systolic blood pressure 108 mm. Hg..

12.3.31. No gross haematuria was observed after this date.

19.3.31. Blood chemistry:- Total protein 7.73, albumin 4.95, globulin 2.78 gm. per cent.. Calculated oncotic pressure 31.1 mm. Hg.. Non-protein nitrogen 39.8 mgm. per cent..

1.4.31. Blood chemistry:- Total protein 7.62, albumin 5.01, globulin 2.61 gm. per cent.. Calculated oncotic pressure 31.2 mm. Hg.. Non-protein nitrogen 27.4 mgm. per cent..

2.5.31. Urine still contained a trace of albumin.

26.9.32. Urine clear. Systolic blood pressure 94 mm. Hg..

CASE 83. A girl aged 7 years who developed headache and began to vomit 5 days before admission. Puffiness of the face was noted.

2.7.31. Well nourished child with puffiness of the face. The urine contained blood and albumin. Blood pressure was 138 mm. Hg. systolic.

3.7.31. Systolic blood pressure 130 mm. Hg. Blood chemistry of the serum:- Total protein 7.33, albumin 4.69, globulin 2.64 gm. per cent. Calculated oncotic pressure 29.4 mm. Hg.. Non-protein nitrogen 67.1 mgm. %.

19.7.31. No oedema was now present. Systolic blood pressure was 90 mm. Hg.. Guaiac reactions on the urine was still positive.

26.8.31. The patient was now apparently well save for a trace of albumin in the urine.

2.10.33. Urine clear.

CASE 84. A girl aged 11 years. A week before admission she complained of backache and sore throat and next day the urine was observed to be red in colour.

11.5.31. On admission no oedema was present. The urine contained blood and albumin. No ophthalmoscopic examination was made. The systolic blood pressure was 110 mm. Hg..

12.5.31. Blood chemistry:- Total protein 7.09, albumin 5.13, globulin 1.96 gm. per cent.. Calculated oncotic pressure 30.9 mm. Hg.. Non-protein nitrogen 49.5 mgm. per cent.. The catheter specimen of urine was sterile on culture.

11.7.31. No abnormality was observed in the urine.

CASE 85. A girl aged five years six months. Six days before admission she complained of sore throat. The urine was dark and scanty. No oedema was observed.

22.6.32. On admission there was no oedema. The urine contained blood and albumin and the systolic blood pressure was 100 mm. Hg.. The fundi were not examined. A basal V.S. murmur was audible but the heart was not enlarged.

27.6.32. The weight was unaltered confirming the absence of oedema on admission. Blood chemistry:- Total protein 5.87, albumin 3.44, globulin 2.43 gm. per cent.. Calculated oncotic pressure 22.3 mm. Hg.. Non-protein nitrogen 57.7 mgm. per cent.. Systolic blood pressure 110 mm. Hg..

6.7.32. No gross haematuria was observed after this date.

20.7.32. The urine was clear on dismissal.

11.9.33. Urine clear.

CASE 86. A girl aged 11 years. A week before admission she became listless and complained of headache.

14.6.31. Oedema was general, and the urine contained blood and albumin. The systolic blood pressure was 146 mm. Hg.. No abnormality was detected in the fundi.

15.6.31. Oedema of the face only was present, 2.0 Kg. in weight having been lost. Blood chemistry:- Total protein 5.18, albumin 3.72, globulin 1.46 gm. per cent.. Calculated oncotic pressure 22.4 mm. Hg.. Non-protein nitrogen 26.6 mgm. per cent..
The systolic blood pressure was 128 mm. Hg..

23.6.31. Systolic blood pressure 90 mm. Hg.. Gross blood was absent from the urine from this date.

31.7.31. A trace of albumin was still present in the urine.

CASE 87. A boy aged 7 years. Swelling of the face was observed two days before admission and next day oedema was general.

28.7.33. On admission there was oedema of the face and extremities of moderate degree. Blood and albumin were present in the urine. Ophthalmoscopic examination revealed no abnormality. Systolic blood pressure 100 mm. Hg..

29.7.33. Blood chemistry:- Total protein 5.06, albumin 2.63, globulin 2.43 gm. per cent.. Calculated oncotic pressure 17.6 mm. Hg.. Non-protein nitrogen 90.9 mgm. per cent..

5.8.33. No oedema.

21.8.33. No gross haematuria observed after this date.

16.9.33. Urea concentration test:- Before urea 1.37, 1 hour after 1.63, 2 hours after 2.42 gm. per cent.. Non-protein nitrogen of the blood 38.6 mgm. per cent..

21.9.33. Tonsillectomy was performed and following the operation haematuria recurred and was still present when the child was removed from hospital by his parents, 16 days later.

CASE 88. A boy aged 11 years. Three days before admission puffiness of the face was seen and urine became dark. On the day before admission he began to take frequent convulsions and to vomit.

8.2.31. On admission oedema of the face was present: he was very drowsy but irritable if roused. Much blood and albumin were present in the urine. The blood pressure was not observed. Retinoscopy revealed dilatation of the retinal veins. Lumbar puncture was performed and 30 c.c. of clear fluid under increased pressure was removed. 180 c.c. of blood withdrawn.

9.2.31. The vomiting and convulsions continued so a further 60 c.c. of blood were withdrawn. The systolic blood pressure after this operation was 120 mm. Hg.. Blood chemistry:- Total protein 6.71, albumin 5.32, globulin 1.39 gm. per cent.. Calculated oncotic pressure 31.3 mm. Hg.. Non-protein nitrogen 50.8 mgm. per cent..

10.2.31. Much brighter. No further fits. Systolic blood pressure 110 mm. Hg. per cent..

11.2.31. Urea concentration test:- Before urea 4.08, one hour after 3.60, two hours after 2.22 gm. per cent..

17.2.31. Non-protein nitrogen of the blood 32.0 mgm. per cent.. Urea concentration test:- Before urea 2.68, one hour after 2.22, two hours after 1.20 gm. per cent.. The systolic blood pressure was 98 mm. Hg..

26.2.31. Gross haematuria ceased.

10.3.31. Urine clear.

11.9.33. Urine clear. Systolic blood pressure 110 mm. Hg..

CASE 89. A girl aged 8 years. 2 days before admission oedema of the face was observed.

30.5.31. On admission oedema of the face was present and the urine contained blood and albumin. No ophthalmoscopic examination was made. The systolic blood pressure was 116 mm. Hg.. Blood chemistry:- Total protein 6.76, albumin 4.01, globulin 2.75 gm. per cent.. Calculated oncotic pressure 25.8 mm. Hg.. Non-protein nitrogen 27.2 mgm. per cent.. Urea concentration test:- Before urea 1.92, one hour after 2.34, two hours after 3.03 gm. per cent..

12.6.31. Systolic blood pressure 90 mm. Hg.. No oedema was present. Gross blood had been absent from the urine for four days.

15.6.31. Urine clear.

5.2.34. Urine clear.

CASE 90. A boy aged 6 years and 10 months. Two weeks before admission he had a sore throat with adenitis of the neck. A few days later oedema of the face was observed.

20.9.31. On admission to hospital he showed oedema of the face only. The urine contained blood and albumin. No ophthalmoscopic examination was made. A V.S. murmur was audible at the base of the heart but no enlargement of dulness was made out. Cough and fever, due to bronchitis, were present.

21.9.31. Systolic blood pressure 130 mm. Hg.. Oedema was unchanged. Blood chemistry:- Total protein 6.99, albumin 4.90, globulin 2.09 gm. per cent.. Calculated oncotic pressure 29.8 mm. Hg.. Non-protein nitrogen 52.6 mgm. per cent..

24.9.31. Systolic blood pressure 104 mm. Hg.. ? if any oedema was present at this date.

30.9.31. No gross haematuria was detected after this date.

14.11.31. Dismissed from hospital - urine clear.

16.4.34. Urine clear.

CASE 91. A boy aged 2 years and 9 months. Ten days before admission swelling of the face and legs was noticed. The urine was dark and scanty and he vomited occasionally.

10.2.33. On admission there was oedema of the face and legs. The urine contained blood and albumin and the systolic blood pressure was 115 mm. Hg.. The fundi were not examined. Blood chemistry:- Total protein 6.32, albumin 4.44, globulin 1.88 gm. per cent.. Calculated oncotic pressure 27.0 mm. Hg.. Non-protein nitrogen 27.1 mgm. per cent..

21.2.33. Oedema gone. The systolic blood pressure was 76 mm. Hg..

15.3.33. No albumin was observed in the urine after this date.

CASE 92. A boy aged 3 years. About 4 days before admission he developed cough and fever. The face was swollen and the urine scanty and dark.

17.4.31. On admission he was found to be very ill with high fever. A right sided pneumonia, ? lobar, was present and in addition there was oedema of the face and blood and albumin in the urine. The fundi were not examined.

18.4.31. Systolic blood pressure 124 mm. Hg.. Blood chemistry:- Total protein 6.58, albumin 4.77, globulin 1.81 gm. per cent.. Calculated oncotic pressure 28.7 mm. Hg.. Non-protein nitrogen 72.3 mgm. per cent..

20.4.31. Non-protein nitrogen 66.0 mgm. per cent.. High fever persisted until death.

24.4.31. Died. Permission for autopsy refused.

CASE 93. A boy aged 8 years. One week before admission his face became swollen.

26.3.34. On admission oedema was general with ascites. The urine contained blood and albumin and the systolic blood pressure was 130 mm. Hg.. The fundi showed no abnormality.

27.3.34. The systolic blood pressure was 130 mm. Hg.. Blood chemistry:- Total protein 5.86, albumin 3.07, globulin 2.79 gm. per cent.. Calculated oncotic pressure 20.8 mm. Hg.. Non-protein nitrogen 89.2 mgm. per cent..

28.3.34. Oedema diminishing. Systolic blood pressure 118 mm. Hg..

30.3.34. No gross haematuria. Oedema much less. Systolic blood pressure 110 mm. Hg..

3.4.34. No oedema. Systolic blood pressure 90 mm. Hg.. Blood chemistry:- Total protein 7.84, albumin 4.97, globulin 2.87 gm. per cent.. Calculated oncotic pressure 31.3 mm. Hg.. Non-protein nitrogen 21.5 mgm. per cent..

8.4.34. Systolic blood pressure 92 mm. Hg.. Urea concentration test:- Before urea 0.57, one hour after 2.57, two hours after 2.37 gm. per cent..

