milk, than demand that any known practicable methods which will remove this danger should be put into operation. Pasteurization is not a new, untried experiment; it operates over a large part of the United States and Canada, and there is much evidence showing its extreme efficiency. One example may be quoted. Price²⁴ examined materials obtained from 320 cases of human tuberculosis, 100 being adults (15 years and over) and 220 children under 14 years. Of the adults the human type of tubercle bacillus was isolated from ninety-seven, the bovine type from two. The human type was isolated from 192 children, the bovine from thirty children. The two adults had both lived all their lives on a farm and had been accustomed to using raw milk. Without exception the children harbouring an infection with the bovine tubercle bacillus came from parts of the province of Ontario where pasteurization of milk was not carried out, and history invariably revealed the fact that the children had been fed on raw milk. The interesting feature of the investigation is that the cases were drawn from Toronto and from other parts of Ontario. In the city of Toronto milk pasteurization is compulsory, and has been rigidly enforced since 1915, but "not a single case of bovine infection has been encountered in the group of children brought up on the pasteurized milk of the district (1915 to 1930)." Less striking but nearer home, Blacklock⁹ notes that of the twenty-one country children in his series with tuberculous cervical adenitis sixteen (76.2 per cent.) were infected with the bovine strain, while of the seven Glasgow city children only two (28.6 per cent.) were infected with the bovine bacillus. Over 80 per cent. of the milk supply in the Glasgow city area is pasteurized.

The medical profession should adopt a definite policy as regards the prevention of the infection of man with the bovine tubercle bacillus, and I venture to recommend the following as such a policy.

1. That the basic aim is the diminution and ultimate elimination of tuberculosis among our dairy herds so that cows entirely free from tuberculosis should be the sole source of milk and milk products for food consumption. This necessitates not only a new active policy, but a reconsideration of present practices, including the utility of the Tuberculosis Order, 1925, the possibility of giving more active encouragement to the producers of tuberculosis-free herds, whether "designated" or undesignated, a simpler and better nomenclature and administrative control for designated milks, and the enforcement of more hygienic methods in connexion with milk production.

2. That pending the elimination of bovine tuberculosis pasteurization should be adopted as a practical and scientific method to make our milk supply safe.

There are technical difficulties in the way of adopting at once a universal system of pasteurization, and my suggestion²⁵ as to procedure is that, as a first instalment, permissive powers should be granted to the larger urban authorities to require that all milk sold within their area shall either be derived from cows free from tuberculosis or be efficiently pasteurized or otherwise heat-treated by some process recognized as efficient by the Ministry of Health.

It may be mentioned that the special committee appointed by the People's League of Health,¹⁵ which made a detailed investigation of the facts, has adopted these proposals as its main recommendations.

REFERENCES

- ¹ Griffith, A. S.: *British Medical Journal*, 1932, ii, 501.
- ² Idem: *Edin. Med. Journ.*, 1932, xxxix, 277.
- ³ Idem: *Journ. Path. and Bact.*, 1930, xxxiii, 1145.
- ⁴ Cumming, W. M., and Foster, Winifred M.: *Ibid.*, 1933, xxxvi, 153.
- ⁵ Cumming, W. M.: *Tubercle*, 1933, xiv, 205.
- ⁶ Lange, B.: *British Medical Journal*, 1932, ii, 503.

- ⁷ Griffith, A. S., and Munro, W. T.: *Journ. Path. and Bact.*, 1933, xxxv, 271.
- ⁸ Cobbett, L.: *The Causes of Tuberculosis*, 1917.
- ⁹ Blacklock, J. W. S.: *Tuberculous Diseases in Children*, Medical Research Council, Special Report Series, No. 172, 1932.
- ¹⁰ Weller: *Arch. Int. Med.*, 1921, xxvii, 631.
- ¹¹ MacCreedy, P. B., and Crowe, S. J.: *Amer. Journ. Dis. Child.*, 1924, xxvii, 113.
- ¹² Wilkinson, H. F.: *Arch. of Otolaryngol.*, 1929, x, 127.
- ¹³ Mitchell, A. P.: *Journ. Path. and Bact.*, 1917, xxi, 248.
- ¹⁴ Savage, W. G.: *The Prevention of Human Tuberculosis of Bovine Origin*, 1929.
- ¹⁵ *A Survey of Tuberculosis of Bovine Origin in Great Britain*, Report of a Special Committee of the People's League of Health, 1932.
- ¹⁶ *The Incidence of Tuberculous Infection and its Relation to Contagion in Children under 15*, Research Department of the Brompton Hospital for Consumption and Diseases of the Chest, No. II.
- ¹⁷ Local Government Board, New Series, No. 88, 1914.
- ¹⁸ Hoy and Stenhouse Williams: *Journ. of Hyg.*, 1930, xxx, 413.
- ¹⁹ Fowler, A. B., and Wright, N. C.: *The Hannah Dairy Research Institute, Bulletin*, No. 2, 1933.
- ²⁰ Jordan, L.: *Hannah Dairy Research Institute*.
- ²¹ *Report of the Reorganization Commission for Milk*, Ministry of Agriculture and Fisheries, Economic Series, No. 38, 1933.
- ²² Savage, W. G.: *Lancet*, 1933, i, 429, 485.
- ²³ Stirling, J. D., and Blackwood, J. H.: *The Hannah Dairy Research Institute, Bulletin*, No. 5, 1933.
- ²⁴ Price, R. M.: *Amer. Rev. of Tuberculosis*, 1932, xxv, 383.
- ²⁵ Savage, W. G.: *Lancet*, 1931, i, 543.

