indeed it would be difficult to have imagined him as angry or impatient.

Fuchs leaves behind him not only a store of most valuable scientific work, but also the example of a fine character and of one who hungered and thirsted after truth.

E.T.C.

RETINITIS NEPHRITICA OR ALBUMINURICA

BY

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"Ceterum censeo ophthalmoscopum quotidie usendum esse."

This paper is the third and last part of one chain of clinical investigation. All the work is the outcome of general practice where the ophthalmoscope was used merely as a means of thorough clinical examination, limited by the comparatively simple resources of routine surgery-work and by the necessity of regarding my retinal findings as a part of the clinical whole. This work is, therefore, as much an essay in general medicine as in ophthalmology and its chief value, if any, lies in demonstrating the importance of an early ophthalmoscopic examination. As an instance it is sufficient to point out the books of Fisher on oedema and McDonagh on the nature of the disease where the ophthalmoscopic examination is wholly omitted. The same applies to many of the cases quoted in D. Russell's remarkable book on Classification of Bright's Disease.

In the special ophthalmological literature up to the present day there still exists a very wide divergence of views on retinitis albuminurica. Putting aside purely pathological or anatomical treatises it will be sufficient to quote the opinions of only a few recognized authorities. In Fuchs' well-known text-book there is no difference between the eleventh and seventeenth editions; in both of them this learned writer considers that "the severity of retinitis albuminurica bears no fixed proportion to the intensity of the kidney disease nor to the amount of albumin in the urine ...... The like is true of the subsequent course; the retinitis may improve, while the kidney lesion grows worse and vice versa ......" Fuchs believes that every form of nephritis, which is accompanied by albuminuria, may be complicated by retinitis albuminurica. Fox, in his text-book, expresses a similar view. Leber, in the Graefe-Saemisch handbook, holds a different view. On page 817, Vol. VII,
he writes that the retinal changes can regress if the basal pathological process in the kidney is healed or improved; in favourable cases even highly advanced retinal changes can regress completely. But though Leber admits the dependence of retinitis on the kidney, he also holds that retinitis albuminurica apoplectica (haemorrhagic retinitis) is most probably connected primarily not with the kidney, but with the vascular system (p. 825). Poulard expresses the opinion that the appearance and prognosis of retinitis is closely connected with the impairment of the function of the kidney as shown by bio-chemical tests. Duke-Elder believes that most probably the aetiology of retinitis albuminurica, diabetica and sclerotica is the same for all of them. For Fox retinitis albuminurica is essentially arteriosclerosis of the smaller and, when advanced, of the larger retinal vessels. Lachmann (Medizin. Welt., Vol. XXXVIII, 1929) thinks that albuminuric retinitis is often the first warning sign of renal disease, but the latter need not necessarily be severe.

My own conclusions are reached on purely clinical observations, only one of my cases having been verified by an operation and a post-mortem examination. This alone makes my exploration of the subject necessarily incomplete, but it still affords an opportunity of discussing many general pathological problems.

The regulation of urinary secretion, roughly speaking, depends on:

1. The chemical composition of the blood which is brought to the vascular tree of the nephron. This alone can produce locally an arterial spasm.

2. The height of the blood pressure and the velocity of the blood circulation, with all their causative factors (central and peripheral heart, elimination of CO₂ from the blood, etc.)

3. The central nervous system through vasomotor, reflex and psychic stimuli; special centres concerned with renal secretion (Hall).

4. The endocrine glands—the most obscure branch of medical knowledge; but diabetes mellitus is a good example of this factor.

5. Local metabolism of the kidney cells, be it increased acidity, alkalinity or otherwise. This is probably the most important factor of all, but extremely difficult to determine in our present state of knowledge.

**Nephritis**

In disease the different parts of the kidney may be attacked—in most cases they are all more or less involved—and this makes the classification and differentiation of the various forms of nephritis
RETINITIS NEPHRITICA OR ALBUMINURICA

extremely difficult. The old classification based chiefly upon the morphological and microscopical aspects of the organ, as seen in the post-mortem room, did not pay sufficient attention to clinical observations, and the attempt to correlate it with the findings of modern bio-chemistry failed. It is more important for the clinician to realize to what extent the efficiency of the kidney is damaged and what part of the whole clinical picture should be attributed to it, than to try and guess what may be the histological state of the organ. When a decapsulation was being performed on a kidney of one of my patients, the surgeon asked the two physicians present the size of the kidney. "Contracted, most probably" one replied; "fairly normal" was the opinion of the other. "It is enlarged, gentlemen!" answered the surgeon, delivering the kidney from the wound and starting the decapsulation. And yet both physicians knew perfectly well all the clinical features of this exceptional case.

"Nephrosis" is the name given to the disease of the tubular or proper kidney cells only. In this country some authorities object to this term; in their opinion nephrosis is simply a form of parenchymatous nephritis. On the Continent and in the United States of America this name is commonly used as distinct from nephritis. Moorhead prefers the term "toxic" kidney to the term "nephrosis" and he is correct from the aetiological point of view. Most authorities state definitely that the cause of this disease is extra-renal; that it does not originate in the kidney, but that some toxic factor attacks all the tissues of the body and that of the kidney as well. (See for instance, "Nephrosis in Children," by Gladys Boyd). Clinically nephrosis is characterized by a marked tendency of the tissues to become oedematous, the cardiac activity usually being unimpaired, the blood pressure normal but the urine shows enormous quantities of albumin, waxy casts, epithelial elements, lipoids or fats and the absence of erythrocytes; the specific gravity is high; and there is oliguria, with diminished chloride content; the alkaline reserve of the blood is very high. It is a disease of the whole organism in which, clinically, the kidneys play an entirely subordinate rôle. It is important to note for the purpose of this paper that in this rare disease three phenomena are never present—erythrocytes in the urine, arterial hypertension and retinitis. There is no disturbance in the nitrogenous metabolism and the oxidation process in the tissues is normal as witnessed by the normal blood urea. The basal metabolism is frequently reduced. In the initial stage ascites and hydrothorax are very marked, but they disappear later. In Schlayer's opinion, oedema following an infectious disease, associated with a haemorrhagic exacerbation in the urine, vascular changes in the fundi oculorum, arterial hypertension with the urea excretion diminished—all these are in favour
of a nephrosis with a "nephrotic" character or chronic glomerulonephritis. Saxl, of Vienna, very definitely states that in nephrosis there is no hypertonia and that the latter appears only with the vascular lesions of nephritis or of nephrosclerosis; as a matter of fact a contracted kidney can develop from pure nephrosis. There is no retinitis so long as the kidney is not contracted, and no tendency to the retention of nitrogen (azotaemic uraemia). Neither are eclamptic attacks (convulsive uraemia) observed because the blood pressure is normal. Histologically the kidney usually shews intact glomeruli and severe fatty, albuminoid or amyloid degeneration of the tubular cells, which contain a lipid, doubly refracting substance. The kidney is enlarged, soft and of a white or yellow appearance. It corresponds to what is called the large white kidney, or to the old name of parenchymatous nephritis. Some authors think that the excretion of urine may be insufficient and thus is caused an occasional attack of diarrhoea (similar to that of amyloidosis), but Schlayer states that usually an increased quantity of urine is passed by the nephrotic kidney. The prognosis is, as a rule, not very unfavourable, the disease generally lasting for years and the chief danger being a secondary infection, because the general defensive apparatus of the body is impaired. Recovery is possible. In Munk's opinion, the prognosis is usually favourable if there are no signs of glomerulo-nephritis (arterial hypertension, retention of nitrogen, erythrocytes in the urine). These are the characteristic signs of a pure nephrosis. But very often "nephrotic" appearances accompany other diseases and then the diagnosis becomes difficult. The albuminuria of fever means an albuminoid degeneration of the tubules—is it a nephrosis or a mild form of nephritis? The same applies to syphilis, especially in the secondary stage. Intoxications may lead to nephrosis and to chronic glomerulo-nephritis. The case of a diabetic patient is ever more striking—is albuminuria here an early sign of a commencing chronic glomerulo-nephritis (as is usually thought) or of nephrosclerosis or is it only nephrosis? Estimation of the blood sugar does not help. Even the sphygmomanometer may not be very useful, as diabetes per se may be accompanied by vascular disease and, moreover, if the myocardium be impaired, it cannot produce a very high systolic pressure. Here again the ophthalmoscope, if used carefully, frequently and in a proper manner, may help in the diagnosis, as pointed out in my previous papers. The same applies to the albuminuria of pregnancy.