24.4.34. A trace of albumin was present in the urine.

24.6.34. Urine still contained a little albumin.

CASE 94. A boy aged 6 years 6 months. A week before admission he developed a sore throat with enlargement of the glands of the neck.

16.10.33. On admission oedema of the face and extremities was present and the urine contained blood and albumin. The fundi were not examined and no observation on the blood pressure was made.

17.10.33. Oedema was unchanged. Blood chemistry:- Total protein 7.25, albumin 3.91, globulin 3.34 gm. per cent. Calculated oncotic pressure 26.2 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent..

5.11.33. No further gross blood was observed in the urine. There was no oedema and the systolic blood pressure was 95 mm. Hg..

23.11.33. On dismissal a faint trace of albumin was present in the urine.

30.4.34. Urine clear.

CASE 95. A boy aged 9 years. Two weeks before admission he had a sore throat with adenitis of the neck. Eleven days later oedema of the hands and face was observed.

12.9.31. On admission there was some puffiness of the face but no oedema elsewhere. The urine contained blood and albumin. The fundi showed no abnormality. No observation of the blood prssure was made.

13.9.31. Oedema was unaltered. Blood chemistry:- Total protein 7.89, albumin 4.50, globulin 3.39 gm. per cent.. Calculated oncotic pressure 29.5 mm. Hg.. Non-protein nitrogen 50.0 mgm. per cent..

16.9.31. No gross haematuria and no oedema were observed after this date.

30.10.31. Urine clear on dismissal.

7.1.32. Urine clear.

CASE 96. A girl aged 5 years and 9 months. Four days before admission the urine was noted to be dark in colour and two days later the face became puffy.

14.10.33. On admission oedema was absent. Blood and albumin were present in the urine and the systolic blood pressure was 110 mm. Hg.. The fundi were not examined. Blood chemistry:- Total protein 8.66, albumin 4.92, globulin 3.74 gm. per cent. Calculated oncotic pressure 32.9 mm. Hg.. Non-protein nitrogen 36.3 mgm. per cent..

22.11.33. No gross blood now present but there was still some albumin.

28.11.33. The child contracted diphtheria and was transferred to a fever hospital. At this time gross haematuria reappeared and albuminuria became more marked.

CASE 97. A boy aged 4 years who had ? mumps 3 weeks before admission. Six days before admission to hospital the face became puffy and the urine red in colour and there was profuse discharge from both ears. Five days later took two convulsions.

23.11.31. On admission he was found to be very irritable if roused but otherwise was drowsy. Oedema of the face and extremities was present. Both ears were discharging. The systolic blood pressure was 116 mm. Hg.. The fundi were not examined. In the urine there was much blood and albumin. No abnormality was detected on examination of the nervous system save for nuchal rigidity. Vomiting was persistent. By lumbar puncture 20 c.c. of fluid were withdrawn under slight increase of pressure. Cell count 15; Pandy ∓. No films were made. Blood chemistry:- Total protein 8.64, albumin 6.12, globulin 2.52 gm. per cent.. Calculated oncotic pressure 37.2 mm. Hg.. Non-protein nitrogen 42.2 mgm. per cent..

25.11.31. Oedema was noted to be less but the child remained very ill, vomiting being incessant. Further convulsions appeared and lumbar puncture was again performed. 50 c.c. of clear fluid were removed under increased pressure. This specimen was not examined. Blood chemistry at 10 a.m.:- Total protein 8.75 gm. per cent.. Non-protein nitrogen 100.0 mgm. per cent.. At 6 p.m. the child was comatose and the blood chemistry was:- Total protein 10.03 gm. per cent.. Non-protein nitrogen 120.0 mgm. per cent.. Death occurred at 10 p.m. At autopsy acute nephritis was found. In addition double acute otitis media and pneumococcal meningitis were present.

CASE 98. A girl aged 8 years. Three months before admission it was noticed that the abdomen was swollen and child became easily tired. Recently the face was noticed to be puffy.

21.8.33. On admission oedema was marked and general. Some bronchitis was present but there was no fever and she was not acutely ill. The heart and fundi were normal. In the urine there was much albumin and scanty casts. Blood was microscopic. Urine culture was sterile. The systolic blood pressure was 107 mm. Hg.. A diet of whole milk giving 32 gm. of protein daily was ordered.

26.8.33. Oedema less, almost 2.0 Kg. in weight being lost. No red cells were now present in the urine.

10.9.33. Oedema rather more marked.

17.9.33. Fever 101-102°F. Slight bronchitis present.

25.9.33. Fever gradually disappeared. The spleen was not palpable and the leucocyte count was 12,400 per c. mm. on 19.9.33. Systolic blood pressure 104 mm. Hg.. A few red cells were observed in the urine for 5 days.

7.10.33. Systolic blood pressure 102 mm. Hg.. Administration of sodium bicarbonate in increasing doses begun, starting with 240 grains daily.

8.10.33. Oedema more marked.

10.10.33. Now receiving 960 grains of sodium bicarbonate daily. Oedema unchanged.

14.10.33. Oedema unaltered. Much vomiting of the sodium bicarbonate.

18.10.33. Stools very loose and frequent. Alkali stopped. Oedema rather less.

24.10.33. In view of the unexplained fever on 17.9.33 and subsequently, when paratyphoid fever was discovered in the ward, this patient was suspected. The Widal reaction was found to be positive for b. paratyphosus B. and she was transferred to a fever hospital. Oedema was rather less on dismissal.

16.4.34. Readmitted to the Royal Hospital for Sick Children. On dismissal from the fever hospital the mother ob-

16.4.34. (contd.) served no oedema but subsequently swelling of the face and ankles recurred from time to time. On examination oedema was general and ascites was present but seemed less than formerly in spite of increased weight. The urine contained much albumin and scanty red cells. The systolic blood pressure was 110 mm. Hg.. Diet whole milk (32 gm. protein per day).

24.4.34. Oedema was less marked. No haematuria.

10.5.34. The systolic blood pressure was 110 mm. Hg.. Oedema slight.

20.5.34. Dismissed as a measles contact.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	mm.Hg. Calculated Oncotic Pressure.	Serum Fat. gm.%	N.P.N. mgm.%
30.8.33	4.18	-	-	-	2.16	40.9
3.9.33	5.36	2.12	3.24	16.1	-	36.1
19.9.33	4.56	1.64	2.92	13.1	3.64	20.1
28.9.33	6.29	2.42	3.87	18.7	2.96	27.4
4.10.33	5.25	1.80	3.45	14.7	2.92	28.5
18.10.33	4.89	1.79	3.10	14.1	3.24	27.1
16.4.34	6.88	2.48	4.40	19.8	-	23.6

Urea Concentration Tests.

Date.	Before urea.	1 hour after.	2 hours after.
31.8.33	1.96 gm. %	2.19 gm. %	2.39 gm. %
18.4.34	1.88 gm. %	1.78 gm. %	3.13 gm. %

CASE 99. A boy of 7 years. Seven months before admission the face and feet became swollen and the mother states that the urine was dark in colour. Since that time oedema has been constant though varying in degree.

11.1.34. On admission oedema of the face and legs of moderate degree was present but no ascites was made out. No abnormality was detected in the heart or fundi. The systolic blood pressure was 108 mm. Hg.. In the urine there was much albumin and scanty casts. No blood, even microscopic, was present. The Wassermann reaction was negative. A diet of half milk was given with a daily protein content of 22.0 gm. of protein. The congo red rest was positive.

17.1.34. Weight unchanged.

22.1.34. Oedema gradually increased. The protein intake was raised to 44.0 gm. daily.

28.1.34. Oedema unchanged. Full diet "salt-free" given.

14.2.34. Oedema increased for past three days and ascites was now present.

23.2.34. Oedema unchanged. Full diet with salt given. 25 millions T.A.B. vaccine intravenously. No reaction followed.

2.3.34. Oedema further increased. 50 millions T.A.B. vaccine intravenously was followed by a rise of temperature to 102.6°.

12.3.34. Oedema diminished. 100 millions T.A.B. vaccine intravenously gave no reaction.

20.3.34. Oedema rather more marked: 200 millions T.A.B. vaccine was again followed by absence of reaction.

28.3.34. Since oedema was still marked a "salt-free" diet was given. Systolic blood pressure 98 mm. Hg..

2.4.34. Oedema began to diminish.

14.4.34. 3.0 Kg. in weight were lost since 20.3.34. Oedema although still present was much less marked. On a "salt-free" diet the condition appeared to be stationary.

24.5.34. No change in oedema. Ammonium chloride grains 120 per day were started.

3.6.34. After a slight gain in weight the boy returned to his weight on 24.5.34. Ammonium chloride was stopped.

13.6.34. The patient was dismissed from hospital, still oedematous.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	mm.Hg. Calculated Oncotic Pressure.	Serum Fat. gm.%	N.P.N. mgm.%
12.1.34	6.86	2.47	4.39	19.7	-	27.2
23.2.34	4.09	1.84	2.25	13.3	2.04	35.2
2.3.34	6.42	1.89	4.53	16.7	-	22.0
12.3.34	4.90	1.86	3.04	14.4	2.13	28.5
20.3.34	5.81	1.81	4.00	15.5	-	29.7
24.4.34	5.89	1.74	4.15	15.4	-	18.3

Urea Concentration Tests.

Date.	Before Urea.	1 hour after.	2 hours after.
19.1.34	2.07 gm. %	2.40 gm. %	3.20 gm. %
22.5.34	3.04 gm. %	2.68 gm. %	2.53 gm. %

CASE 100. A boy aged 11 years. A week before admission he lost appetite and began to vomit. Complaint was made of headache. On the day before admission he was drowsy; declared he could not see. Muscular twitchings were noted. Two hours before admission a generalized convulsion occurred followed by coma.

15.7.33. On admission he was unconscious and taking frequent short convulsions. A catheter specimen of urine contained much blood and albumin. The systolic blood pressure was 120 mm. Hg.. No oedema present. In both lungs much râle was present. Blood chemistry:- Total protein 10.06, albumin 3.98, globulin 6.08 gm. per cent.. Calculated oncotic pressure 30.3 mm. Hg.. Non-protein nitrogen 190.0 mgm. per cent.. In spite of withdrawal of 110 c.c. of blood and lumbar puncture, by which 40 c.c. of clear fluid under increased pressure were withdrawn, he did not improve. 25 c.c. of 10 per cent. magnesium sulphate were given by intravenous injection. Death occurred 12 hours later. Autopsy showed acute nephritis and bronchopneumonia involving both lungs.