THE RENAL ASPECTS OF ESSENTIAL VASCULAR HYPERTENSION

(HYPERPIESIA OF CLIFFORD ALLBUTT)*

BY

W. W. D. THOMSON, M.D., B.Sc., F.R.C.P.

PROFESSOR OF MEDICINE IN THE QUEEN'S UNIVERSITY OF BELFAST

Sir Clifford Allbutt's definition¹ of hyperpiesia as "a disease which, *independent of the kidneys*, has its own characters, of which high arterial pressures, systolic and diastolic, seem to be the chief," emphasizes the essentially vascular nature of the disease and the secondary importance of the renal aspect. Persistent high arterial pressure leads to hypertrophy of the heart, and to characteristic degenerative lesions in the arterioles of many organs of the body^{2 3 4 5 6}—of the kidney almost universally, of the retina, spleen, pancreas, liver, and brain frequently, of the gastro-intestinal tract, lungs, skin, myocardium, and skeletal muscles less often. Recent investigations,⁷ however, have demonstrated the frequency of changes in the arterioles of skeletal muscles, especially in the severer type of the disease.

Sixty years ago Sir William Gull condemned the narrow pathology which regarded the kidney lesion as the *fons et origo* of this disease, which he and Sutton³ called arterio-capillary fibrosis, emphasizing the widespread thickening of the arterioles (and erroneously of the capillaries) throughout the body and the fact that the kidneys merely shared in this generalized fibrosis. Never did Sir William Gull⁸ plead more forcibly for a wider outlook on the pathology than in a clinical lecture to the students of Guy's Hospital, a lecture which has become one of the classics of medical literature. On that occasion there was on the table a museum specimen of a large hypertrophied heart and a very contracted kidney, mounted under Dr. Richard Bright's personal supervision to demonstrate that the wasting of the kidney had been the cause of the thickening of the heart.

"I think," said Sir William, "with all deference to so great an authority, that the systemic capillaries, and had it been possible, the entire man, should have been included in this vase, together with the heart and the kidneys, and then we should have had, I believe, a truer view of the cardiac hypertrophy and of the disease of the kidney."

* Read in the Section of Medicine at the Annual Meeting of the British Medical Association, Dublin, 1933.

To-day it is accepted that both hypertrophied heart and shrunken kidney are the result of a common cause—namely, persistently raised arterial pressure, which is known as hyperpiesia or essential vascular hypertension.

Even at the risk of wearisome repetition let me stress those points in the pathology which have an important bearing on my subject.

1. Essential hypertension produces a characteristic lesion in the arterioles of many organs in the body.

2. This lesion consists of a hyaline thickening of the sub-endothelial layer of the intima, leading to narrowing and sometimes to occlusion of the arteriole.

3. This change is seen most frequently and to best advantage in the afferent arterioles of the kidney, and may lead to atrophy and obliteration of the glomeruli and tubules through deficient blood supply and disuse. The interlobular arteries are also often affected (see figure).

Kidney of essential hypertension (arteriosclerosis).

4. The number of glomeruli affected is relatively small in proportion to the number of arterioles which appear occluded.⁹ The impermeability of many of the arterioles is more histologically apparent than physiologically real. Evidence has been produced by Hueck¹⁰ that the hyaline material is of a semi-fluid consistency, which, yielding easily, offers little resistance to the flow of blood through the arteriole. The circulation, too, is rendered more efficient by the raised blood pressure.

5. Glomerular and tubular atrophy is patchy in character, with normal areas of kidney parenchyma between the islands of sclerosis.