Osler points out the important fact that the glomeruli and tubules may temporarily substitute one another in their action to a certain degree, but the tubular cells, not used to the "high speed and pressure" of the glomeruli, will suffer considerably. The more so because the tubular cells are supplied by the afferent artery
of the glomerulus and any toxins affecting the latter will affect the former also. If we add to this a possible damage from the toxins that pass through the glomeruli and travel down the tubules we shall readily understand how early "nephrosis" may accompany the other forms of nephritis. Such may be the case in glomerulonephritis. A patient may be seen with hypertension, haematuria, retinitis, a tendency to uraemia—all signs of glomerulonephritis. But his urine may be saturated with protein and his body may be markedly oedematous. If the Fates are benevolent, the haematuria will disappear, as will also the tendency to uraemia. The blood pressure may become nearly normal, but the retinal changes, even if regressed, will remain as a silent and permanent witness of a vicious vascular past. The urine may remain very dark in colour and contain large quantities of protein and lipoid, and oedema of the body will persist—the nephrosis has not disappeared. Even pure vascular disease of the kidney vessels, such as arteriosclerosis and atheroma, according to some writers may lead to nephrosis by interfering with the nutrition of the tubular epithelium.

It will take us far away from the theme of this paper if we describe or discuss the many other features of nephrosis; but some important points are already clear. Fisher considers that every albuminuria means a loss of kidney substance. The patient would soon succumb, as the kidneys are not very voluminous organs, if later on the albumin were not supplied by the damaged glomeruli and ruptured kidney vessels. But the latter source means the appearance of erythrocytes in the urine and their absence is characteristic of nephrosis. The course of nephrosis is a very prolonged one—eo ipse the albumin is not the result of a loss of kidney substance. The same objection—absence of erythrocytes in the urine of a nephrotic—applies to the filtration theory of urine, which always presupposes damage to the glomeruli in every case of albuminuria. Albumin in the urine may be present in an enormous amount as the result of a pathological metabolism of the tubular cells, produced by an extrarenal cause, without occasioning death of these cells, without arterial hypertension and without producing retinitis albuminurica.

In acute nephritis all the elements of the kidney are most probably involved, but any one of them may be more seriously affected than the others. In haemorrhagic nephritis we have a more benign form of the disease; it commences without oedema, which if present, only occurs late; arterial hypertension and hypertrophy of the heart are seldom observed; retinitis albuminurica is extremely rare, but if it be present the prognosis is very serious indeed. Haematuria remains the chief symptom, and transition to chronic glomerulo-nephritis seldom occurs. In the majority of
cases the cause of the disease is in the tonsils, nasal accessory sinuses, etc. The second form—acute oedematous nephritis is much more serious. The heart is usually affected and the blood pressure increased. The prognosis and treatment depend on careful clinical observation, paying special attention to the heart, blood pressure and fundus oculi (Schlayer). Retinitis albuminurica may be seen and, if present, makes the prognosis very gloomy. Isaac thinks that the dyspnoea, oedema, increase of blood pressure, scanty diuresis and the inclination to convulsions are due more to the disturbance of the circulation than to the kidney itself. Eppinger thinks that hypertonia and oedema (especially hydrothorax, as demonstrated by X-rays) may occur even before albuminuria is evident. An increase of blood pressure was at one time regarded as almost certain evidence of old-standing nephritis. It is now, however, universally recognized that even in primary acute attacks of every variety of nephritis the blood pressure may rise rapidly (Moorhead). The reader will see later that this point is still not settled in regard to the kidney of pregnancy. It is important for us to note that in acute nephritis retinitis albuminurica is fortunately very rare and is always preceded by arterial hypertension and other signs of serious damage to the glomeruli and to the general cardio-vascular system.

In the great majority of cases acute nephritis subsides and the kidney recovers, but in other cases the latter becomes chronically affected, the disease spreading slowly and insidiously, involving one nephron after another, crippling them or putting them out of action. Volhard ingeniously explained the difference by the degree of impairment of the blood supply to the glomeruli. And may I suggest that one of the causes may be the same collapse of the artery, a result of an oedematous perivascularis as seen on the retina? If the tubular elements are chiefly involved, the patient will suffer from chronic parenchymatous nephritis with considerable albuminuria and normal or moderately raised blood pressure. The heart will be involved and will suffer from myocarditis, or if hyperpiesis be present, from hypertrophy and enlargement. Retinal changes may be present or absent; if present, this will be in a patient with hyperpiesis and the prognosis will be bad. The blood urea may be normal for a long time and become increased only later, in the terminal stage. Oedema of the tissues is usually definitely marked and the excretion of sodium chloride by the kidney may be impaired. This form of nephritis is the "chlorure" or "hydraemic" type of Widal and other French authors. If the glomerular involvement is the greater we have the "azotaemic" type of Bright's disease, with traces of albuminuria, no oedema of the tissues, elevated blood pressures, hypertrophy of the heart and retinal changes. The blood urea is raised, and dyes and, of
course, urea are badly excreted by the kidneys. In a very interesting paper on chronic nephritis in childhood (Brit. Med. J., Aug., 1928), Spence stated that retinitis occurred in cases with high blood pressure. Very rarely does one see such a case of primary arteriosclerosis with secondary contraction of the kidney as occurred in a child of ten with a systolic blood pressure of 220 mm.; renal efficiency tests were normal, but so-called uraemic symptoms occurred, such as transient amaurosis and monoplegia of the left arm, which, in the presence of albuminuria and retinitis, were regarded as uraemic, although they were more likely due to a cerebral vascular disturbance. In all the cases of chronic interstitial nephritis with normal or low blood pressure retinitis was absent, and Spence concluded that when it did occur retinitis was a manifestation of hypertension or vascular disease. Davies saw many case of uraemia in children: even when very ill these children maintained an alert mental condition. The blood pressure was not raised and absence of eye-signs was the rule. Remarkably high blood urea, 300 mg. per 100 c.c., was noted.