CASE 101. A boy aged 5 years. 3 days before admission a purpuric rash appeared and next day bleeding was observed from nose and gums.

15.7.32. On admission a profuse and general purpuric eruption was present. Bleeding was occurring from the nose and the gums and a small conjunctival haemorrhage was present. The spleen was not palpable. Clot retraction was absent and diminution of capillary resistance was observed after the application of a tourniquet. Platelets were 400,000 per c.mm. The Wassermann reaction was negative.

16.7.32. Bleeding was unabated. Blood chemistry:- Total protein 9.11, albumin 6.17, globulin 2.94 gm. per cent.. Calculated oncotic pressure 38.0 mm. Hg.. Non-protein nitrogen 42.0 mgm. %. Calcium 9.0 mgm. per cent..

18.7.32. Because bleeding continued he was transfused with 120 c.c. of father's blood.

19.7.32. Again transfused with 120 c.c. of father's blood.

24.7.32. No further bleeding.

CASE 102. A girl aged 1 year and 10 months. For a few days, 6 months before admission, a purpuric rash was observed. Two days before admission the rash reappeared, there was some bleeding from the mouth and nose and bright red blood appeared in the urine.

17.5.32. On admission a profuse purpuric eruption was present, chiefly on the limbs. There was no blood observed in the stool or the urine. The temperature was 103°F. The bleeding time was greatly prolonged (1½ hours) and the platelets were reduced to 56,000 per c.mm. The spleen was just palpable. Blood chemistry:- Total protein 9.56, albumin 5.35, globulin 4.21 gm. per cent.. Calculated oncotic pressure 35.3 mm. Hg.. Non protein nitrogen 22.4 mgm. per cent..

6.6.32. Dismissed from hospital well.

CASE 103. A girl aged 8 years. A year before admission a ?purpuric rash was present for a few weeks. Since then there have been several attacks of joint pains. Two days before admission the gums began to bleed and a purpuric rash appeared on the limbs and body.

13.5.33. On admission petechiae and ecchymoses were profuse on the limbs and slight on the trunk. A small conjunctival haemorrhage was present and oozing from the gums was occurring. The spleen was not palpable. The capillary resistance test was slightly positive and the platelets were 52,000. Bleeding time was prolonged. The Wassermann reaction was negative. No blood or albumin was present in the urine.

14.5.33. No further bleeding observed.

15.5.33. Blood chemistry:- Total protein 8.22, albumin 5.20, globulin 3.02 gm. per cent.. Calculated oncotic pressure 32.8 mm. Hg.. Non-protein nitrogen 27.2 mgm. per cent..

1.6.33. Dismissed from hospital well.

CASE 104. A boy aged 8 years. Since he was 5 years old the patient has bruised easily and has had frequent epistaxis. Three days before admission a purpuric rash appeared.

6.10.33. On admission petechiae and extensive ecchymoses were present on the trunk and limbs. The urine was clear. Clotting time was normal but bleeding time was prolonged. The capillary resistance test was positive and the clot was non-retractile. Spleen was not palpable. Platelets 24,000. Wassermann reaction negative.

13.10.33. Blood chemistry:- Total protein 9.56, albumin 5.36, globulin 4.20 gm. per cent.. Calculated oncotic pressure 35.4 mm. Hg.. Non-protein nitrogen 24.0 mgm. per cent..

22.10.33. Because of persistent epistaxis transfused with 400 c.c. of the father's blood.

4.11.33. Since bleeding did not cease after transfusion splenectomy was performed after a further transfusion of 400 c.c. of blood.

6.4.34. Out-patient. No further bleeding since operation.

CASE 105. A girl aged 6 years. Four weeks before admission was listless and feverish and was kept in bed for a fortnight. Since that date was easily tired and inclined to be cyanosed. In the three days prior to admission she fainted twice and swelling of the face was noted. There was no history of rheumatism.

2.1.34. On admission there was oedema of the face and legs and slight ascites: the heart was slightly enlarged to the left and to mid-sternum on the right; the sounds were soft and foetal in character. Vomiting was frequent and a moderate degree of cyanosis was present. In the urine there was much albumin - 2.5 parts Esbach, numerous casts, but no blood. No abnormality of the nervous system was present. Throat-swabs on two occasions were negative for b. diphtheriae.

3.1.34. The systolic blood pressure was 80 mm. Hg.. Blood chemistry:- Total protein 6.22, albumin 5.08, globulin 1.14 gm. per cent.. Calculated oncotic pressure 29.5 mm. Hg.. Non-protein nitrogen 53.7 mgm. per cent.. The congo red test was negative. Urea concentration test:- Before urea 2.83, one hour after 2.10, two hours after 3.40 gm. per cent..

10.1.34. Vomiting had ceased, cardiac dulness was normal and there was no oedema. A considerable degree of albuminuria was still present.

15.1.34. While the general condition was improving absence of knee jerks was observed for the first time. Albumin in urine was but a trace.

22.1.34. Complete palatal paralysis was observed. No abnormality was detected in the heart. Signs of a consolidation of the right base were now present with fever.

23.1.34. Today the diaphragm was observed to be immobile and screening confirmed this.

24.1.34. Child died. At autopsy bronchopneumonia was found. The kidneys were apparently normal.

CASE 106. A girl aged 10 years. When aged 8 years she had rheumatic fever when the heart was damaged. Four months ago she took tonsillitis and about 15 days later arthritis and praecordial pain developed. Although no oedema was observed she became very orthopnoeic one month before admission.

12.1.34. On admission she was acutely ill, breathless and cyanosed. Slight fever was present throughout. Slight oedema of the legs was present. The liver was three fingerbreadths below the costal margin but no ascites was present. Cardiac dulness was increased to the right and left of the middle line. V.S. and V.D. murmurs were audible at the apex and a V.D. murmur at the inner and lower left sternal margin. The pulse was water-hammer in character and there was marked pulsation over the whole praecordium. The urine contained no albumin or blood. There was no vomiting throughout the stay in hospital.

21.1.34. The heart was increased in size and oedema more marked. Ascites was now present. Blood chemistry:- Total protein 6.38, albumin 4.05, globulin 2.33 gm. per cent.. Calculated oncotic pressure 25.5 mm. Hg.. Non-protein nitrogen 48.7 mgm. per cent.. The child died the same night. Permission for autopsy was refused.

CASE 107. A boy aged 5 years. Eight months before admission he became listless and easily tired.

25.8.32. On admission the heart dulness was found to be within normal limits but a V.S. murmur was audible at the apex which well conducted to the axilla. There was no arthritis or oedema and the urine was clear.

13.9.32. About this time short bouts of slight fever began to occur and elevation of the pulse rate was observed while considerable increase of cardiac dulness to right and left of mid-sternum was found. Friction was audible at times.

12.12.32. Oedema developed. Great enlargement of the liver with ascites was now a marked feature. Puffiness of the face was considerable.

29.12.32. Albumin appeared in the urine reaching on occasion 3.5 parts Esbach.

1.2.33. The condition was unchanged. Blood chemistry:- Total protein 6.48, albumin 2.41, globulin 4.07 gm. per cent.. Calculated oncotic pressure 18.9 mm. Hg.. Non-protein nitrogen 33.0 mgm. per cent..

8.2.33. The child died and permission for autopsy was refused.

CASE 108. A girl aged 4 years. At 2 years and 6 months this patient had an attack of acute arthritis lasting 2 months. One month before admission another attack developed involving ankles, elbows and shoulders.

10.1.34. On admission to hospital arthritis was present involving the ankles and the right knee. There was no fever. Cardiac dulness was within normal limits but a loud apical V.S. murmur was audible.

18.1.34. On treatment with sodium salicylate gr. 90 per diem arthritis disappeared and weight rose from 12.0 to 12.9 Kg. in 4 weeks.

1.2.34. Temperature became elevated to 102°F.

4.2.34. Cardiac dulness increased to right and left of the mid-sternum, the murmur remaining unaltered. The liver was palpable three fingerbreadths below the costal margin.

6.2.34. Cardiac dulness was further increased but no oedema could be made out.

9.2.34. Definite oedema was present. Cyanosis and orthopnoea marked, which were ascribed in part to the presence of fluid in both plural cavities. Blood chemistry:- Total protein 7.17, albumin 3.69, globulin 3.48 gm. per cent.. Calculated oncotic pressure 25.2 mm. Hg.. Non-protein nitrogen 53.0 mgm. per cent.. The right chest, which seemed to contain more fluid than the left, was tapped and 300 c.c. of clear fluid were removed. The chemistry of this was:- Total protein 3.37, albumin 1.76, globulin 1.61 gm. per cent.. Calculated oncotic pressure 11.9 mm. Hg.. Non-protein nitrogen 43.0 mgm. per cent.. The systolic blood pressure was 84 mm. Hg.. A trace of albumin was found in the urine.

11.2.34. Child died. Autopsy showed:- rheumatic carditis. The kidneys showed merely oedema and congestion.

CASE 109. A boy aged 8 years. Eighteen months before admission he had rheumatic arthritis. Since that time he was never really well and sixteen months later he became easily tired and breathless. Soon after swelling of the feet was noted.

5.1.31. On admission there was marked oedema of the legs and considerable ascites. The heart was enlarged to the right and left of mid-sternum and an apical V.S. murmur was audible. The urine was clear. Vomiting was frequent in the latter part of the stay in hospital.

7.1.31. Blood chemistry:- Total protein 5.96, albumin 3.04, globulin 2.92 gm. per cent.. Calculated oncotic pressure 20.2 mm. Hg.. Non-protein nitrogen 28.7 mgm. per cent..

3.3.31. The general condition was unchanged on the death of the patient. Permission for autopsy was refused.

CASE 110. A boy aged 4 years and six months. He was admitted to hospital on 21.12.33 with complaint of arthritis 6 weeks before when the hands and feet became swollen and painful.

21.12.33. Well nourished: no oedema: urine normal: rheumatic nodules on elbows: heart not enlarged but a loud apical V.S. murmur was present well conducted to the axilla: weight 16.2 Kg.

16.1.34. In spite of rest pulse rate was still rapid and cardiac dulness unaltered. Nodules more plentiful. Weight 16.0 Kg.

20.1.34. Heart now enlarged to right of middle line and to the left. Liver three fingerbreadths below costal margin and oedema of feet and face present. Weight 17.0 Kg.