6. The kidney of essential hypertension, or the arteriosclerotic kidney, so called from the characteristic lesions in its arterioles, must be clearly distinguished from the arteriosclerotic kidney, in which the renal artery and its branches share in that generalized arteriosclerosis so often present in the old. This "senile" kidney, generally unaccompanied by hypertension, is of little, if any, clinical importance. In the kidney of essential hypertension, especially if the subject be elderly, similar arteriosclerotic changes are often found in the renal artery and its main divisions, superadded to the arteriolar changes already described. Gross¹¹ has demonstrated these vascular changes by x-ray photographs after the injection of the renal artery with barium sulphate suspended in gelatin. He describes the normal kidney as "a spreading chestnut tree," while the contracted hypertensive kidney suggests rather an aged and gnarled oak.

The enormous reserve power possessed by the kidneys has been recognized since the classical experiments of Rose Bradford¹² in 1892. The brilliant researches of Richards¹³ have demonstrated that while some glomeruli are active others are resting, the total number of renal units functioning at the same period being only a fraction of the huge number available, computed at some two millions. In essential hypertension the destruction of

glomerular and tubular tissue lags behind the arteriolar lesions, and is focal in nature and not diffuse. In consequence, many years may elapse before sufficient glomerular tissue is affected to produce evidence of renal inadequacy. This period of the disease, often unmarked by renal damage, Mahomed¹⁴ referred to as "the pre-albuminuric stage of Bright's disease." As actual evidence of arteriosclerotic changes was still often wanting Huchard¹⁵ named this initial period "presclerosis."

There is some evidence that nocturia may be the earliest symptom to raise the suspicion of renal mischief. Rise-man and Weiss¹⁶ found this symptom in 25.9 per cent. of 1,090 hypertensive cases in which cardiac, cerebral, or renal complications had not occurred, while in 500 cases presenting evidence of such complications Paullin, Bowcock, and Wood¹⁷ found that nocturia was the most frequent symptom, occurring in 49 per cent. It is, however, difficult to evaluate the importance of nocturia. Acquired habits of nocturnal micturition, the fluid intake of the previous evening, and insomnia may be the underlying cause. In males the consideration of prostatic enlargement must not be neglected. Fishberg¹⁸ considers that in the majority nocturia is of cardiac origin, the increased volume of the night urine being due to the improved circulation while the patient is at complete rest.

Albuminuria is inconstant, often slight, and intermittent. Janeway¹⁹ found in his analysis of a series of cases of hypertensive cardiovascular disease that out of 246 cases alive 127, or 52 per cent., did not suffer from albuminuria, while out of 212 fatal cases albumin was absent in only thirty-eight, or 18 per cent. The incidence of albuminuria becomes much more frequent as the disease progresses. With the albumin may appear hyaline casts, while the presence of an occasional granular cast points to tubular degeneration. Addis and Oliver,²⁰ who lay great stress on the examination of the urinary sediment, point out that the relatively small number of casts, of white blood corpuscles, and epithelial cells, and especially of red blood corpuscles, differentiates the inactive lesion due to slow vascular occlusion in the kidney of essential hypertension from the actively destructive processes at work in nephritis. Glycosuria secondary to arteriosclerotic changes in the pancreas is not uncommon, but yields generally to dietetic treatment.²¹

Polyuria does not intrude itself so noticeably as in chronic nephritis, but if the quantity of urine be measured some slight increase will generally be found. The various methods of testing the urine concentrating power of the kidneys are found to give results which, though sometimes lower than the average, still fall within the normal limit. The non-protein nitrogen of the blood is not raised.

At necropsy, even after years of hypertension, the kidneys may appear almost normal, the microscope revealing only minimal arteriolar change. On the other hand, dissection may reveal grievous structural damage in kidneys which, during life, gave little evidence of functional derangement. In his writings Richard Bright²² himself several times remarked on this paradox.

DIFFERENTIAL DIAGNOSIS

In essential hypertension the frequent presence of albumin in the urine during life and the contracted kidney found after death have caused much confusion, both clinically and pathologically, with chronic nephritis. The majority of cases of so-called chronic interstitial nephritis are, in truth, examples of hyperpiesia, while the remainder are examples of a focal glomerulonephritis with late development of renal failure and secondary arteriosclerotic changes, as Shaw Dunn²³ has demonstrated. One of the most important advances in our