The kidney may be the seat of a vascular disease that has attacked all the organs of the body, e.g., the angio-fibrosis of Sutton, the involutionary arterio-sclerosis of Allbutt, etc. It will also be involved in essential hyperpiesis, called "vascular disease" by many authors. Involutionary arterio-sclerosis implies only a limitation of function that occurs pari passu with the same process throughout the body; the kidney is, therefore, quite capable of serving the organism's needs and no danger to life exists from that circumstance. The bio-chemical tests are usually normal. The kidney changes are only slightly progressive and in view of the reduced metabolism the patient does not reach the stage of renal insufficiency. In the benign form of essential hyperpiesis the renal vessels are also attacked, and I agree with Lewandowsky and others when they suggest that a permanent systolic blood pressure of over 200 mm. means a wide-spread sclerosis of the kidney (nephro-sclerosis) or ischaemic nephritis (D. Russell). The glomeruli may be moderately involved or be only partly out of action and a sufficient number remains to give satisfactory bio-chemical tests and enable one to carry on for many years. The sclerosis may involve chiefly the afferent arteries and the glomeruli will suffer secondarily and not primarily. In years, if this process advances and an insufficient portion of the kidney is left for action, the patient will reach the stage of renal insufficiency—"malignant nephrosclerosis." Essential hyperpiesis may be malignant from the onset and then it means a rapid progress of the disease; the expectation of life may be reduced to five or six years, and in the end the clinical picture will be identical with the terminal stage of true interstitial nephritis. In spite of
relatively good results from bio-chemical renal tests we have to watch the cardio-vascular system very carefully in both forms. One cannot agree with the opinion of D. Russell, that primary ischaemic nephritis never interferes with renal function. It may lead to albuminuric retinitis and it was so in her own case No. 28.

In "uraemic conditions" Volhard and many other authorities distinguish two different pathological agencies—vascular disease and renal insufficiency. If both kidneys are excised from an animal, the latter preserves until the end mental alertness, good vision and complete consciousness. The same phenomena have been mentioned previously when describing nephritis in children. The animal dies from gradual wasting and weakness, vomiting, etc. Experimental injections into animals of large quantities of urea failed to produce a state of uraemia, and many authors believe that urea per se is most probably a quite innocuous substance. Generally speaking not one of the chemical substances that are employed clinically for renal efficiency tests has been proved to be the cause of uraemia. The convulsions, the cerebral disturbance, the diseased heart are all, in Volhard’s opinion, the result of vascular disease. Fisher goes much further than this. On page 883 he writes: "It is not the kidney disease that leads to the high blood pressure, cardiac hypertrophy, etc., but it is the vascular disease, which when it happens to affect the kidney gives rise to albumin and casts." The high blood pressure, cardiac hypertrophy, etc., so frequently observed with this type of chronic interstitial nephritis are not the consequence of the kidney disease, but expression of the vascular disease here held responsible for the kidney lesion ....... Blood vessel disease, high blood pressure and cardiac hypertrophy are not secondary to loss of kidney function " (p. 24). The first sign of impaired renal function is given by a simultaneous rise in the urea and sodium chloride in the blood as well as of the systolic blood pressure, and it is only when the renal lesion has become more or less pronounced that it is detected by examination of the urine and general condition. (Brasiello).

Blacklock and MacDonald in their paper on blackwater fever conclude that in this disease a state of anoxaemia is present, which causes an increase of sarcolactic acid either locally or generally. "We produce evidence from experiments, both in vitro and in vivo, that sarcolactic acid is haemolytic ...... to whole human blood ...... The sarcolactic acid is the causal agent in the production of the haemolysis in blackwater fever and these haemoglobinurias." Moreover it is quite a common occurrence to find albuminuria, casts and even occasional erythrocytes in the urine after strenuous muscular exercise. The brain in the living animal produces lactic acid very rapidly from some precursor, so rapidly that, when all possible haste is made in killing, exciting, and fixing the tissue
only a very little extra lactic acid can subsequently be formed in vitro, unless glucose be supplied artificially." (Holmes).

McLean says: "The increased blood pressure of the acute disease is almost invariably present when oedema is well marked and it quickly returns to a normal or even an unusual low level with subsidence of the oedema" (p. 187). "Hydremia ..... is closely connected with the rise of blood pressure." Although in the account of his cases McLean does not give a description of their fundi (this, in my opinion, considerably diminishes their clinical value), he says on page 27: "There is a constant amount of evidence pointing to the conclusion that these eye changes are connected with the raised blood pressure." "Speaking very broadly, it may be taken for granted that in chronic renal disease, the more serious the renal damage, the higher the blood pressure and the greater the cardio-vascular involvement" (p. 75). "Arterio-sclerosis in a patient with comparatively active kidneys is often not so hopeless as it would be if the kidney were badly involved, and it is now generally admitted by those who have carefully studied the subject that arterio-sclerosis may sometimes be present without the kidneys being much, if at all, involved." A perfectly true sentence, which is difficult to understand, because McLean uses the vague term of arterio-sclerosis. If he means "involuntary arterio-sclerosis" or "athero-sclerosis," he is correct; if "essential hyperpiesis" he is wrong. "Extensive renal disease may exist with little or no increase of blood pressure ..... arterio-sclerosis may be present without much renal involvement."

Elwyn in his "Nephritis" states that in the senile kidney the renal artery is sclerotic; in hyperpiesis the primary cause of the changes in the kidney is the sclerosis of the arterioles of the kidney. In nephrosis the tubules are involved, but the blood pressure is not raised and no eye changes are met with. Diminution of kidney efficiency is usually combined with a rise of blood pressure. The hypertrophy of the heart is the result of the raised blood pressure. Osler describes the microscopic findings in chronic interstitial nephritis as a general increase in the fibrous tissue, thickening of the vessel walls, destruction of the glomeruli and more or less marked degeneration of the renal epithelium. "The glomerular lesion, however, is not necessarily primary. The more correct conception is to regard the process as from the first more or less diffuse, and to look upon a change in one part as necessarily leading to a change in another, often in the manner of a vicious circle." (p. 896). "An endarteritis or even mesarteritis can usually be made out ..... the smaller intertubular vessels are specially involved and are often entirely obliterated ..... The sclerosis is sometimes patchy, even in the individual artery, one portion of the circum-
ference shewing an extreme lesion, while the remainder of the ring is nearly normal." "Exceptionally typical contracted kidney has been found unaccompanied by arterio-sclerosis, or cardiac hypertrophy. Roth reports six such cases. Death was generally from uraemia. In most of the cases blood pressure had been low" (p. 899). He does not mention the importance of the diastolic blood pressure. The secretion of water by the kidneys depends in his opinion on the rapidity of the flow of blood through the renal vessels; this may or may not be influenced by a rise or fall of the blood pressure. The local activity of the vasomotors in the kidney vessels is much more important. "The tubular cell is prompt to suffer from the effects of even transitory toxicity of the blood and lymph (p. 772) ..... The toxicity, which is sufficient to kill a tubule cell, only irritates the interstitial tissue—the cell perishes and its work is thrown on to the other cells; the interstitial tissue grows under the double influence of the toxin and the empty space left by the cell."