23.1.34. Oedema was more marked. Slight cyanosis present but no orthopnoea. Urine clear. Blood chemistry:- Total protein 7.40 gm. per cent. Albumin 5.21 gm. per cent.. Globulin 2.19 gm. per cent.. N.P.N. 45.8 mgm. per cent..

24.1.34. Digitalis minims 10 every 4 hours. Weight 18.0 Kg.

27.1.34. Oedema less. Weight 16.1 Kg.. Faint trace of albumin present in the urine.

28.1.34. Right cardiac border now at middle line. ? oedema. Weight 15.7 Kg..

7.3.34. Dismissed. Heart still large. No oedema.

CASE 111. A boy aged 4 years. An unsatisfactory history of abdominal swelling and vague pains in the limbs of three weeks' duration was obtained. Till then he had been healthy.

25.12.31. On admission there was oedema of the legs, ascites and double pleural effusion. Cardiac dulness was increased to the right and left of the mid-sternum. No murmur was heard but the sounds were of very poor quality. Albumin was present in the urine throughout up to 4.0 parts Esbach. A radiological examination showed a heart shadow of peculiar shape.

9.1.32. Blood chemistry:- Total protein 6.71, albumin 3.79, globulin 2.92 gm. per cent.. Calculated oncotic pressure 24.9 mm. Hg.. Non-protein nitrogen 43.0 mgm. per cent..

13.1.32. On the development of chicken-pox he was transferred to a fever hospital. Since admission oedema had, if anything, become more marked. A week after transfer the patient died. No post-mortem examination was made.

CASE 112. A girl aged 12 years and 6 months. When 9 years old she had chorea. At 10 years she was in the Royal Hospital for Sick Children with rheumatic arthritis at which time mitral disease was diagnosed. Nine months and six months before readmission she had short attacks of arthritis. Two weeks before admission joint pains and swelling reappeared and in addition she became very breathless.

13.3.34. On readmission the heart was much enlarged to the right and left of mid-sternum and V.S. and V.D. murmurs were audible at the apex. No oedema was present and the urine was clear. She was very thin.

20.4.34. The condition remained unchanged save for occasional slight rises of temperature and the appearance of rheumatic nodules on the elbows.

2.5.34. Oedema of the feet was observed.

29.5.34. Oedema was now general and cyanosis and orthopnoea were present. The urine contained a trace of albumin. Blood chemistry:- Total protein 7.82, albumin 3.98, globulin 3.84 gm. per cent.. Calculated oncotic pressure 27.0 mm. Hg.. Non-protein nitrogen 20.0 mgm. per cent..

4.6.34. The child died. Permission for autopsy was refused.

CASE 113. A girl of 3 years and 7 months. Six weeks before admission to hospital the child took an indefinite illness which was diagnosed as pneumonia. Although in bed since, swelling of the legs and later of trunk and face appeared 5 weeks later.

29.4.34. On admission she was acutely ill, cyanosed and orthopnoeic. Oedema was very marked, involving the body generally, including the face. Ascites was present and fluid in both pleural cavities. There was no fever and no vomiting throughout. The heart was very much dilated to right and left of the middle line. A loud V.S. murmur was audible all over the praecordium and back. The liver was 4 fingerbreadths below the costal margin.

1.5.34. Friction was audible at the base of the heart. Blood Chemistry:- Total protein 7.32, albumin 3.97, globulin 3.35 gm. per cent.. Calculated oncotic pressure 26.5 mm. Hg.. Non-protein nitrogen 29.2 mgm. per cent..

6.5.34. The child died, the general condition being unchanged. Permission for autopsy was refused.

CASE 114. A girl aged 16 months. Three days before admission swelling of the face and feet was observed. From birth she was breast-fed till three months old when the diet was changed to Nestlé's milk owing to insufficiency of breast milk. Only half the amount proper for the age was given owing to vomiting. Bread or pudding was given once a day.

24.1.33. On admission she was a poorly nourished child with oedema of the legs and face. Marked rickets was present and the liver and spleen were palpable: nasal discharge was profuse. No abnormality was detected in the urine. A diet containing 46.0 gm. of protein per day was given.

30.1.33. Fever was present and a pyogenic infection of the urinary tract was found due to bacillus coli. Oedema had diminished.

13.2.33. There was now no fever and no oedema. The urine was clear. The Wassermann reaction was positive.

28.2.33. Neokharsivan 0.15 gm.

2.3.33. Neokharsivan 0.15 gm.

9.3.33. Neokharsivan 0.15 gm.

16.3.33. Neokharsivan 0.15 gm.

23.3.33. Neokharsivan 0.15 gm.

31.3.33. Neokharsivan 0.15 gm. The child was dismissed from hospital: 0.5 kilo in weight had been gained and oedema was absent.

Blood Chemistry.

Date.	Total Protein Gm.%	Albumin Gm.%	Globulin Gm.%	mm. Hg. Calculated oncotic pressure.	N.P.N. mgm.%
28.1.33	4.51	2.51	2.00	16.6	29.4
30.1.33	4.08	2.94	1.14	17.8	30.0
13.2.33	6.59	4.09	2.50	25.8	31.0

CASE 115. A girl aged 16 months. She was admitted to hospital on 18.9.33 with complaint of oedema of face, hands and feet of about 3 weeks' duration. Still entirely breast fed.

18.9.33. Oedema fairly marked. Urine clear. No abnormality detected in heart, lungs, alimentary or nervous systems on physical examination. Light diet given. Weight 8.2 Kg.

19.9.33. Weight 8.0 Kg. Urea concentration test:- Before urea 1.44 gm. per cent.. 1 hour after 2.75 gm. per cent.. 2 hours after 3.88 gm. per cent.. Blood chemistry:- Total protein 2.98 gm. per cent.. Albumin 1.17 gm. per cent.. Globulin 1.81 per cent.. N.P.N. 18.8 mgm. per cent..

27.9.33. Oedema just present. Urine clear. Weight 7.4 Kg.. Ileo-colitis developed with much blood and mucus in the stool. Blood chemistry:- Total protein 4.09 gm. per cent.. Albumin 2.81 gm. per cent.. Globulin 1.28 gm. per cent.. N.P.N. 20.1 mgm. per cent..

2.10.33. Weight 6.9 Kg. No oedema.

17.10.33. Stool normal. Weight 6.8 Kg. No oedema. Light diet.

10.10.33. Blood chemistry:- Total protein 5.15 gm. per cent.. Albumin 3.28 gm. per cent.. Globulin 1.87 gm. per cent.. N.P.N. 21.0 mgm. per cent.. Weight 6.5 Kg.

19.10.33. Weight 7.5 Kg. Dismissed well.

17.6.34. Out-patient. Child thriving. Weight 9.5 Kg. Blood chemistry:- Total protein 6.80 gm. per cent.. Albumin 4.21 gm. per cent.. Globulin 2.59 gm. per cent.. N.P.N. 24.0 mgm. per cent..

CASE 116. A girl aged 1 year. Till 10 months she was breast-fed and apparently throve till she was weaned and received 4 oz. of milk and one teaspoonful of sugar 4 times a day.

26.1.34. On admission she was found to be a typical cretin and was 63 per cent. of the normal weight for the age. Otitis media was present with fever. The urine was clear at this time and there was no oedema. Thyroid, grains 2 daily, was given and milk giving a protein intake of 42 grams of protein per day.

9.1.34. Pus was found in the urine and bacillus coli on culture. Sodium bicarbonate, grains 90 per day, was given. At this point thyroid extract was omitted.

14.1.33. Gastro-enteritis developed with frequent vomiting and passage of loose motions.

17.1.33. Dehydration very marked. 210 c.c. of normal saline were given into the peritoneal cavity. Weight 4.8 Kg..

27.1.33. The weight was now 6.0 Kg. and oedema of legs and face was present. Vomiting was less frequent and also the number of stools per day was smaller. Blood chemistry:- Total protein 5.64, albumin 3.08, globulin 2.56 gm. per cent.. Calculated oncotic pressure 20.5 mm. Hg.. Non-protein nitrogen 21.8 mgm. per cent.. Sodium bicarbonate was stopped.

7.2.33. No oedema was present. The weight was 4.9 Kg.. High fever was present and signs of broncho-pneumonia.

10.2.33. Child died. Permission for autopsy was refused.

CASE 117. A female aged 18 months. Seven weeks before admission she began to vomit and pass loose green stools.

6.3.34. On admission a pyogenic infection of the urinary tract was found, the urine containing much pus with a growth of bacillus coli in the catheter specimen. No abnormality was detected in heart, lungs or nervous system. Much dehydration was present and some irregular fever. For the urinary infection hexamine and calcium chloride, 5 grains of each, were given every four hours. These drugs were increased to a daily intake of 75 grains of

13.3.34. each. After 3 days on the latter dose a severe acidosis with diarrhoea and vomiting appeared. Blood CO_2 31.0 vols. per cent.. The hexamine and calcium chloride were omitted and sodium bicarbonate gr. 30 every 4 hours given along with intraperitoneal saline and intravenous glucose daily.

19.3.34. Vomiting ceased. Sodium bicarbonate stopped.

20.3.34. Weight rising rapidly. Parenteral fluid therapy stopped.

22.3.34. Pitting oedema present in legs. Face puffy. Catheter urine sterile. No pus or albumin.

23.3.34. Weight falling. Blood chemistry:- Total protein 6.89, albumin 2.90, globulin 3.99 in grams per cent.. Calculated oncotic pressure 21.5 mgm. per cent.. N.P.N. 23.5 mgm. per cent..

25.3.34. No oedema. Child now dehydrated. Pus still present in urine.

19.4.34. Urine sterile. Child was now putting on weight.

CASE 118. A boy aged 9 years. Always a physically backward child: prominence of the abdomen and the passage of large, pale, loose stools were the complaints. Till the day of admission diarrhoea had been present.

15.6.31. On admission he was a small child 105 cm. in height (normal 127 cm.) who weighed 16.7 Kg. (normal 25.8 Kg.) Slight oedema of feet and of the face was present. The heart and urine were normal. There was no fever.

16.6.31. Blood chemistry:- Total protein 3.76, albumin 2.85, globulin 0.91 gm. per cent.. Calculated oncotic pressure 16.9 mm. Hg.. Non-protein nitrogen 33.0 mgm. per cent..

17.6.31. A typical coeliac motion was passed.

19.6.31. No oedema.

30.7.31. Dismissed from hospital.

CASE 119. A boy aged 17 months. From birth he was breast fed and this was the main article of diet. Eggs and tea were occasionally added. One month before admission enteritis developed and breast milk alone was given.