knowledge of Bright's disease is the separation of hyperpiesia with secondary renal changes from hyperpiesis (high blood pressure) following primary nephritis. The differential diagnosis is of great importance, and arises in practice every day. It has been stressed by many writers.^{24 25 26 27} Hyperpiesia is much the commoner condition, carries a much more favourable prognosis, and demands a different type of treatment. The diagnosis of essential hypertension is quite compatible with several decades of useful life; the chronic nephritic is always in danger, and if renal insufficiency is progressive, as shown by a gradual lowering of the maximum specific gravity of the urine, death is rarely delayed beyond a year or two. The restrictions in diet and in mode of life, justifiable in a case of chronic nephritis, are unnecessary and even harmful in essential hypertension. The peace of mind and the renewal of hope which a confident and cheery prognosis affords to a non-nephritic hyperpiesic are worth all the drugs in the *Pharmacopoeia* or the various much-vaunted proprietary remedies.

A patient of middle age complains of shortness of breath, of fatigue on exertion, of headache and dizziness, and, perhaps, of rising several times at night to pass urine. On examination are found an enlarged heart, a systolic blood pressure raised to over 200 mm. Hg, a diastolic of 120, and some sclerosis of the retinal arteries. The urine contains a slight cloud of albumin. If the specific gravity of this sample is above 1020 the case is, in all probability, one of hyperpiesia. But the sample is a casual one, passed perhaps on a cold day and after a meal generous in fluid intake, and the specific gravity may be low, say, 1010 or under. The concentrating power of the kidney is next investigated. This requires no complicated urinary analysis, since the information required can often be obtained by the systematic study of the specific gravity of the urine. A striking characteristic of the healthy kidney is its amazing capacity to adapt its work to the requirements of the body. A healthy individual who drinks little fluid or who sweats profusely passes a small quantity of urine of a high specific gravity. On the other hand, when much fluid is taken or when the weather is cold the same person passes larger quantities of urine of a lower concentration. Korányi²⁸ recognized that the fundamental evidence of impaired renal function is a loss of this "physiological flexibility," and in such cases the urine passed, regardless of the coexisting conditions, shows little variation in its range of specific gravity or in the amount secreted from hour to hour. Many methods of testing this power of accommodation have been introduced, chiefly modifications of the procedure described by Volhard.²⁹

The vogue of renal tests involving some knowledge of biochemistry and the use of more or less complicated apparatus has frightened the general practitioner. He is inclined to regard the investigation of renal function as the province of the specialist. On the contrary, using the following procedure suggested by Calvert³⁰ in his range of urea concentration test, the only apparatus required is a reliable urinometer. The importance of the urinometer as a simple and reliable indicator of renal insufficiency within the scope of even the busiest practitioner cannot be too strongly stressed. The patient is instructed to take no fluid after 5 p.m., and at 11 p.m. to empty the bladder and discard the urine passed. At 7 a.m. the bladder is again emptied, and this specimen (A) is kept for examination. Immediately after micturition the patient drinks a large quantity of fluid, say two breakfast cups of weak tea without sugar and two glasses of water. Two hours later urine is again voided, and this specimen (B) is also sent for examination. In the normal kidney specimen A should be concentrated, having a high specific gravity 1025 and upwards; failure to reach 1020 must

be viewed with suspicion. Specimen B should have a low specific gravity, probably 1005 or under. Any fixation of the specific gravity, both specimens ranging below 1020, points to renal inefficiency—for example, 1007 to 1015; the nearer the fixation is to 1010, say 1009 to 1012, the more extensive the damage. Inability to concentrate urine above a specific gravity of 1010 represents maximum impairment of concentrating power. Apart from the vital information given by renal function tests there are many other points of value in the differential diagnosis as presented in the following table.

TABLE I

	Essential Hypertension	Chronic Nephritis
History ...	Often family history of cardio-renal cerebro-vascular disease. ³¹ Common at menopause	Sometimes previous history of acute or subacute nephritis
Age ...	Above 40 ...	Below 40
Heart ³² ...	Cardiac hypertrophy more marked	Cardiac hypertrophy less marked
Blood pressure ³³ ...	Higher average; often over 250 mm. Hg. May fluctuate with rest and other circumstances	Raised generally, but lower average and less fluctuation. May not be raised
Fundus ^{34 35} ...	Marked sclerosis in the retinal arteries. Arterio-venous compression striking feature. Discrete, sharp-edged exudates. Oedema less common. Retinitis may be unilateral. Haemorrhages commoner	Less sclerosis in retinal arteries. Cotton-wool patches and oedema more common. Always bilateral. Retinal detachment commoner
Oedema ...	No oedema, unless cardiac	Oedema may occur
Anaemia ...	Generally absent	Often present
Polyuria ...	Not obtrusive	Marked
Albumin ...	Inconstant and intermittent	Generally present
Urinary sediment ³⁶ ...	Hyaline casts alone generally. Sometimes hyaline and granular. Red blood cells few in number	Both hyaline and granular casts; often excess of red blood corpuscles, white blood corpuscles, and epithelial cells
Blood urea ...	Under 40 mg. per cent.	Over 40 mg. per cent.
Urea concentration	Over 2 per cent.	Under 2 per cent.
Fixation of specific gravity	No	Yes
Maximum specific gravity	1025 or over	1010 to 1020
Histology ...	Afferent arterioles primarily affected; glomeruli and tubules secondarily	Glomeruli primarily affected; arterioles secondarily
Prognosis ...	Depends chiefly on cardiac condition; relatively favourable	Depends on degree of renal insufficiency. Grave
Mode of death	Cardiac failure. Cerebral haemorrhage	Uraemia