Stevens divides nephritis into three groups. The first—tubular nephritis; the second—inflammation and degeneration in and around the Malpighian bodies; and the third—increase of the fibrous connective tissue around the glomeruli and between the tubules and sclerosis of the small blood vessels (renal sclerosis). "Renal sclerosis is always an end stage of some earlier process affecting the kidneys." "In chronic glomerular nephritis the blood pressure is usually almost invariably increased, a systolic pressure of 200 to 250 (Osler's figure starts from 170) and a diastolic figure of 120 to 160 being not unusual."

Lyon recognizes four types of nephritis:

(1) Simple albuminuric nephritis without any oedema, cardiovascular changes or "uraemic" symptoms. The albuminuria is not influenced by rest or dieting. The prognosis is favourable because the evolution of the disease is very prolonged.

(2) Chronic hydraemic nephritis. The urine is scanty and concentrated. Oedema of the tissues is present. Sodium chloride is not excreted by the kidney, but is retained in the tissues. The water is retained by the tissues to dissolve this sodium chloride. This is the cause of the oedema. This form of nephritis is apt to be complicated by nitrogen retention.

(3) Uraemigenic nephritis. The blood urea is raised. "L'azotémie se traduit par les troubles nerveux, surtout cérébraux, et par les troubles gastro-intestinaux."

The nervous features include fatigue, torpor, headache and retinitis albuminurica, the gastro-intestinal disorders, intense anaemia and loss of flesh.
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(4) Nephritis with arterial hypertension, the blood pressure being extremely raised (he mentions only the systolic, omitting the diastolic) and cardiac hypertrophy. Albuminuria is only slight or absent. The blood urea is not raised. There is no retention of chlorides. The patients are subject to haemorrhages including epistaxis and retinal haemorrhages.

From this imperfect review of the observations of a few modern authorities, necessarily incomplete because it is adapted only to the subject matter of this paper, the reader will realize that there is no uniformity of opinion about the physiology and pathology of the kidney and, moreover, that the opinions on some vital points are contradictory. See also page 14 in H. French's book. So far as retinitis albuminurica is concerned, I believe that an analysis of my cases will help to some extent to bring order out of the present chaos, and it may probably throw light upon some doubtful points of general significance. Further work is needed, in D. Russell's opinion, to determine what other clinical criteria can help to separate primary ischaemic nephritis from the latent stage of nephritis repens. And it is my deep conviction that the ophthalmoscope may be the ultimate judge in this difficult problem.

Retinal Oedema

The general view is that oedema of the tissues is of extra-renal origin. Such, for instance, is the view of McLean and of Bennett. It is held that toxins damage the metabolism of the cells, causing water to be retained by the tissues. Our ignorance of the functions of the so-called interstitial tissue prevents us from understanding why the fluid collects in the different parts of the body in certain varieties of oedema. We still do not possess a theory that would solve all the difficulties of this thorny problem. It seems to me that Fisher comes nearer than anybody else to the correct solution. By very ingenious experiments he excluded the influence of the blood circulation. For instance, he placed a ligature over the knee of a frog and tied it sufficiently to stop the arterial and venous circulation. The other leg was left intact. The frog was put into distilled water sufficient to cover both legs and the ligatured leg with time swelled enormously, but the other did not. The explanation according to Fisher lies in the fact that the colloids become acid very quickly after their supply of oxygen is cut off. Being more acid the colloids absorb water and become oedematous. If the frog is put into a dry vessel the ligatured leg does not swell; it mummifies with time. The same explanation applies to the swelling of dead animals or of individual organs when separated from the body. Fisher thinks that the cause of the acidity is CO₂, which is the result of cell metabolism. At its arterial end the cell
receives nutritious material and oxygen and the formed CO₂ is washed away at the venous end of the cell by the lymph or blood. Modern investigators tacitly admit the truth of this theory, but they add other acids, especially lactic acid, to the CO₂. "In pneumonia there are two things wrong with the patient, a general toxaemia and the local changes in the lungs. Usually the toxaemia is the cause of death, and the oxygen seems to do good by neutralizing the effects of the toxaemia as well as possibly by its action on the micro-organisms. Toxaemia kills by producing anoxaemia, with reduction of the alkalinity of the blood, and the condition of acidosis is produced .... The kidney and liver, the organs apparently responsible for maintaining the proper alkalinity of the blood, may both be upset." (Kirk, Brit. Med. Jl., Aug., 1928). In my opinion, the above theory of Fisher taken along with what we know from Pal about vascular spasm is the best explanation of what is seen in the retina when there is an interference with its oxygen supply. All the brain tissue and, therefore, the retina "uses a considerable amount of oxygen and its metabolism must be of considerable magnitude. Lactic acid is formed by the brain tissue and this so rapidly that it is extremely difficult to eliminate it when preparing tissue for microscopical examination." (Eric Holmes, Brit. Med. Jl., Sept., 1928). Menzies ascribes to anoxaemia of toxic origin the explanation of many problems of psychiatric pathology. This by itself is a sufficient explanation of what we see ophthalmoscopically in the living retina. Fisher entirely ignores the backward pressure of the blood circulation and, in my opinion, he is wrong in this minor detail.

As an illustration of the onset of retinal oedema as the result of local metabolic disturbances, cases of embolism or of sudden thrombosis of the central retinal artery or one of its branches, serve well. In such cases larger arteries can still be seen as very narrow lines; the smaller ones disappear entirely. Later, within a few days or weeks, the arteries can again be seen and the retina is once more transparent. I had an opportunity of examining a patient a few hours after he had suddenly become hemianopic in the right eye as a result of thrombosis of the upper branch of the retinal artery. I knew the appearance of his fundus before. I could see all his arteries, even the smaller ones, but they were covered with white sheaths of oedematous perivascular membrane. He did not present the well-known areas of retinal exudation, so characteristic of retinitis albuminurica; the retina was uniformly oedematous, but the vessels were sharply differentiated as swollen and whitish lines. The blood stream in them, although diminished, was not completely interrupted. Many of the arteries were free, and a few of them well covered in certain parts. That it was a transitory interference with the arterial circulation was evident
from the fact that I could see the blood stream in the artery immediately after the attack and later on as well. It was sufficient to cause irreparable damage to the function of the cells of the retina, as witnessed by permanent blindness, but not powerful enough to cause severe degeneration with scarring. The retina was absolutely transparent three months later. Sometimes, after an exudation or a haemorrhage disappears, an area of atrophy is left as witnessed by a whitish colour. But the oedema of the retina seen in such cases of vascular disturbance, was not confined to a localized area, nor did it cover the retinal vessels; the latter were concealed only by their oedematous perivascular sheaths. As the blood supply was interrupted or considerably diminished, it is difficult to explain the resulting oedema otherwise than by increased acidosis of the retinal cells with retention by them of water and possibly different salts, and, consequently, with impediment of the back-flow of lymph in the perivascular channels.