20.5.31. On admission he was a poorly nourished child with oedema of the face and feet. No abnormality was detected on physicial examination save tonsillitis. The urine was clear. Slight fever-102°F.-was present. Blood chemistry:- Total protein 5.99, albumin 2.71, globulin 3.28 gm. per cent.. Calculated oncotic pressure 19.5 mm. Hg.. Non-protein nitrogen 33.0 mgm. per cent..

26.5.31. No fever. Oedema gone.

15.6.31. One kilo in weight gained. No oedema.

CASE 120. A girl aged 2 years. She was admitted to hospital on 10.10.33 with oedema of face and extremities of 2 days' duration. History of vomiting for two weeks but nothing more definite. Diet not stated. Small child 71 per cent. of expected weight (oedema-free). Urine - tr. albumin. No blood or casts. Oedema of face, hands and feet present.

11.10.33. Blood chemistry:- Total protein 4.58 gm. per cent.. Albumin 2.71 gm. per cent.. Globulin 1.87 per cent.. Calculated oncotic pressure 17.0 mm. Hg.. N.P.N. 22.4 mgm. per cent..

18.10.33. Oedema and urine unchanged. Light diet given.

23.10.33. Catheterised - urine clear. No albumin. Culture sterile. Oedema still present.

2.11.33. Oedema gone. Urine clear.

20.11.33. Weight rising rapidly but no oedema present. Very well.

CASE 121. A boy aged 7 years. Three days before admission he developed a cough and complained of feeling cold.

19.10.32. On admission a consolidation of the right upper lobe was found. High fever was present. The urine contained no albumin and the chlorides were not tested for.

20.10.32. Temperature was 104°F.. Blood chemistry:- Total protein 7.72, albumin 5.14, globulin 2.08 gm. per cent.. Calculated oncotic pressure 31.2 mm. Hg.. Non-protein nitrogen 32.5 mgm. per cent..

23.10.32. The temperature fell by lysis.

8. 11.32. Recovery was uninterrupted and the patient was dismissed well.

CASE 122. A male aged 22 months. Four days before admission cough and fever developed.

7.10.33. On admission the child was sharply ill with a temperature of 103°F. Rickets was present. Over both lung bases much râle was present. Blood chemistry:- Total protein 8.13, albumin 5.58, globulin 2.55 gm. per cent... Calculated oncotic pressure 34.2 mm. Hg.. Non-protein nitrogen 26.3 mgm. per cent..

15.10.33. The temperature fell gradually by lysis. The lungs were clear.

23.10.33. Dismissed well.

CASE 123. A boy aged 7 months. On the day before admission he became acutely ill with fever following a cough of a few days' duration.

27.3.32. On admission the child appeared to be acutely ill with a temperature of 105°F. Râle was general over the back and an area of consolidation was present in the left lateral region. Blood chemistry:- Total protein 6.04, albumin 4.83, globulin 1.21 gm. per cent.. Calculated oncotic pressure 28.2 mm. Hg.. Non-protein nitrogen 16.3 mgm. per cent..

29.3.32. The child died. Autopsy showed bronchopneumonia.

CASE 124. A male aged 29 weeks. Three days before admission he began to cough and fever and vomiting developed.

10.4.31. A well-nourished child who was acutely ill, the temperature being 104°F. Much loose râle was audible at both bases with impairment of the percussion note at the right base.

15.4.31. The condition was unchanged. Blood chemistry:- Total protein 6.43, albumin 5.08, globulin 1.35 gm. per cent.. Calculated oncotic pressure 29.8 mm. Hg.. Non-protein nitrogen 22.5 mgm. per cent..

18.4.31. The temperature fell by lysis.

20.4.31. No fever was present and the lungs were clear.

22.4.31. Dismissed well.

CASE 125. A girl of 5 years. Six days before admission she lost appetite and next day was jaundiced. Stool pale. There was no pain or fever.

15.1.32. On admission jaundice was deep. The urine contained bile and the stool was pale. The liver was 2 finger-breadths below the costal margin. The temperature was 101°F. Blood chemistry:- Total protein 10.00, albumin 6.94, globulin 3.06 gm. per cent.. Calculated oncotic pressure 42.5 mm. Hg.. Non-protein nitrogen 49.0 mgm. per cent..

10.1.32. Liver normal; no jaundice: urine and stool normal. Dismissed well.

CASE 126. A boy aged 11 months. About 2 weeks before admission he began to vomit and the mother observed that he was very irritable.

25.3.31. On admission meningitis was diagnosed from the presence of a bulging fontanelle and nuchal rigidity. The spleen was palpable and scanty tuberculides were present on the thighs. On lumbar puncture a clear fluid was obtained containing 65 cells per c.mm. These were for the most part lymphocytes. The temperature was 101.8°F. Blood chemistry:- Total protein 7.56, albumin 4.82, globulin 2.74 gm. per cent.. Calculated oncotic pressure 30.3 mm. Hg.. Non-protein nitrogen 25.6 mgm. per cent..

30.3.31. The child died. No autopsy.

CASE 127. A boy aged 4 years. About three months before admission the child began to vomit occasionally and to complain of headache.

7.5.32. On admission he was found to be very thin. Signs of increased intracranial pressure were present as shown by the presence of starting of the sutures in the x-ray plate of the skull and optic neuritis. Lumbar puncture at this time gave normal findings. The tuberculin skin reactions were markedly positive.

15.5.32. The condition was unchanged. The temperature was normal. Blood chemistry:- Total protein 7.25, albumin 4.97, globulin 2.28 gm. per cent.. Calculated oncotic pressure 30.5 mm. Hg.. Non-protein nitrogen 40.0 mgm. per cent..

13.6.32. The child subsequently developed tuberculous meningitis and died.

CASE 128. A boy aged 3 years. A week before admission he was "unwell" and became jaundiced. Right-sided abdominal pain was present and the urine was noted to be very dark in colour. Vomiting took place several times.

21.10.32. On admission he was a fairly well nourished boy who was deeply jaundiced. There was no fever or vomiting during his stay in hospital. The urine contained much bile and the stool was pale.

25.10.32. Blood chemistry:- Total protein 7.61 albumin 4.47, globulin 3.14 gm. per cent.. Calculated oncotic pressure 33.3 mm. Hg.. Non-protein nitrogen 37.0 mgm. per cent..

2.11.32. There was now very slight jaundice, the stool was normal in colour and the urine contained only a trace of bile.

11.11.32. Dismissed well.

CASE 129. A boy aged 19 months. Previously well till a week before admission when he began to vomit. Irritability and constipation were noted.

7.9.31. On admission he was found to be well nourished. Drowsiness was present. The temperature was 102°F. No abnormality was detected in the lungs or abdomen and the spleen was not felt. On lumbar puncture a clear fluid under increased pressure was obtained: the cells present were lymphocytes and numbered 31 per c.mm.. Blood chemistry:- Total protein 6.03, albumin 4.28, globulin 1.75 gm. per cent.. Calculated oncotic pressure 26.0 mm. Hg.. Non-protein nitrogen 25.5 mgm. per cent..

27.9.31. The child became gradually more drowsy and died. Autopsy showed miliary tubercle and tuberculous meningitis.

CASE 130. A boy aged 5 years. Five days before admission it was noticed that he was jaundiced and that the urine was dark in colour.

27.4.32. On admission jaundice was very marked, the stool was very pale and the urine contained much bile. The liver was palpable 2-3 finger-breadths below the costal margin. The temperature was 102°F. Blood chemistry:- Total protein 8.75, albumin 4.49, globulin 4.26 gm. per cent.. Calculated oncotic pressure 30.1 mm. Hg.. Non-protein nitrogen 27.0 mgm. per cent..

29.5.32. The child was dismissed well.

CASE 131. A boy aged 8 years. Till the present illness he throve well. 6 months before admission complained of epigastric pain of a spasmodic nature - many attacks daily. These gradually became less frequent - 5 days between attacks. Vomiting was present. For weeks motions have been pale and urine dark. Jaundice was noticed only 4 days before admission on 14.2.32.

15.2.32. Skin slightly jaundiced. Conjunctivae yellow. Cervical glands palpable. Abdomen distended, liver palpable 2 finger-breadths below costal margin. Spleen 2 finger-breadths. Stool normal in colour. Child ill and drowsy with a normal temperature. The urine contained a small quantity of bile but no albumin. Blood: R.B.C. 2,710,000. W.B.C. 10,200. Hb. 50%. Films showed only aniscytosis and poikilocytosis. Wassermann reaction negative. Van den Bergh biphasic 15 units. Weight 23.0 kilos. Blood chemistry:- Serum total protein 5.88, albumin 2.88 and globulin 3.00 in grams per cent.. N.P.N. 34.0 mgm. %. Calculated oncotic pressure 20.0 mm. Hg.

20.2.32. All the time during admission vomiting was very frequent. On the last two days of life there was fever and wild delirium. Blood chemistry:- Serum total protein 9.87, albumin 3.62; globulin 6.25 gm. per cent.. N.P.N. 70.6 mgm. %. Calculated oncotic pressure 28.6 mm. Hg.. Died. The clinical diagnosis was Hanot's cirrhosis. At autopsy the liver was large and showed a fine cirrhosis.

CASE 132. A girl aged 8 years. For 2 years recurring attacks of jaundice were observed during which the motions became pale and the urine dark.

19.1.31. On admission a slight degree of jaundice was present. The liver and spleen were both greatly enlarged. Blood:- R.B.C. 3,490,000 millions per c. cmm. White cells 6,200 per cmm., haemoglobin 48 per cent.. Films showed no abnormality. The fragility of the red cells was slightly diminished. The Wassermann reaction was negative. In the urine bile was not present but urobilin was ++.

20.1.31. No fever. Blood chemistry:- Total protein 5.31, albumin 2.68, globulin 2.63 gm. per cent.. Calculated oncotic pressure 18.4 mm. Hg.. Non-protein nitrogen 25.2 mgm. per cent..

2.3.31. For three days some oozing from the gums and nose occurred during which the temperature rose to 102.6°F.

9.3.31. No fever. Jaundice was rather less than on admission. Blood chemistry:- Total protein 8.28, albumin 2.95, globulin 5.33 gm. per cent.. Calculated oncotic pressure 23.7 mm. Hg.. Non-protein nitrogen 24.4 mgm. per cent..

13.5.31. Dismissed from hospital.

CASE 133. A boy aged 3 years and 3 months. He was perfectly well till the day before admission when he vomited. A few hours later he was noticed to be pale and rather yellow in colour. The urine was observed to be bright red.