Sir Clifford Allbutt,³⁶ in discussing this subject, wrote:

"One or two recent writers seem disposed to revert to the notion that these cases of hyperpiesia are but early stages of chronic renal disease—especially of primary contracted kidney. The clinical physician knows better. He sees, on the one hand, in young as well as in middle-aged persons, the weariness, the headache, the gradual impoverishment of the blood, the sallowing of the complexion, the puffy eyelid, symptoms becoming more and more distinct as the glomeruli are successively attacked, and these sufferers he contrasts with the non-renal hyperpiesics; active, well-coloured persons, free from nausea, headache, and all other symptoms of incipient uraemia. And in these it is that a blood examination reveals no excess of non-protein nitrogen."

This, then, is the clinical picture, as far as the kidney is concerned, in the great majority of cases of pure or benign essential hypertension: a slow development over a decade or two with a marked paucity of clinical or biochemical evidence of renal damage, death resulting from cardiac failure, cerebral haemorrhage, or from some unrelated disease.

The small minority of patients who develop marked renal insufficiency and die with uraemic symptoms

remains to be considered. Such cases furnish one of the still unsolved problems of renal pathology. Table II affords an index of the percentage who die a renal death.

TABLE II.—Cause of Death in Essential Vascular Hypertension

Observer	Cardiac Failure	Cerebral Haemorrhage	Renal Failure	Other Causes
Christian ⁸⁷ ...	32 per cent.	25 per cent.	4.5 per cent.	38.5 per cent.
Bell and Clawson ⁸⁸	60.4 "	19.3 "	8.5 "	11 "
Granger ⁸⁹ ...	52 "	31.5 "	5.5 "	11 "
Sir T. Lewis ⁴⁰ ...	"One in three, or rather more"	"One in four or five"	"Very few"	Less than 50 per cent.

It must be remembered that in hyperpiesia uraemic symptoms may be closely imitated by those of hypertensive encephalopathy. Probably in the past, before renal function tests were in general use, the convulsions characteristic of this latter condition were confused with uraemia.

In some cases cardiac failure is the precipitating cause. The arteriolar lesions in the kidney, almost constantly present and often of considerable extent and severity,

called "the malignant phase of essential hypertension." To Volhard and Fahr⁴³ we owe the idea of this malignant stage in the disease (malignant nephrosclerosis); in some 10 to 15 per cent. of their cases proliferative and exudative phenomena in the glomeruli, indicative of an acute or sub-acute nephritis, were superadded to the arteriosclerotic changes already present. Hence the term "Kombinations form." To these changes, which Volhard and Fahr regarded as inflammatory in nature, the onset of uraemia was considered due. That such changes in the glomeruli do occur in varying degrees must be admitted, but most pathologists consider these as indicative not of an inflammatory process, but of a rapidly progressive arteriolar lesion, which grossly interferes with the circulation. Volhard and Fahr have modified their ideas as to the inflammatory aetiology of these changes. Fahr⁴⁴ ⁴⁵ considers the cause to be a rapidly developing necrosis of the arterioles, while Volhard⁴⁶ holds that the onset synchronizes with a generalized vaso-constriction of the arterioles of the body, producing pallor of the skin, glomerular ischaemia, and neuroretinitis.