In contrast to the exudates associated with oedema that are seen in albuminuric retinitis there is the fundus of retinal sclerosis. Here the characteristic feature is the absence of noticeable oedema. Apart from haemorrhages one often sees a small area of sharply defined bluish-white exudation. It is usually situated not very far from a vessel, sometimes even adjoining it. The colour differs from the "fat" colour of an albuminuric exudation. The surface is always flat—it seems to be on the same level as the retina; the albuminuric type sometimes looks prominent or elevated. The most important feature is that its edge is sharply limited; there is no oedema, no gradual transition into the surrounding retina as is the case with an albuminuric exudation. A vessel crossing such a sclerotic fundus will be clearly seen, sharply outlined, not oedematous and not covered by a veil. Sometimes in a very advanced exudation which leads to a scar in the retina the vessel, especially a vein, will be narrowed at this place, but will still be clearly seen—in my opinion, the best proof that it is the perivascular channel which is involved in the scarring originating from below the vessel. Careful attention must be paid to local perivasculitis, as I described elsewhere. (It may be advisable to mention here that even a normal retinal artery may shew a slight constriction of the lumen in some parts, especially on the disc. This phenomenon is not described till now and I would warn against considering those physiological local constrictions of the vessels as being pathological. In a few cases I saw one of the large arteries become gradually narrower from the periphery of the disc towards its centre exactly in the same way, as veins show this appearance). I have seen whole branches of the central artery such as the inferior temporal artery remain unchanged on the surface of a wide exudation that quickly led to scarring of the
retina. This was accompanied by chorio-retinitis, as witnessed by pigmentation which appeared later around each spot. The form of this sclerotic exudation is, as a rule, irregular. This distinguishes it from sclerotic chorio-retinitis, which forms small, round, more or less uniform spots all over the retina. In a few cases I have observed a very remarkable picture. The irregular area of exudation was surrounded at the periphery by comma-like new vessels. Were they newly-formed vessels or capillaries distended by the *vis a tergo*? It is difficult to decide. Most probably they are newly-formed vessels for one can follow their development almost day by day. In a patient whose fundus is represented in illustration No. 23 (see "Sclerotic retinal vessels") it took me six weeks to decide whether I saw new-formed vessels or a haemorrhage. After seven weeks from its first appearance the exudation was smaller and a definite vascular ring was formed around it. Two weeks afterwards this ring started to contract and advance and eleven weeks after its appearance this exudation disappeared without leaving any trace.

This sclerotic exudation appears in advanced cases and may be quite independent of the height of even the diastolic blood pressure; it may be absent when the latter is at its maximum and appear when it has dropped a good deal. I did not see it in mild cases, the systolic blood pressure always being 200 or more, the diastolic 100 or more when the patients were *first* seen. The retinal vessels were always in an advanced state of sclerosis. This exudation may remain stable for weeks or even months and yet disappear without leaving a scar or any other trace in the majority of cases. In a minority, a whitish spot is left permanently and later this may become surrounded by pigmentation, a sign of a corresponding chorio-retinitis. It also forms whole fields of white atrophic areas sometimes closely resembling in their direction the course of retinal vessels, but one can never see any vessels. This exudation is, in my opinion, the result of insufficient oxygenation of the retinal cells. It does not mean an actual and permanent blockage of the capillaries and arterioles, for then it would not disappear and would lead to scarring. Most probably it means a combination of perivasculitis, endarteritis and actual constriction or spasm of the fine vessels—the same process that I discussed at length when describing the "silver-wire" artery. I say "most probably" because this is purely a microscopical problem and I am concerned here only with the ophthalmoscopic picture. It is possible that the retinal vessels are independent of the "selfishness" of the respiratory and vasomotor centres, which will constrict all other vessels of the body to a maximum to have their own free supply of oxygen and blood. Therefore, the spasm may be purely a local one—a reflex of a diseased vessel wall, and we have seen in the
paper on "Sclerotic retinal vessels" that this disease is always patchy, that even in the same circumference of a vessel a portion may be changed and the rest not affected. That is why I did not see spasm or contraction of a large adjoining vessel in these cases. It was not involved, as it certainly would have been if the contraction had been of a vasomotor origin. The condition corresponds to the localized vascular crises of Pal. These only occur in pathological vessels; they may even lead, according to Oertel, to actual gangrene of the intestine, if the mesenteric artery be affected. They are the cause of angina pectoris. They explain the numerous cerebral manifestations of sclerotic patients, which can pass away without leaving any trace or can lead to actual cerebral lesion—the exact parallel to what is seen in the sclerotic exudation in the retina. Be that as it may, it always means a diminished supply of oxygen, a local starvation of the retinal cells and a local limitation of their metabolism of vascular causation. It is very gradual, very slow in onset, although the last drop may suddenly cause an already full cup to overflow. That is why the resulting acidosis is not sudden and not extreme, and the oedema of the retina is therefore so insignificant as not to be detected by the ophthalmoscope.

In two cases I have observed this blocking of the arterioles affect a very large portion of the central part of the retina. In both of these oedema was absent or only slightly marked. One case I have fully described elsewhere. The other one (see illustration No. II) is that of a woman aged 72 years. She was seen in the out-patient department of the London Jewish Hospital on June 8, 1928, with translucency of her retinal vessels lost, copper-wire colour, and the light reflex dotted. Severe arterio-venous compression was present. There was a great deal of retinal exudation, but the vessels were not covered; they were clear. There were many haemorrhages of different forms. The small and round ones were situated near the macula. The right eye was more affected. Blood pressure 150/85. Urine contained no sugar or albumin. Blood sugar 0.1 per cent., blood urea 33 mg. per 100 c.c. The haemorrhages gradually disappeared in the right eye, and the exudation gave place to scarring of the retina, the round foci being surrounded by pigmentation. In the left eye, the same process was going on. Then, a week or so later, the patient presented herself with the left eye showing all the central part of the retina around the macula, an area three or four discs in diameter, whitish, not oedematous, being sharply demarcated from the rest of the retina, with a cherry-red macula in the centre. In the macula there was a large flat haemorrhage; small flat haemorrhages were scattered here and there in the whitish area. Central vision was lost. The same picture was seen a few weeks
afterwards. All this, in my opinion, was simply due to a blockage of the arterioles and capillaries. Why are the larger vessels clearly seen? Simply because they are situated superficially in the nerve fibre layer of the retina, whilst their branches pass backwards, deeper into the retina, to form there the end capillaries. The oedema of the tissue is too slight and too slowly progressive to go so far forwards and cover the large vessels also. The intermediate step between this kind of retinal exudation and real albuminuric retinitis I saw in a woman, aged 33 years, who had lost a tremendous amount of blood through a miscarriage. (Illustration No. I). About three weeks afterwards I examined her fundi. Translucency of the retinal vessels was lost, copper-wire colour, light reflex dotted, no white lines and no arterio-venous compression seen; a few slight retinal haemorrhages, many areas of exudation, irregular in shape, slightly oedematous, i.e., not sharply demarcated from the surrounding retina. This exudation covered some of the vessels exactly as in albuminuric retinitis. But the fact that there was no arterio-venous compression, or other signs of vascular disease, that the retina was healthy and clear and the vessels clearly seen and sharply defined immediately excluded the diagnosis of albuminuric retinitis. Her blood pressure proved to be 140/75; the urine was normal. These two
cases together give a composite picture of albuminuric retinitis. In the first all the vascular components of albuminuric retinitis are present; in the second the element of oedema. This illustrates very well the complex aetiology of retinitis albuminurica—the vessel changes caused by hyperpiesis and oedema of the retina which may be independent of hypertension per se. Evidently in the above case the oxygenation and nutrition of the retina suffered