15.4.31. On admission there was moderate fever. He was very pale but his colour was not that of obstructive jaundice. Air-hunger was present. The red cell count was 1,280,000 per c.mm.: white cells were 40,000 per c.mm.: the haemoglobin 40 per cent.. Films showed that polymorphs formed 72 per cent. of white cells: numerous normoblasts were present. The spleen and liver were not palpable and there was no oedema. The urine contained much haemoglobin but no red cells. Albumin was +. Culture was negative. The Wassermann reaction was negative.

16.4.31. Excretion of haemoglobin in the urine continued. Blood chemistry:- Total protein 6.68, albumin 2.11, globulin 4.57 gm. per cent.. Calculated oncotic pressure 18.0 Hg.. Non-protein nitrogen 130.6 mgm. per cent.. On centrifuging the blood it was found that a marked degree of lysis was present. Transfused with 300 c.c. of blood. Frequent vomiting was still taking place.

19.4.31. Haemoglobinuria was still present but was much less marked.

1.5.31. As the red cells were still 2,100,000 millions in spite of the fact that no haemoglobin, blood or albumin had been present in the urine for a week a further transfusion of 350 c.c. of blood was given. Following this uninterrupted recovery ensued.

10.6.31. Dismissed well.

CASE 134. A boy aged 7 years and 9 months. Save for measles at three years he had no illnesses. Apparently he had always wet the bed: this, and his small size, were the subject of the mother's complaint. She also noticed that he drank a great deal. No oedema was ever noted or any abnormality in the urine.

8.5.31. On admission he weighed 16.8 Kg. (normal 24.1) and was 106 cm. in height (normal 121). The urine contained a trace of albumin. Ophthalmoscopic examination showed a slight degree of optic neuritis. The systolic blood pressure was 108 mm. Hg.. The urea clearance test was 8 per cent. of normal and only 8.6 per cent. of the dye appeared in the urine 2 hours after the injection of phenolsulphonephthalein.

11.5.31. Blood chemistry:- Total protein 7.55, albumin 5.69, globulin 1.86 gm. per cent.. Calculated oncotic pressure 33.9 mm. Hg.. Non-protein nitrogen 96.1 mgm. per cent..

9.6.31. Non-protein nitrogen of the blood was 136.3 mgm. per cent.

12.6.31. Dismissed from hospital, the condition being unchanged.

?.3.32. It was discovered that child took convulsions (at home) about this time and died a few days later.

CASE 135. A girl aged 4 years. Admitted to hospital on 17.3.31. with rheumatic arthritis. There was no carditis.

10.6.31. She was afebrile and there were no joint manifestations. Blood chemistry:- Total protein 6.84, albumin 5.32, globulin 1.52 gm. per cent..

CASE 136. A girl aged 3 years. For three weeks before admission on 17.5.34. Two or three generalized convulsions occurred every day.

21.5.34. Afebrile. The Wassermann reaction was negative. Blood chemistry:- Total protein 6.87, albumin 4.49, globulin 2.38 gm. per cent.. A diagnosis of epilepsy was made.

CASE 137. A boy aged 5 years. The history was bed-wetting since birth.

21.1.32. On admission he was found to be healthy child. No abnormality of the urine or the urinary tract was detected. He was afebrile. Blood chemistry:- Total protein 7.75, albumin 4.81, globulin 2.94 gm. per cent.. A diagnosis of enuresis was made.

CASE 138. A boy aged 5 years. For a long period short "turns" had been observed to occur many times daily in which the child seemed to forget what he was doing.

27.7.33. In hospital he was afebrile and apparently healthy. No "turns" were observed. Blood chemistry:- Total protein 6.84, albumin 4.74, globulin 2.10 gm. per cent..

CASE 139. A boy aged 5 years. On 25.4.31., three weeks before admission he developed arthritis.

3.7.31. Save for a V.S. murmur at the apex, which was conducted to the axilla, no abnormality was present. Blood chemistry:- 8.01, albumin 5.22, globulin 2.79 gm. per cent..

CASE 140. A boy aged 5 years. Shortly before admission on 20.5.31 arthritis developed.

18.7.31. There was now no evidence of active rheumatism. He was afebrile and the heart was apparently normal. Blood chemistry:- Total protein 8.24, albumin 5.43, globulin 2.81 gm. per cent..

CASE 141. A girl aged 5 years. For some weeks before admission on 16.2.32 incontinence of urine had been present.

21.2.32. No abnormality in the urine or in urinary tract was observed, and a diagnosis of enuresis was made. Blood chemistry:- Total protein 7.25, albumin 4.97, globulin 2.28 gm. per cent..

CASE 142. A boy aged 7 years. Three weeks before admission on 8.8.31 he developed chorea.

5.11.31. Chorea was now gone. He was afrebile and the heart was apparently unaffected. Blood chemistry:- Total protein 7.38, albumin 5.10, globulin 2.28 gm. per cent..

CASE 143. A boy aged 7 years. Two years previously he was in hospital when a diagnosis of epilepsy was made. Two days before admission on 5.4.32 convulsions became very frequent and of long duration.

26.4.32. He was now apparently well and had had no convulsions for 20 days. There was no fever. Blood chemistry:- Total protein 7.54, albumin 5.18, globulin 2.36 gm. per cent..

CASE 144. A boy aged 8 years. Three days before admission on 1.2.33 arthritis developed.

28.4.33. There had been no arthritis or fever for over six weeks. A V.S. murmur was still audible at the apex of the heart which was not enlarged. Blood chemistry:- Total protein 7.22, albumin 4.72, globulin 2.50 gm. per cent..

CASE 145. A girl aged 8 years. Two weeks before admission on 24.8.32 chorea appeared.

20.11.32. No chorea was observed three weeks after admission, there was no fever and the heart was apparently normal: Blood chemistry:- Total protein 6.84, albumin 4.45, globulin 2.39 gm. per cent..

CASE 146. A girl aged 9 years. Four days before admission on 22.11.31 she developed severe chorea.

2.4.32. There had been no chorea for 8 weeks and she was afebrile. A loud apical V.S. murmur was audible at the apex of the heart which was not dilated. Blood chemistry:- Total protein 7.58, albumin 5.94, globulin 1.64 gm. per cent..

CASE 147. A girl aged 9 years. Three weeks before admission on 6.6.33 rheumatic arthritis developed.

27.8.33. Afebrile: No arthritis: A short V.S. murmur was audible at the base of the heart. Blood chemistry:- Total protein 7.43, albumin 4.70, globulin 2.73 gm. per cent..

CASE 148. A boy aged 10 years. Two days before admission on 19.2.34 he took a generalized convulsion.

23.2.34. No abnormality was detected. He was afebrile. Blood chemistry:- Total protein 7.10, albumin 4.72, globulin 2.38 gm. per cent.. Epilepsy was diagnosed.

CASE 149. A girl aged 10 years. One month before admission on 3.8.31 she developed arthritis and three weeks later chorea appeared.

12.9.31. She was afebrile: chorea was gone and there was no arthritis. Blood chemistry:- Total protein 7.64, albumin 5.28, globulin 2.36 gm. per cent..

CASE 150. A girl aged 11 years. In 1931 she had rheumatic arthritis. Three days before admission on 12.2.34 arthritis reappeared.

14.4.34. There was no arthritis and she was afebrile. Cardiac dulness was within normal limits but a V.S. murmur was audible at the apex. Blood chemistry:- Total protein 7.78, albumin 5.27, globulin 2.51 gm. per cent..

CASE 151. A girl aged 11 years. A week before admission on 17.12.32. chorea appeared.

2.3.33. Chorea was now absent. A short apical V.S. murmur was present but the cardiac dulness was not increased. She was afebrile. Blood chemistry:- Total protein 7.27, albumin 5.52, globulin 1.75 gm. per cent..

CASE 152. A girl aged 11 years. Three days before admission on 12.9.31 arthritis appeared.

24.11.31. While there was now no arthritis V.S. and V.D. murmurs were audible at the apex of the heart which was normal in size. There was no fever. Blood chemistry:- Total protein 7.34, albumin 5.12, globulin 2.22 gm. per cent..

CASE 153. A girl aged 11 years. Four days before admission on 23.1.33 arthritis developed.

3.3.33. There was now no arthritis. A V.S. murmur was audible at the apex of the heart which was not enlarged. Blood chemistry:- Total protein 6.83, albumin 4.99, globulin 1.84 gm. per cent.. Fever was absent.

CASE 154. A boy aged 10 years. For three years he had been subject to epileptic convulsions. On the day of admission, 17.4.34, he took a very severe fit.

20.4.34. There was no fever and no abnormality was detected on physical examination. Blood chemistry:- Total protein 8.02, albumin 5.92, globulin 2.10 gm. per cent.. Haematocrit 41 per cent. R.B.C. Haemoglobin 102 per cent.. R.B.C. 5,350,000 millions per c. mm.

CASE 155. A boy aged 8 years. For some years prior to admission on 8.11.31 he had suffered from enuresis.

15.11.31. No abnormality was detected on physical examination and he was afebrile. Blood chemistry:- Total protein 7.78, albumin 5.62, globulin 2.16 gm. per cent.. Haematocrit 40 per cent. R.B.C.. Haemoglobin 94 per cent.. R.B.C. 5,390,000 millions per c.mm.

CASE 156. A girl aged 9 years. Five days before admission on 15.2.32 chorea appeared.

17.5.32. Chorea was now gone and she was afebrile. A V.S. murmur was audible at the apex of the heart which was not dilated. Blood chemistry:- Total protein 8.04, albumin 5.25, globulin 2.79 gm. per cent.. Haematocrit 40 per cent. R.B.C.. Haemoglobin 90 per cent.. R.B.C. 4,870,000 millions per c.mm.

CASE 157. A boy aged 8 years. Three days before admission 27.2.31 he developed arthritis.

26.4.31. There was no arthritis and fever was absent. In the heart V.S. and V.D. murmurs were present at the apex but there was no enlargment. Blood chemistry:- Total protein 7.03, albumin 5.42, globulin 1.61 gm. per cent.. Haematocrit 41 per cent. R.B.C.. Haemoglobin 96 per cent.. R.B.C. 5,080,000 millions per c.mm.

CASE 158. A boy aged 10 years. Ten days before admission on 27.2.31 chorea appeared.