In America, Keith⁴⁷ and his co-workers in the Mayo School have widened the definition of malignant hyper-

TABLE III

Date	Symptoms	Blood Pressure	Heart	Albumin	Renal Function	Remarks
November, 1927	Melaena, severe enough to require transfusion	—	—	—	—	Duodenal ulcer? Cirrhosis of liver?
March, 1928	"Too full blooded," Haemoglobin 105 per cent.	205/130	Nil	Trace	Normal	Diagnosis changed to essential hypertension. No evidence of polycythaemia vera
January, 1931	Failing sight. Hypertensive neuroretinitis	230/135	Apex beat 4 in. from mid-sternal line	Cloud	Normal	Onset of malignant phase of essential hypertension. Marked papilloedema of disk
March, 1931	Haematemesis and melaena	220/120	5 in.	Cloud	Normal	—
January, 1932	Haemoptysis	240/150	6 in.	Marked cloud	Blood urea 40 mg. per cent.	Renal involvement manifesting itself
August, 1932	Nocturia; dyspnoea on exertion	250/170	As above	Heavy cloud	Reduced concentration	Cardiac symptoms, steady rise of blood pressure, and advance in renal insufficiency
March, 1933	Haematuria. Nocturnal attacks of dyspnoea—cardiac or uraemic?	Petechial haemorrhages under armband 230/135	As above	Much albumin Many casts; granular + "renal failure" casts and blood casts	114 mg. per cent. Specific gravity fixed at 1010	Severe renal failure. Onset of haematuria ominous
April, 1933	Uraemic symptoms and death	—	—	—	—	Post-mortem was not obtained

make the kidneys a weak link in the circulation, and when cardiac failure sets in oliguria with a rise in the non-protein nitrogen in the blood follows, and even uraemic symptoms manifest themselves. Sir Clifford Allbutt⁴¹ has emphasized this, and points out that uraemia is often but an episode in the disease, and, if the embarrassed circulation be relieved, may pass away. This type of renal insufficiency is easily recognized by the signs and symptoms of cardiac failure. As the concentrating powers of the kidney have not failed there is no lowering of the specific gravity of the urine although the amount passed is greatly decreased. An intercurrent infection, especially of the respiratory passages, may also produce a failure of renal function.

Theoretically, renal failure can be explained by the gradual destruction of more and more glomerular tissue. The kidney passes through what Fishberg⁴² calls the stage of compensated hypofunction (increased flow of urine compensating for the decreased concentrating power of the kidney) to reach the condition of uncompensated hypofunction, characterized by scanty urine of low specific gravity and the rise of non-protein nitrogen in the blood. But though this is the natural course pursued in chronic nephritis, it is a relatively rare event in essential hypertension. Although a few cases of hyperpiesia may live for a surprising number of years with compensated hypofunction, yet marked polyuria and lowering of the maximum specific gravity should be viewed with grave suspicion as heralding the approach of what has been

tension to include not only cases characterized clinically by acutely progressive renal failure, but also those in which a persistent high blood pressure, especially diastolic, leads to a rapidly progressive arteriolar lesion widely spread throughout the body, including even the arterioles of skeletal muscle, and which, in its turn, produces severe neuro-retinitis and the rapid development of cerebral, cardiac, or renal symptoms or combinations of these. Hypertensive neuro-retinitis, characterized by papilloedema and retinal signs similar to those formerly called "albuminuric retinitis," is often the first evidence of the onset of the malignant phase. The development of malignant hypertension is well exemplified by the case of B. H., a man of fine physique, one who worked and played hard and was moderate in neither his eating nor his drinking, and who enjoyed excellent health till the age of 47. Table III tells the story of his illness.

This case illustrates the transition of a symptomless benign hypertension into the malignant phase, of which the first evidence was given by severe hypertensive neuroretinitis. Frequent and severe haemorrhages from gastrointestinal tract and lungs, and bleeding into retinae and skin, pointed to a widespread and severe degeneration of the arterioles. Blood pressure rose quickly, and evidence of cardiac involvement rapidly followed. Later the kidneys shared in the general debacle; the onset of haematuria should be especially noted, owing to its ominous clinical significance and its frequency in the malignant stage. Death occurred about one year after the onset of renal

damage and a little over two years from the discovery of the neuroretinitis. The evil prognosis accompanying either neuroretinitis or the onset of definite renal symptoms in hyperpiesia is well recognized.