suddenly and considerably with resulting oedema, because of the sudden loss of the oxygen carriers—the erythrocytes. A similar, but much more severe case of post-partum haemorrhage followed by retinal oedema was described by A. Fuchs (Med. Klinik, Sept. 28, 1928) with a striking and immediate improvement after transfusion of blood. This interference with nutrition also applies to retinitis albuminurica. In the latter the outstanding feature as already pointed out by Rochon-Duvigneaud is the oedema of the retina. The "wool-patches" are of "fatty" colour; their margins are oedematous, gradually merging into the retina. If they are near to vessels they cover them. The vessels are not altogether clearly seen; they are not sharply defined but appear as if submerged in a tiny layer of water or covered with a very fine veil. Sometimes only a few vessels look
like this; in severe cases nearly all of them. The disc may be very oedematos, but one cannot rely on this alone, as essential hyperpiesis may give a similar papillitis, because the sclerotic perivascular sheath may make the outflow of lymph very difficult. (The same mechanical explanation may suffice for many cases of papillitis or papilloedema of quite different origin and that is why the same picture of papillitis is common to many diseases and one cannot therefore rely solely on it in diagnosis. The retina, which does not stand in such a direct communication with the intra-cerebral pressure and whose lymphatic vessels are not so compressed, naturally does not suffer so much and therefore its oedema is not usually so complicated in its causation as oedema of the disc may be.) This oedema of the retina covering the vessels may vary from an inconstant veil that remains for a few days only and then disappears only to reappear again and again, or the oedema may be of a type that allows one to follow a medium vessel from the disc to the periphery and, in spite of all one's efforts, not be able to see some portion of it clearly. Usually the patient presents all the signs of advanced arterial sclerosis with slight exudation or haemorrhages in the retina. The blood pressure is very much raised; the urine has a specific gravity of 1,000 to 1,005 and contains traces of albumin or none at all. This oedema of the retina which covers the vessels is, in my opinion, the decisive factor in the diagnosis of retinitis albuminurica. If seen fully developed, it means that the prognosis is very grave and that most probably in a short time (at most, two or three years) the patient will succumb. Again I have to repeat that the ophthalmoscopic picture is only a part, although a very essential one, of the clinical whole. A considerably raised blood pressure is a conditio sine qua non. This oedema of the retina, very protean in character, presents so to speak a close analogy to all the finest gradations between the "normal" and the "inefficient" kidney of the vascular or sclerotic type and sometimes the ophthalmoscopic diagnosis may be extremely difficult.

Elsewhere I have suggested that nephro-sclerosis due to essential hyperpiesis may finally, when very advanced, be identical with malignant nephro-sclerosis or terminal stage of glomerulonephritis, i.e., the stage of absolute kidney inefficiency. In the retina the above described peculiar phenomenon of oedema is the key to what is taking place. If the patient was originally a hyperpiesic, this oedema will only indicate that the reserve power of the kidney is becoming exhausted. Altogether it is a very slow process, as every case of hyperpiesis is, and if by medication or dieting or in some other way the disease regresses, the patient may recover and the signs of "albuminuric" retinitis, especially of the "apoplectic" variety may disappear. Such a case is described
in my paper on "Arterial hypertension and retinal changes." In my opinion to such cases are applicable these words of Leber that "the retinal changes can regress if the basal pathological process in the kidney is healed, or is improved; in favourable cases even the highly advanced retinal changes can regress completely." (p. 817). Those are the cases that are described under interstitial nephritis as going on for many years—10 or 20 or not even suspected during life and suddenly discovered post-mortem. Hence the importance of the ophthalmoscopic diagnosis when it is made with all the foregoing reservations, for the presence especially of retinal oedema is a sure sign that the patient is fast approaching the stage of absolute kidney inefficiency.

I have watched a patient, aged 40 years, for two years, who at first shewed signs of vasculo-renal affection of the retina. The condition did not progress but on the contrary slowly improved.


In another case, that of a woman suffering from diabetes mellitus and described in my two previous papers, I was inclined to think that she was developing true interstitial nephritis, but she proved to have nephro-sclerosis. In spite of getting insulin and a normal blood-sugar, her blood pressure is 200—230/109. The blood urea in 1927 was 49 per cent. and urea concentration test 1'1 per cent. and 1'7 per cent. (first and second hours). Phenolphthalein test 6'6, 22:2, 4'4. Her retinae are full of haemorrhages and enormous scars. In 1928 her blood urea was 22 per cent., blood sugar 0'22 per cent. and urea concentration test 0'35 per cent. and 0'4 per cent. (first and second hours). She is in the same state of health now, 1930, but the destruction of the retina is enormous without actual and persistent oedema.

It is my impression that I have not come across a case of albuminuric retinitis without the blood pressure being considerably raised. That is why in my opinion only definite forms of nephritis, and not every type as Fuchs and Fox evidently think, are accompanied by retinitis albuminurica. Swanzy believes in the association of high blood pressure with retinitis; "The arterial tension is always high when retinitis is present, even in the young."
Parsons says (p. 351) that "Generally the history of severe headache may be elicited and the blood pressure is high, usually about 200 mm." The opinion of Foster Moore is that "It is very unusual to meet with retinitis except in the presence of a considerably increased blood pressure," and furthermore that "some degree of oedema of the retina is probably present in all cases." Rochon-Duvigneaud, as quoted by Bailliart, always found renal retinitis in association with considerable hypertension. And if one adds to the above authorities the partisans of the theory that retinitis albuminurica is entirely the result of vascular changes, as, for instance, Duke-Elder and Fox, then the overwhelming majority always find arterial hypertension present in combination with albuminuric retinitis. One must not forget, that even arterial hypertension is relative in its character: a reading of 160/95 is not very pathological of itself, but it may be so, if the normal one for the same person was 120/70.

It is a clinical fact that the urine most saturated with albumin is met with in "nephrosis," where the blood pressure is normal and retinal changes do not appear. On the other hand retinitis is seen in patients with nephritis associated with raised blood pressure and scanty or even absent proteinuria. Therefore the old term of "albuminuric" retinitis is not a satisfactory one: "renal" would be much more appropriate, although it implies that the aetiology of retinitis is dependent upon the kidney affection, a theory which, as will be shewn later, is not yet proved.

When the diagnosis of retinitis albuminurica is made, the changes are so advanced that it is impossible to state whether any healthy vessels are left. This and the fact that arterial hypertension accompanies the retinitis give support to the theory of vascular disease being the cause of retinitis. The first to maintain this view were Michel and Herzog Karl Theodor. On the other hand Rochon-Duvigneaud has shown that in many microscopic sections he could demonstrate retinal vessels sufficiently healthy to exclude the possibility of their being the cause of marked retinal changes. In this he is supported by Ginsberg, Schieck and many others. Of modern writers Fisher is, of course, entirely for the vascular theory, "The ophthalmologist who discovers ocular changes should not make the diagnosis of nephritis, but one of vascular disease, which may presumably be affecting also the patient's kidneys" (p. 631). "The retinitis is not a sequel of the kidney disease. In parenchymatous nephritis the retinitis is the result of toxaemia and therefore the "blindness" may disappear. In interstitial nephritis it is caused by insufficient oxygen supply to the tissue and is therefore mostly immovable." Duke-Elder holds (p. 191) "That the basis of pathology of all three (arterio-sclerotic, diabetic, and renal retinitis) is in all probability the same." Fox
writes "Although albuminuric retinitis may be seen in any form of kidney disease, it is encountered most frequently by the ophthalmic surgeon in connection with the cirrhotic kidney." (p. 313). He also refers to the veiling of the retinal vessels by the exudation. "Coincidentally with the changes in the retina there is a progressive degeneration of the vascular system, accompanied by high arterial pressure." Poulard is of Rochon-Duvigneaud's opinion that retinitis albuminurica is a disease sui generis and is not the result of vascular changes. Swanzy thinks that the retinal changes "are probably toxic in origin and not caused by arteriosclerosis." Parsons writes: "There is no constant relationship between the retinitis and the vascular disease. The retinitis is, therefore, not directly due to the vascular disease, but probably to toxins circulating in the blood-stream."