19.4.31. Chorea was absent and there was no fever. The heart was apparently undamaged. Blood chemistry:- Total protein 7.62, albumin 5.59, globulin 2.03 gm. per cent.. Haematocrit 41 per cent.. R.B.C.. Haemoglobin 90 per cent.. R.B.C. 5,090,000 millions per c.mm.

CASE 159. An infant aged 15 weeks. Owing to injury at birth convulsions had been frequent throughout life.

15.4.31. Afebrile. Blood chemistry:- Total protein 6.87, albumin 4.49, globulin 2.38 gm. per cent..

CASE 160. An infant aged 16 weeks. A week before admission the child began to take frequent convulsions.

12.7.33. Afebrile. Blood chemistry 7.19, albumin 5.10, globulin 2.09 gm. per cent..

CASE 161. An infant aged 17 weeks. The day before admission the child took a convulsion.

7.3.32. Afebrile. Rickets marked. Blood chemistry:- Total protein 7.22, albumin 4.96, globulin 2.26 gm. per cent..

CASE 162. An infant aged 19 weeks. For some time before admission increase in the size of the head was observed.

22.3.34. Hydrocephalus was marked. No fever was present. The Wassermann reaction was negative. Blood chemistry:- 7.10, albumin 4.48, globulin 2.62 gm. per cent..

CASE 163. An infant aged 27 weeks. Four days before admission on 12.3.31 fever and cough developed. Broncho-pneumonia was present.

19.3.31. Fever gone and chest clear.

26.3.31. Blood chemistry:- Total protein 6.56, albumin 5.43, globulin 1.13 gm. per cent..

CASE 164. An infant aged 9 months. Labour was difficult. The complaint was that the child could not raise the head and made no effort to play with toys.

Afebrile. Blood chemistry:- Total protein 7.63, albumin 5.38, globulin 2.25 gm. per cent..

CASE 165. An infant aged 9 months. Afebrile. Rickets marked. Blood chemistry:- Total protein 6.94, albumin 4.12,globulin 2.82 gm. per cent..

CASE 166. An infant aged 9 months. Three days before admission on 20.3.33 cough and fever appeared and next day the child had a convulsion. Tetany and rickets were well marked.

28.3.33. No fever. Tetany gone. Blood chemistry:- Total protein 7.33, albumin 4.77, globulin 2.56 gm. per cent..

CASE 167. An infant aged 10 months. Afebrile. Marked rickets was present. Blood chemistry:- Total protein 6.79, albumin 4.92, globulin 1.87 gm. per cent..

CASE 168. An infant aged 11 months. Rickets was marked and tetany was present. There was no fever. Blood chemistry:- Total protein 7.72, albumin 4.95, globulin 2.77 gm. per cent..

CASE 169. An infant aged 11 months. For some weeks prior to admission convulsions had been present. The Wassermann reaction was negative. There was no fever. Blood chemistry:- Total protein 6.82, albumin 4.14, globulin 2.68 gm. per cent..

CASE 170. An infant aged 1 year. Two days before admission on 17.2.31 otitis media developed and next day crowing was marked.

24.2.31. No fever or tetany. Blood chemistry:- Total protein 6.04, albumin 4.83, globulin 1.31 gm. per cent..

CASE 171. An infant aged 1 year. Three days before admission on 17.3.32 crowing and carpopedal spasm were observed.

28.3.32. No fever and no evidence of tetany. Blood chemistry:- Total protein 6.41, albumin 4.92, globulin 1.49 gm. per cent..

CASE 172. An infant aged 1 year and 1 month. On admission rickets was marked. Afebrile. Blood chemistry:- Total protein 6.31, albumin 5.05, globulin 1.26 gm. per cent..

CASE 173. An infant aged 1 year and 2 months. On admission rickets was marked. Afebrile. Total protein 7.69, albumin 5.21, globulin 2.48 gm. per cent..

CASE 174. An infant aged 1 year and 4 months. On admission there was mild rickets. No fever. Total protein 7.64, albumin 4.95, globulin 2.69 gm. per cent..

CASE 175. An infant aged 1 year and 5 months. Rickets was very marked. Afebrile. Blood chemistry:- Total protein 7.91, albumin 5.39, globulin 2.52 gm. per cent..

CASE 176. An infant aged 1 year and 5 months. On the day before admission on 17.2.33 a convulsion occurred.

2.3.33. Child apparently well. Afebrile. Blood chemistry:- Total protein 6.38, albumin 5.04, globulin 1.34 gm. per cent..

CASE 177. An infant aged 1 year and 6 months. Rickets was present on admission. Blood chemistry:- Total protein 8.00, albumin 5.22, globulin 2.78 gm. per cent..

CASE 178. An infant aged 1 year and 6 months. Rickets present. Afebrile. Blood chemistry:- Total protein 6.55, albumin 4.84, globulin 1.71 gm. per cent..

CASE 179. An infant aged 1 year and 8 months. For 4 months prior to admission convulsions had been frequent. Afebrile. Blood chemistry:- Total protein 7.33, albumin 4.82, globulin 2.51 gm. per cent..

CASE 180. An infant who on admission showed evidence of rickets. Blood chemistry:- Total protein 7.31, albumin 5.91, globulin 1.40 gm. per cent..

CASE 181. A boy aged 7 years. During an attack of scarlet fever seven months before admission albuminuria was observed for nine days, commencing on the eleventh day of the fever. Neither haematuria nor oedema was present. Six days after dismissal oedema of the face and legs was noted.

25.1.34. On admission oedema of the face and shins was present. The heart and fundi showed no abnormality and the systolic blood pressure was 100 mm. Hg.. The urine contained much albumin but no blood, even microscopic. Milk only was permitted on admission.

29.1.34. No change in oedema was observed. Diet with salt was permitted.

31.1.34. In two days 2.0 Kg. in weight were gained. The congo red test was positive.

10.2.34. Oedema was still increasing. Diet "salt-free."

17.2.34. No change in oedema. Fever (103°F.) and cough present. Clinically fluid was present in both pleural cavities and this was confirmed by X-ray. Fluid diet - "salt-free."

21.2.34. The right chest was explored and pus found. The organism was a pneumococcus.

27.2.34. Oedema unchanged.

14.3.34. Oedema rather less. On three occasions during the past fortnight the empyema had been treated by aspiration of the pus. Since no improvement took place he was transferred to a surgical ward where rib-resection was performed.

2.5.34. Transferred to a medical ward. There was no oedema. The urine contained much albumin but no blood. The systolic blood pressure was 90 mm. Hg.. For the past three weeks he had been receiving full diet (with salt): this was continued.

8.6.34. Dismissed from hospital. There was no oedema but the urine still contained much albumin.

9.7.34. The patient now looked very well and there was no oedema. Marked albuminuria was still present.

Blood chemistry:-

Date	Total protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure mm.Hg.	N.P.N. mgm.%
26.1.34.	-	-	-	-	22.5
2.3.34	-	-	-	-	22.5
8.5.34	7.97	2.17	5.80	20.2	30.0

Urea Concentration Tests:-

Date.	Before urea.	1 hour after.	2 hours after.
1.2.34.	0.54 gm.%	2.43 gm.%	3.50 gm.%
3.5.34.	2.72 gm.%	2.67 gm.%	4.04 gm.%

CASE 182. A boy aged 10 years. On the occasion of his third admission to hospital with haemophylia there was very marked anaemia associated with multiple haemarthroses.

7.4.33. Slight fever - 101°F. Red blood corpuscles 1,500,000 millions per c.mm. Haemoglobin 30 per cent.. Blood chemistry:- Total protein 6.41, albumin 4.20, globulin 2.21 gm. per cent..

CASE 183. A girl aged 15 months. The complaint was pallor.

5.3.32. On admission a well-marked degree of anaemia was present which responded well to iron. Red blood corpuscles 2,800,000 millions per c.mm. Haemoglobin 60 per cent.. Blood chemistry:- Total protein 6.38, albumin 5.04, globulin 1.34 gm. per cent..

CASE 184. A boy aged 8 years. Seven weeks after admission for acute rheumatism he appeared to be well. Afebrile. Red blood corpuscles 4,290,000 millions per c.mm. Haemoglobin 85 per cent.. Blood chemistry:- Total protein 6.56, albumin 4.16, globulin 2.40 gm. per cent..

CASE 185. A boy aged 10 years. A week before admission oedema of the face was observed. Six days later headache, vomiting, and dimness of vision appeared.

23.12.32. On admission oedema was general and ascites was present. The urine contained much blood and albumin and the systolic blood pressure was 150 mm. Hg.. Twitching of the face was observed after admission. Lumbar puncture was performed and 30 c.c. of clear fluid under increased pressure were withdrawn. 130 c.c. of blood were removed. This relieved the headache and no further twitching was noted.

27.12.32. Oedema was considerably less and the systolic blood pressure was 118 mm. Hg.. Examination of the fundi showed the vessels to be very prominent.

9.1.33. No oedema.

12.1.33. Systolic blood pressure 90 mm. Hg..

30.1.33. No oedema. Systolic blood pressure 98 mm. Hg..

4.2.33. Gross haematuria ceased.

21.2.33. Moderate fever. Tonsils enlarged and inflamed with follicular exudation present. Swab negative for b. diphtheriae.

22.2.33. Gross haematuria again present but no increase in albumin occurred. No oedema. Blood pressure not observed.

25.3.33. Gross haematuria ceased. Systolic blood pressure 110 mm. Hg..

6.4.33. A trace of albumin was present in the urine.

Blood chemistry/

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%
23.12.32	7.47	-	-	-	80.0
27.12.32	6.72	-	-	-	49.0
12.1.33	7.73	4.66	3.07	29.9	89.5
19.1.33	6.23	3.87	2.36	24.6	30.0
30.1.33	6.19	3.53	2.66	23.1	37.7
1.3.33	7.34	4.66	2.68	29.4	26.0

Urea Concentration Tests.

Date.	Before urea.	One hour after.	Two hours after
12.1.33	1.73 gm.%	1.73 gm.%	1.73 gm.%
30.1.33	1.46 gm.%	1.82 gm.%	2.08 gm.%
1.3.33	1.76 gm.%	1.76 gm.%	2.10 gm.%

CASE 186. A female aged 1 year and 3 months. She was an only child of healthy parents. Throve well on the breast till 9 months. She continued to thrive till 6 weeks before admission when double otorrhoea developed and she became listless and vomited occasionally. Two weeks later a purulent nasal discharge appeared.

7.9.33. On admission the face was puffy and there was some pitting of the legs. The fundi were normal. The urine contained much albumin but no blood macroscopically. Very scanty red cells were detected by the microscope.