The clinical association of hypertensive neuroretinitis with renal failure⁴⁸ on the one hand and with cerebral vascular catastrophes⁴⁹ on the other has been emphasized by many observers, and has a solid foundation in fact. Although it is true that neuroretinitis may exist for considerable periods with apparently normal renal function⁵⁰ (as in the case cited), and without evidence of cerebral arteriosclerosis, yet, provided such cases be kept under observation, provided they be not carried off by cardiac failure or intercurrent malady, evidence of renal or cerebral damage will become manifest within a period of two years. The onset of neuro-retinopathy is the writing on the wall which proclaims the onset of the malignant and final phase of the disease. The pathological changes in disk and retina are but an index of co-ordinated arteriolar disease in other vascular fields.⁵¹

The arteriolar system of the body may be compared with the extended front line of the last war. Always under steady pressure, it is at any time liable to intensified attack. The line will yield first at the weakest point, the retinal area; but this is not a vital spot, and the line as a whole stands. As the strain is maintained the line gives at an area essential for its existence—cardiac, renal, or cerebral—with resulting disaster. As to the mysterious agency which causes this speeding up in the degeneration of the arterioles throughout the body, and converts a comparatively benign condition into a rapidly fatal one, we are still absolutely ignorant. Unless a case of malignant hypertension has been under observation before the onset of renal insufficiency it may be quite impossible to differentiate it, clinically or biochemically, from chronic nephritis. Even at necropsy, even after histological examination, pathologists may differ. But then indeed the problem is one of academic rather than of practical importance, for at this stage the prognosis is equally hopeless.

REFERENCES

- ¹ Allbutt, T. Clifford: *Arteriosclerosis: A Summary View*, 1925, p. 44.
- ² Johnston, George: *Med.-Chir. Trans.*, 1868, li, 57.
- ³ Gull, W. W., and Sutton, H. G.: *Ibid.*, 1872, lv, 273.
- ⁴ Jones, L.: *Virchow's Arch. f. Path. Anat.*, 1904, clxxviii, 367.
- ⁵ Evans, G.: *Quart. Journ. Med.*, 1920-1, xiv, 215.
- ⁶ Fishberg, A. M.: *Hypertension and Nephritis*, second edition, 1931, p. 179.
- ⁷ Kernohan, J. W., Anderson, E. W., and Keith, N. M.: *Arch. Int. Med.*, 1929, xlv, 395.
- ⁸ Gull, W. W.: *British Medical Journal*, 1872, ii, 673, 707.
- ⁹ Gray, J.: Medical Research Council, Special Report Series, 1933, No. 178, p. 121.
- ¹⁰ Hueck: *Munch. med. Woch.*, 1920, lxvii, 835.
- ¹¹ Gross, L.: *Journ. Med. Research*, 1917, xxxvi, 327.
- ¹² Bradford, J. Rose: *Journ. Physiol.*, 1899, xxiii, 415.
- ¹³ Richards, A. N.: *Kidney Function*, Harvey Lectures, 1920, vol. xvi.
- ¹⁴ Mahomed, F. A.: *British Medical Journal*, 1874, i, 585.
- ¹⁵ Huchard, H.: *Traité clinique du cœur et des vaisseaux*, third edition, 1899, i, 45-126.
- ¹⁶ Riseman, J. E. F., and Weiss, Soma: *Amer. Journ. Med. Sci.*, 1930, clxxx, 47.
- ¹⁷ Paullin, J. E., Bowcock, H. M., and Wood, R. H.: *Amer. Heart Journ.*, 1926-7, ii, 613.
- ¹⁸ Fishberg, A. M.: *Loc. cit.*, p. 546.
- ¹⁹ Janeway, T. C.: *Arch. Int. Med.*, xii, 755.
- ²⁰ Addis, T., and Oliver, J.: *The Renal Lesion in Bright's Disease*, 1931, p. 96.
- ²¹ Christian, H. A., and O'Hare, J. P.: *Oxford Medicine*, iii, p. 772 (38).
- ²² Bright, Richard: Goulstonian Lectures, *Medical Gazette*, 1833, xii, 381.
- ²³ Dunn, J. Shaw: *British Medical Journal*, 1922, ii, 1166.
- ²⁴ Shaw, H. Batty: *Hyperpiesia and Hyperpiesis*, Oxford Medical Publications, 1922.
- ²⁵ Ellis, A. W. M., and Marrack, J. R.: *Lancet*, 1923, i, 891.
- ²⁶ Calvert, E. G. B.: *British Medical Journal*, 1925, i, 64.
- ²⁷ Hunt, T. C.: *Lancet*, 1929, ii, 751.
- ²⁸ Korányi: *Zeit. f. klin. Med.*, 1897, xxxiii, 1.
- ²⁹ Volhard, F.: Mohr and Staehelin's *Handbuch der inneren Medizin*, Berlin, 1918, iii, 1197.
- ³⁰ Calvert, E. G. B.: *Loc. cit.*
- ³¹ O'Hare, J. P., Walker, W. G., and Vickers, M. C.: *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, 27.