Vascular disease of the retina, as characterized by accompanying hypertension, is of very slow development, although it commences very early. It presents a picture of gradually developing perivascular sclerosis and is really an adaptation of the body to the new conditions of the circulation. It follows the general rule that the parenchyma of an organ, where the vessels only are affected by sclerosis, may function pretty well for a long time, even for many
years. This applies to the hyperpietic retina as well as to the hyperpietic heart or kidney. It is surprising how far the retinal cells may accommodate themselves to extreme degrees of vascular anoxaemia without developing oedema, although they may be completely destroyed by a haemorrhage (See the illustration No. III, the late stage of thrombosis of the temporal superior vein).

If the parenchyma of the retina is involved, the process is also a very slow one of gradual strangulation, gradual starvation, very patchy, as every sclerotic process is, and therefore is not accompanied by considerable oedema. In albuminuric retinitis the process is rapid and strong. It is a sudden invasion of the parenchyma as well as of the vessels. We shall therefore see in the vessels actual degeneration of the vessel wall more pronounced—"non-true"—silver-wire artery, haemorrhages and oedema of the wall; the perivascular sheath will be oedematos. In short, it will be a rough, deformed, aggraved vascular picture, instead of the fine, beautiful sclerotic vessels full of nuances. Thus the retina will be brick-red from hyperaemia, swollen, oedematos, with "wool-patches," macular star and large haemorrhages. It is a fact of minor importance and may be even a coincidence, as my number of cases is so small, but I never saw a true silver-wire artery; evidently, the vessels are attacked by a powerful toxin and in such a short period of time, that they are not capable of developing the more delicate signs of vascular degeneration. Only the more frequent use of the sphygmomanometer in the routine examination of patients and the regular, frequent and careful examination of the fundus in every case of hypertension can decide in our present state of knowledge the important pathological question of the cause of renal retinitis. It is my belief that the retina suffers pari passu along with the vessels, the same toxin attacking both of them, which makes a pre-existent renal lesion in the previous history unnecessary. Moreover, I shall later quote a case where the patient was suffering for a year from fully developed retinitis albuminurica and yet all his renal tests were normal. What reason then have we to incriminate the kidney as the cause of retinitis, if the kidney still functions normally? I am obliged to the courtesy of Dr. J. Burnford for seeing a young girl, aged 20 years, with arterial hypertension of advanced degree, albuminuria and nearly normal fundus. Therefore, I did not feel justified in making the diagnosis of chronic interstitial nephritis. Six months afterwards she came again with a fully developed and typical albuminuric retinitis.

In toxaemia of pregnancy we have another striking instance of the same state of affairs. There the retinitis is always preceded by hypertension. Both the retinitis and hypertension will rapidly disappear if the pregnancy is terminated. The kidney is
obviously as much a victim of the intoxication as the vascular system, and the pregnancy is undoubtedly the cause of all the mischief.

Why then of all the higher sense-organs is the retina the first and foremost to be involved? Three explanations are possible.

(a) The kidney has an endocrine secretion, which is in intimate association with the vascular system and with the brain, especially the retina. According to De Schweinitz, Zur-Nedden believes that toxin is elaborated by decomposition of the kidney substances, which toxin possesses a selective affinity for the retinal vessels. One wonders what Zur-Nedden means by "kidney substances"; if tubular cells, then nephrosis is free from retinal changes. At present, this attractive hypothesis is insufficiently confirmed to be accepted as an explanation.

Bailliart claims to have discovered a local vascular hypertension of the retina only out of all proportion to the increased brachial pressure in every case of retinitis albuminurica, even before the oedema and exudation appear. If confirmed, and Bailliart is a very good authority indeed, this fact would at least point to the retinal affection preceding that of any other organ of the body in its reaction to the kidney disease.

(b) If the reader will recall the complex structure of the retinal capillaries as demonstrated by Krückmann, he will realize under what difficulties the metabolism of the retinal cells is carried on. The blood has to pass through the endothelium and the basal membrane on which the former is situated to enter the perivascular channel. Here it mixes with the lymph, which flows in an exactly opposite direction from the retinal cells to the vessel. The slowed stream has now to pass through two or three strong glial membranes to reach the intercellular space of the retina proper. Most probably the vis a tergo exhausts itself completely in traversing all these obstacles and it is left only to the physico-chemical force of the colloids of the retinal cells to select and absorb the necessary substances out of the mixture of lymph and blood—a very fine and delicate process indeed. If the retinal cells are comparatively healthy and only the vessels are sclerotic, the metabolism may still be normal although proceeding more slowly and with some difficulty. With increasing oxygen deficiency the retinal cells, half-starved, become oedematous, part of the poisonous products of their own metabolism—most probably acid in nature—being unable to find any outflow; with relief of any associated spasm of the vessels the crisis may be got over. If, however, the metabolism of the cells themselves be impaired and altered and, furthermore, the outflow of their waste products (more poisonous than usual) be also impaired by degeneration and continuous spasm of the vessels, the result will be that the
arterial hypertension, perivascular and selective retina diseased purely vascular unanimous that Weigert retinitis is nature and although the syphilis of that succeeded in making retina. the syphilis of the anterior layers of the retina is very rare. On the other hand syphilis is a very common affection of the retina. The difference cannot be caused by the blood supply, the arteria ophthalmica being the common main trunk. We must therefore look for the cause in the local condition of vascularization. Be the cause of syphilis the spirochaeta pallida or spore of this parasite which lives and develops in the endothelial cells, either must penetrate through the wall of the capillaries, fight its way against the stream of lymph and then pass through strong glial membranes. Is it any wonder then that such a large parasite as the spirochaete fails to get over all these obstacles? The same applies even more to the immobile bacillus of Koch, and again tuberculosis of the retina is very uncommon while choroiditis is not infrequent. In the uvea the vascularization is different and as a result the condition for infection is more favourable. The embryological similarity between the retina and the kidney is of some interest too. In both we can differentiate two parts, the proper parenchyma cells that are ectodermic in origin, and the mesodermic vascular and supporting tissue that grows in later. We have seen that in the retina both parts are segregated by a special membrane and that, as Weigert stated, the vascular system is treated by the central nervous system as a foreign body. Should similar histological conditions exist in the kidney, the Bowman capsule and its prolongation down the nephrone corresponding to the glial retinal membranes, it would satisfactorily explain why the organ is so closely connected with the retina. So far as I know, nobody has succeeded in making the same fine and precise injection-preparations of the human kidney as Krückmann has done in the case of the retina. One has only again to point out the remarkable fact that syphilis of the kidney, like that of the retina, is extremely rare although the kidney is a "vascular" organ par excellence.