9.9.33. No change in the condition. The systolic blood pressure was 98 mm. Hg.. Wassermann reaction negative. Fever was now present and a purulent nasal discharge again appeared. Blood chemistry:- Total protein 3.80, albumin 2.40, globulin 1.40 gm. per cent.. Calculated oncotic pressure 15.2 mm. Hg.. Non-protein nitrogen 29.2 mgm. per cent..

17.9.33. Enteritis. Vomiting frequent.

18.9.33. No oedema. Blood chemistry:- Total protein 5.21, albumin 2.13, globulin 3.08 gm. per cent. Calculated oncotic pressure 16.0 mm. Hg..

21.3.33. Child irregularly dismissed from hospital. Albuminuria still marked.

14.10.33. The infant was now very dehydrated owing to continuous diarrhoea and vomiting since dismissal. A catheter specimen of urine contained neither albumin, blood nor casts.

19.10.33. Child died at home.

CASE 187. A boy aged 8 months. Till 4 weeks before admission he throve well. Generalized oedema appeared and urine was observed to be dark in colour.

17.10.31. On admission oedema was general and ascites was present. Much albumin and blood were present in the urine.

20.10.31. Fever was present and some râle over both bases.

21.10.31. Blood chemistry:- Total protein 6.78, albumin 2.66, globulin 4.12 gm. per cent.. Calculated oncotic pressure 20.4 mm. Hg.. Non-protein nitrogen 29.1 mgm. per cent.. Serum calcium 9.2 mgm. per cent..

24.10.31. Temperature rose steadily, the stools became loose and vomiting frequent. Much generalized râle audible throughout the lungs. Oedema steadily diminishing.

26.10.31. Child died.
At autopsy broncho-pneumonia was present and acute nephritis. There was no evidence of congenital syphilis.

CASE 188. A boy aged 4 months. He was breast-fed and throve till 2 weeks before admission when oedema of the face was noted.

4.2.33. On admission oedema was general with ascites and the urine contained albumin but only microscopic blood. Culture of the urine was negative.

6.2.33. If anything oedema was more marked. Blood chemistry:- Total protein 4.84, albumin 1.60, globulin 3.24 gm. per cent. Calculated oncotic pressure 13.3 mm. Hg.. Non-protein nitrogen 50.0 mgm. per cent..

12.2.33. For past few days the motions had been loose and diarrhoea was now severe.

14.2.33. Child became very drowsy and took several convulsions. Lumbar puncture was performed and 25 c.c. of clear fluid under increased pressure were removed. Cell count six per c.mm. Pandy's test negative. The child died 6 hours later.

At autopsy marked oedema of the brain was present. No evidence of congenital syphilis was found. Areas of intense congestion in the bowel. The kidneys were swollen and the capsule slightly adherent. Histologically subacute nephritis was present with well-marked tubular involvement and extensive proliferation of the interstitial tissue with foci of round-cell infiltration.

CASE 189. A girl aged 7 months. Three weeks before admission swelling of the face was observed and of the abdomen 2 weeks later.

23.6.31. On admission moderate generalized oedema was present with slight ascites. The urine contained much albumin but no gross blood. Culture was negative.

24.6.31. Acute gastro-enteritis present.

27.6.31. The child died, no oedema being present.

Autopsy showed the presence of broncho-pneumonia and acute nephritis. No evidence of congenital syphilis was present.

CASE 190. A boy aged 1 year. Two weeks before admission oedema was observed.

26.10.31. On admission oedema was very marked and ascites was present. The fundi were normal and the systolic blood pressure was 98 mm. Hg.. In the urine much albumin and blood were found. Culture of the urine was negative. Blood chemistry:- Total protein 4.23, albumin 1.96, globulin 2.27 gm. per cent.. Calculated oncotic pressure 13.9 mm. Hg.. Non-protein nitrogen 36.3 mgm. per cent..

27.10.31. Acute enteritis present.

1.11.31. Oedema was much less marked. Child died. Autopsy refused.

CASE 191. A boy aged 1 year and 4 months. He throve on cow's milk and light diet till 4 weeks before admission when he went "off colour." Two weeks later oedema of the face was noted.

7.9.33. On admission oedema was general and ascites was present. The urine contained much albumin but blood was present in only microscopic amount. The systolic blood pressure was 100 mm. Hg.. No abnormality was detected in the fundi. The Wassermann reaction was negative.

10.9.33. Urine culture was sterile.

15.9.33. Dismissed with condition unchanged.

26.9.33. Gastro-enteritis present. No oedema.

1.10.33. Motions normal. No oedema. Albuminuria was still marked.

29.10.33. Albuminuria much less.

26.11.33. Urine clear.

15.5.33. Urine clear. Child was very well.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%
8.9.32	4.51	2.92	1.59	18.3	28.5
14.9.32	5.63	2.25	3.38	17.1	35.7
15.5.33	7.31	5.32	1.99	31.8	31.8

CASE 192. A boy aged 1 year and 4 months. On 18.3.32 the baby was admitted to the Royal Hospital for Sick Children suffering from convulsions. A diagnosis of?encephalitis was made. At that time the urine was clear and the Wassermann reaction of blood and cerebrospinal fluid was negative. He was discharged with a right-sided hemiplegia on 25.6.32. Two months later, a week before readmission, oedema of the legs was observed and the urine was thought to be dark.

29.8.32. On admission oedema was general and ascites was present. The urine contained much blood and albumin. No observations were made on the blood pressure or fundi.

31.8.32. Blood chemistry:- Total protein 4.54 gm. per cent.. Non-protein nitrogen 24.1 mgm. per cent..

7.9.32. Condition unchanged. Ammonium chloride gr. 15 five times a day begun.

14.9.32. Vomiting frequent.

17.9.32. Ammonium chloride stopped because of the vomiting. Oedema was now considerably less.

20.9.32. Oedema again marked. No further vomiting since ammonium chloride was omitted.

9.10.32. High fever.

18.10.32. Temperature normal since left ear began to discharge on the previous day. Oedema less.

8.11.32. No oedema.

10.12.32. Oedema again present.

20.12.32. No oedema. The child was now much better and no gross haematuria was observed from this date.

8.2.33. Dismissed from hospital. Much albumin was present in the urine but haematuria was microscopic only. There was no oedema.

6.6.33. The urine contained a trace of albumin but no red cells were seen. Blood chemistry:- Total protein 9.95, albumin 5.83, globulin 4.12 gm. per cent.. Calculated oncotic pressure 37.8 mm. Hg.. Non-protein nitrogen 25.0 mgm. per cent.. A severe cough was present which subsequently was found to be whooping cough. It was also apparent that mentally defective to a degree. he was

CASE 193. A boy aged 9 months. A week before admission swelling of the face was observed which spread gradually over the whole body.

18.2.33. On admission there was very marked oedema with ascites. In spite of this he did not seem acutely ill and there was no fever. The urine contained much blood and albumin. No examination of the fundi was made. The Wassermann reaction was negative.

19.2.33. A high protein diet - 68 gm. daily - was instituted.

5.3.33. Oedema increasing slightly.

13.3.33. Marked diuresis began.

15.3.33. Scrotum very inflamed. Temperature 103°F.

19.2.33. High protein diet stopped. Half-milk given - 16 gm. protein daily.

29.3.33. Definite abscesses present in both testicles. No gross haematuria was observed after this date.

1.4.33. Abscesses discharging pus.

10.4.33. No oedema. Albuminuria was much less.

15.4.33. Abscesses healed. Albumin in the urine was now but a trace.

25.9.33. The urine was quite clear and the child seemed to be well.

7.2.34. Urine clear.

Blood chemistry.

Date	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure mm.Hg.	N.P.N. mgm.%
19.2.33	3.67	1.80	1.87	12.5	28.0
27.2.33	4.24	1.80	2.44	13.3	27.0
13.3.33	3.92	2.38	1.54	15.2	27.2
22.3.33	4.34	2.19	2.15	15.0	20.0
24.3.33	6.22	2.16	4.05	17.5	25.3
29.3.33	6.78	2.24	4.54	18.7	25.0
10.4.33	5.83	2.93	2.89	20.2	41.6
13.4.33	5.86	3.54	2.32	22.7	37.0
25.9.33	6.99	4.18	2.81	26.9	27.0

CASE 194. A boy aged 6 months. Following an attack of enteritis, one week before admission oedema was noticed.

16.6.31. On admission oedema was marked and ascites was present. The urine contained much blood and albumin (11 gm. per litre). Culture was negative. The systolic blood pressure was 85 mm. Hg. and the fundi showed no abnormality. Blood chemistry:- Total protein 4.09, albumin 1.63, globulin 2.46 gm. per cent.. Calculated oncotic pressure 12.4 mm. Hg.. Non-protein nitrogen 27.5 mgm. per cent.. Serum calcium 5.4 mgm. per cent..

24.6.31. Enteritis, which was present on admission, became progressively worse and was associated with very frequent vomiting. Oedema was quite gone and dehydration present at death.

Autopsy:- Acute nephritis. No evidence of congenital syphilis was found.

CASE 195. A boy aged 1 year and 1 month. Fifteen days before admission the face became puffy and the urine dark. Since then oedema became general.

4.4.34. On admission oedema was very marked and general: ascites was present. The urine contained much blood and albumin. No examination of the fundi was made. The Wassermann reaction was negative. A protein intake of 40.0 gm. daily was given.

6.4.34. Oedema was unaltered.

30.4.34. Blood and albumin were still present in large amount and the oedema was unchanged. On this date an extensive cellulitis of the thighs and abdomen appeared with high fever.

1.5.34. Child died. Permission for an autopsy was refused.

Blood chemistry.

Date.	Total Protein gm.%	Albumin gm.%	Globulin gm.%	Calculated Oncotic Pressure. mm.Hg.	N.P.N. mgm.%
6.4.34.	4.32	2.46	1.86	16.1	65.2
11.4.34	4.91	2.52	2.39	17.2	39.9
1.5.34	4.27	1.39	2.88	11.7	29.2

CASE 196. A man aged 22 years. Six months before the sample of blood was received there was a rather insidious onset of oedema without any gross haematuria. At time of observation oedema was extreme; there was no elevation of blood pressure: the urine was free of blood but albuminuria was very profuse. Blood chemistry:- Total protein 2.99, albumin 1.76, globulin 1.23 gm. per cent.. Non-protein nitrogen 40.0 mgm. per cent. The course of this case is not known.