- ³² Turnbull, H. M.: Quoted by Ellis and Marrack, *loc. cit.*
- ³³ Lewis, T.: *Diseases of the Heart*, 1933, p. 234.
- ³⁴ Moore, R. Foster: *Medical Ophthalmology*, 1922, p. 154.
- ³⁵ Evans, P. J.: *Brit. Journ. Ophthalmol.*, 1933, xvii, No. 5.
- ³⁶ Allbutt, T. Clifford: *Loc. cit.*, p. 54.
- ³⁷ Christian, H. A.: *Journ. Amer. Med. Assoc.*, 1926, lxxxvii, 931.
- ³⁸ Bell and Clawson: *Arch. Path.*, 1928, v, 939.
- ³⁹ Granger: *Journ. Amer. Med. Assoc.*, 1929, xciii, 820.
- ⁴⁰ Lewis, T.: *Loc. cit.*, p. 64.
- ⁴¹ Allbutt, T. Clifford: *Loc. cit.*, p. 64.
- ⁴² Fishberg, A. M.: *Loc. cit.*, p. 544.
- ⁴³ Volhard, F. and Fahr, T.: *Die Brightsche Nierenkrankheit*, Berlin, 1914.
- ⁴⁴ Fahr, T.: *Virchow's Arch. f. Path. Anat.*, 1919, ccxxvi, 119.
- ⁴⁵ Idem: Heucke and Lubarsch's *Handb. d. Path. Anat. u. Hist.*, Berlin, 1925, vii, 405.
- ⁴⁶ Volhard, F.: *Verhandl. d. deut. Gesellsch. f. inn. Med.*, 1923, xxxv, 134.
- ⁴⁷ Keith, N. M., Wagener, H. P., and Kernohan, J. W.: *Arch. Int. Med.*, 1928, xli, 141.
- ⁴⁸ Fishberg, A. M., and Oppenheimer, B. S.: *Ibid.*, 1930, xlvi, 901.
- ⁴⁹ Moore, R. Foster: *Loc. cit.*, p. 59.
- ⁵⁰ Wagener, H. P., and Keith, N. M.: *Arch. Int. Med.*, 1924, xxxiv, 374.
- ⁵¹ Salus: *Med. Klinik*, 1931, xxvii, 1885.

REPORT ON TWO CASES OF PSITTACOSIS

BY

E. J. PYE-SMITH, M.A., B.CHIR.

AND

DENTON GUEST, M.D.

PATHOLOGIST, HUDDERSFIELD ROYAL INFIRMARY

With a Note on the Serological Investigation of the Two Cases by S. P. BEDSON, M.D., M.Sc.

The two cases described occurred in Huddersfield during April, 1933, in the house of a local millowner. Resident in the house were the owner and his wife, their son, and two maids, one of whom (S. H.) and the mistress (E. H.) contracted the disease.

CASE I

S. H., a female aged 41, had a chronic duodenal ulcer. On April 10th, 1933, she complained of chilliness and headache. She was first seen on April 12th, when her temperature was 103° F., and she was complaining of generalized aching, especially in the back, and of severe occipital headache. A troublesome dry cough was present, but except for a furred tongue there were no physical signs. On April 13th the air entry to the right base was diminished, but it was not until the 17th that definite signs of consolidation in the right base appeared. During this first week the temperature remained high, the pulse rate was not correspondingly raised, and the respiration rate was never more than 37. The aching passed away, an irritating cough with very little sputum persisted, the tongue remained thickly furred, and the bowels were loose. The patient had vivid hallucinations during this week. On April 19th the temperature reached 105° F., the pulse rate was 108, and the respiration rate 35.

On April 20th a Widal test was performed for typhoid, paratyphoid A and B, *B. aertrycke*, *B. enteritidis* Gaertner, and *Br. melitensis*; also the blood was cultured aerobically. The Widal reaction was negative for all except *Br. melitensis*, which organisms were agglutinated to a titre of 1 in 50, with slight agglutination to a titre of 1 in 125 after standing overnight. The blood culture proved sterile. At this stage, in view of the presence of several budgerigars in the house, an infection by psittacosis virus was thought to be possible. Accordingly sputum was collected on April 21st for bacteriological examination and for injection into mice as described later. No tubercle bacilli were detected in the sputum. Direct Gram films showed some streptococci and pneumococci, and cultures confirmed the presence of these organisms. On the same date the faeces were examined for organisms of the typhoid-paratyphoid groups, with negative results.

During the second week of illness the patient's general condition was poor. There was cyanosis at times, and the pulse was intermittent. Insomnia was troublesome, there was profuse perspiration, and the stools were frequent, fluid, and most offensive. On April 26th the temperature dropped