At a recent discussion on retinitis albuminurica, held at the 30th Congress of German Biologists and Doctors, all the speakers were unanimous that retinitis albuminurica is always accompanied by arterial hypertension, but opinions were sharply divided on the nature and aetiology of retinitis albuminurica, some claiming a purely vascular origin and others denying this. Volhardt main-
RETNITIS NEPHRITICA OR ALBUMINURICA

Obtained a view identical with mine, that retinitis albuminurica means a pathological local metabolism of the retinal cells. Like myself, he also believes that the chief mischief is caused by the disorder of local cellular respiration; but on many other points his views are different. So far as the retina is concerned the features of vascular sclerosis in essential hyperpiesis may be explained by fibrotic changes of the perivascular sheath and not by a maximal contraction. If this explanation be correct, then retinitis albuminurica means an actual pathological metabolism of the retinal cells in combination with a vascular disease.

(c) Nephritis is the actual *fons et origo* of retinitis albuminurica. This was the general opinion until quite recently and is widespread even now. However, the question may be viewed differently. It is quite possible that both the kidney and the retina may suffer from the same general toxin and the gravity of the prognosis simply depends upon the fact that all the other vital organs of the body—brain, heart, liver—are involved to nearly the same extent, but we cannot examine them clinically with the same degree of precision as we can do in the case of the retina.

Animal experiments have failed up till now to shew any definite connection between inefficiency of the kidneys and raised blood pressure and, consequently, retinitis albuminurica. On the other hand benign nephro-sclerosis *per se* does not give rise to retinitis albuminurica for many years and, if it does so, it is always questionable if some superadded infection be not the real cause. In nephrosis *per se* retinitis albuminurica does not appear either. Therefore, we have to presume that a combination of glomerulitis and nephrosis is the cause of retinitis. But though both glomeruli and tubular cells are always involved in every form of nephritis, retinitis does not always appear; this may only mean that not enough of glomeruli and tubules are involved, or that the involvement is not very severe. It may be argued that perhaps complete elimination of all of them by extirpation of the kidneys would cause retinitis and even to a greater degree hyperpiesis. However, this is not the case. Spence describes cases of renal dwarfism dying from uraemia, but with a normal blood pressure and the absence of retinitis. It may be that there is a *special pathological factor*, or a combination of several pathological factors, which give rise to nephritis and retinitis alike. And this is my opinion. In the majority of the text-books, including even McDonagh's, the kidney is the cause of hyperpiesis. I think it is nothing of the kind. I mentioned this elsewhere, quoting endarteritis obliterans as an instance. Briefly, my opinion is that hypertension is always caused by the muscular contraction of the vessels, and a sufficient number of them is always affected at the time when the kidney-vessels are involved too. The kidneys are as
innocent of arterial hypertension as the hypertrophied heart. On the other hand, it is my opinion that essential hyperpiesis is the cause of nephro-sclerosis, an opinion also held by Fishberg and Gray. Generally speaking, in glomerulo-nephritis we have an inflammatory and in nephrosclerosis a degenerative process of the nephron-vessels.

Clinically we can verify this theory by testing the kidneys as to their efficiency by the methods known to us to-day. These are: Volhard's water test, McLean's urea concentration test, the estimation of urea and of creatinin in the blood, and the intramuscular injection of different dyes. All of them are a tremendous step forward, but the exaggerated hopes that they aroused have not been realized. In the great majority of cases retinitis albuminurica is, as shewn by these tests, combined with kidney inefficiency. The opinions of authorities are sharply divided as regards their prognostic value. If in retinitis kidney inefficiency were always demonstrated by the various tests, it would be difficult to deny that nephritis is the cause of retinitis, but if fully developed retinitis be present and the kidney efficiency tests are normal, then we may assume that the body is being poisoned by a toxin which is not a product of nitrogen metabolism. Every toxin is a complex protein so far as our present knowledge goes. It is possible that the retina is more sensitive and shews the pathological process earlier than the kidney, and that both are afflicted by a common foe. Such cases are not common, but I have had one under my care.

The patient was a man, aged 24 years, first seen in 1924. Urine: sp. gr., 1015; much albumin present. Blood pressure 180/120. In the fundi translucency of the vessels had disappeared; the arteries were copper-wire, and shewed dotted light reflex. White lines were seen at arterio-venous crossings, where the veins were crushed. The retinae were hyperaemic but not oedematous. A small haemorrhage was present in the left eye.

To this picture of retinal sclerosis there were added two months later exudates, wool-patches and oedema around the macula. At that time his kidney function was investigated at a hospital by means of intravenous indigo-carmine and was pronounced "normal." A month later there was a definitely established albuminuric retinitis. His blood pressure and urine were very much as before. A urea concentration test shewed 25 urea. In the meantime the patient was going steadily downhill, suffering from many attacks of minor uraemia, and a second investigation of his kidney function three months after the first still gave fairly normal results. (Blood urea 40 per mille; serum-indican negative; water concentration, excretion and dilution normal). The fundi shewed minor changes in the fully established albuminuric retinitis during this time, and four months later a third examination of kidney
function still gave a fairly good result. (Blood urea 38 per mille; urea concentration test 1'7 per cent., 1'8 per cent., 2'3 per cent., 2'6 per cent., before administration of urea, one hour, two hours and three hours after, respectively). A year after he was first seen he developed a right Bell’s palsy. The blood urea at the time was only 26 per cent. and decapsulation of the right kidney was performed. The kidney was only slightly enlarged. In spite of some immediate improvement the patient died within six weeks. His blood urea rose from 77 per cent. to 188 per cent. within 17 days, and the patient died 17 days afterwards. Dr. J. Burnford kindly furnished me with the following report on the post-mortem examination of the kidney.

"This case was an example of a subacute nephritis, contracting. The kidneys were mottled, finely granular, fairly large. Microscopically—chronic interstitial inflammation (round cells in great numbers between the tubules) with some parenchymatous changes; some glomeruli degenerated and inflamed; some tubules cystic. Arteries thickened, especially in the tunica media."

Which is more important in such a case, for prognosis and treatment, the retinal picture or the kidney efficiency tests? Is it a case of gross cardio-vascular disease, benign nephro-sclerosis, or true interstitial nephritis (malignant nephrosclerosis)? McLean is a staunch advocate of the kidney efficiency tests, even though in the experience of others they are not altogether reliable. "Indeed, cases of alleged chronic interstitial nephritis have been described, in which renal tests gave good results quite incompatible with the supposed conditions of the kidneys, and those anomalous results have been brought forward as an indication that the renal tests are not always reliable. In such a case it is the diagnosis that is at fault and not the tests." (p. 78). Elwyn holds that retinitis albuminurica, especially if the "star" around the macula be present, is a sure sign that the patient is fast approaching the stage of absolute kidney inefficiency, although the blood chemistry be normal. But though it is true that retinitis bears no direct relationship to the blood chemistry, one is not warranted in holding as Parsons does that "The degree of retinitis bears no fixed relationship to the nature or intensity of the renal mischief," a view shared by Fuchs: "The severity of retinitis bears no fixed proportion to the intensity of kidney disease .... the like is true of the subsequent course; the retinitis may improve while the kidney lesion grows worse or vice versa."

(To be Continued.)