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COMMUNICATIONS

ARTERIO-SCLEROSIS AND THE EYE

THE RICHARD MIDDLEMORE POSTGRADUATE LECTURE, 1919*

BY

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I MUST first express my gratitude to those who have done me the honour to invite me to deliver the Middlemore Postgraduate Lecture this year. The idea of the lecture, I believe, is that the subject chosen should be one that is of interest to all members of the profession and it is with that end in view that I have selected as my subject arterio-sclerosis and the eye.

There can be no question, I think, as to the extreme importance of this subject to our patients, to the practitioner of general medicine, and to the ophthalmic surgeon.

In considering the subject of arterio-sclerosis the first point of importance to remember is that this is not a disease of itself, but rather the result of several different pathological processes, some of which are but dimly understood.

This subject is best divided into three groups :

First group, called Hyperpiesia by Clifford Allbutt,¹ characterized by simple high tension, without signs of arterial or renal disease.

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Second group: Arterio-sclerosis with associated high tension, renal, and heart changes.

Third group: Chronic nephritis, with secondary high pressure, arterio-sclerosis, and heart changes.

Hyperpiesia.—In many ways this is the most important group of cases from our point of view, for reasons which I shall endeavour to show.

It was Clifford Allbutt¹ who recognized that high pressure preceded actual arterial changes, and it is to this condition that he gives the name of hyperpiesia.

If treated appropriately, he states, it may be cured, or at any rate recur with less persistence. On the other hand, if neglected, it tends to recur and to progress, and ultimately to become associated with true arterio-sclerotic changes. These facts show that high arterial blood pressure is at any rate one of the earliest signs of arterio-sclerosis; and if not a direct cause, is, seeing that it may be made to disappear without arterio-sclerosis resulting, at any rate associated with conditions which give rise to this condition.

Williamson² in a very practical paper on this subject, states that it is now generally recognized that in hyperpiesia, the increased resistance to the blood flow is associated with a contraction of the muscular coat of the medium and smaller arteries, causing a diminution of their lumen. This fact was first emphasized by W. Russell³ and called by him "arterial hypertonic contraction."

Russell's explanation of the phenomenon is as follows:

Toxic substances cause a hypertonic contraction of the arterioles and of the arteries, from as large as the brachial downwards. That an increased pressure is thus caused, which if recurring or continuous, leads to hypertrophy of the muscular coat of the arteries.

"If hypertonus persists, it must lead to hypertrophy, hypertrophy being the normal result of such a condition."

According to Osler⁴, the changes in these cases are not in the heart, or main drainage system, nor in the supply pipes, but to keep up the normal irrigation in the capillary beds, there has to be a widespread increase in pressure in the smaller arteries. He believed that the primary mischief lay between the capillary wall and the lymph space, or as he graphically put it: "There is a row between the manufacturer, the middle man, and the sanitary authorities." In consequence of this, an increase of pressure is necessitated in the supply pipes to overcome this.

Mackenzie⁵ states that the arterial pressure is maintained by the force of the left ventricle, the peripheral resistance, and the elastic recoil of the arteries, and unless the pressure is kept up there is not a regular and sufficient supply of blood to the tissues. He

believes that there is an intimate association between the heart and the tissues, whereby the supply is moderated to their requirements.

As age advances three chief changes occur in the blood-vessels—

(1) The elasticity of the arteries diminishes, *i.e.*, they become more like rigid tubes and there is no longer the same equable pressure during diastole. Therefore the pressure must be increased during the ventricular systole to compensate for this.

(2) There may be increase of the muscular tissue in the arterioles, which implies an increase in functional activity, with increase in the peripheral resistance.

(3) There is great diminution in the capillary fields, owing to thinning and wasting of the skin and subcutaneous tissue, causing a considerable narrowing of the passage of outflow.

According to Mackenzie⁵, the conditions which induce degenerative changes in the arterial system are—

- (1) High blood pressure ;
- (2) Toxic conditions ;
- (3) Senile changes ;

and he lays special stress on the obliteration of the capillaries, which causes degenerative changes in the heart, and narrows the communication between the arterial and venous system, entailing more work on the heart in forcing blood through the constricted area.

In what type of patient, then, is it that these changes are most liable to occur?

Osler⁴ says it is the man who works hard, drinks hard, and smokes hard, particularly the keen business man with many responsibilities, and also occasionally gouty or neurasthenic persons. To these, one may truthfully add, I think, the man who plays hard and loves hard. In fact it is the penalty of the man who adopts as his life's motto : "Whatsoever thy hand findeth to do, do it with thy might."

The next point to consider is the symptoms that such patients complain of.

Williamson² gives the following, which I have arranged in two groups :

(1) Heaviness or fulness of the head, drowsiness, insomnia, and fatigue especially in the morning. Inability to concentrate, despondency, giddiness, noises in the ears, migraine, neuralgia, and nervousness.

(2) Local syncope of the extremities, rheumatic pains or cramps in the limbs, tendency to hæmorrhage, hæmoptysis or epistaxis, dyspnoea on exertion, and intermittent polyuria.

On thinking over this list, we find that we, as ophthalmic surgeons, are frequently consulted for many of them, on the supposition that they may be caused by eye strain or want of glasses.

It is the symptoms placed in the first group, which are more usually complained of by our patients, and I should like to add to them, headaches on waking in the morning, and pains in the muscles at the back of the neck. The headache that patients complain of when they first wake, or that even wakes them up in the night, but passes off after a cup of tea and getting up, is, I believe, never caused by the eyes and always raises a suspicion of high blood pressure in my mind. At the same time it is not an unusual complaint of women at the menopause. Pain at the back of the neck again may be caused by errors of muscle balance, particularly exophoria, but this is more so in young subjects, and when occurring for the first time in middle age, is, I believe, a symptom suggestive of raised pressure.

Cases of migraine again are frequently sent to the ophthalmic surgeon to discover if the attacks are caused by eye strain. In my experience, it is the exception, rather than the rule, to find an error of refraction sufficient to account for the condition. I am not implying that migraine is usually caused by arterio-sclerosis, but in those patients who have their first attack somewhere about the age of 50, with tendency to frequent repetition, I believe the trouble often lies in heightened blood pressure.

Giddiness is another symptom which, to my mind, is rarely caused by eye strain or refractive error, though sometimes patients with astigmatism will complain of this, and are relieved by appropriate glasses. Those cases of giddiness which come on, on change of position, such as getting up after sitting in an easy chair for some time, or getting out of bed in the morning, seem obviously due to circulatory disturbance, and yet I have had many people sent to me to have their eyes tested for glasses on account of this symptom, the confusion arising, I believe, from the fact that the patient was reading in the chair before getting up.

Williamson² also draws attention to the fact that the symptoms of hyperpiesia may be mistaken for neurasthenia.

First, then, we see that there are many symptoms of hyperpiesia which are liable to be confused with those caused by eye strain.

Secondly, all the medical authorities whom I have consulted agree that the most important consideration, as regards the prognosis and treatment of the hyperpietic condition, is its early recognition.

Thirdly, we, as ophthalmic surgeons, see an enormous number of patients between the ages of 40 and 55, the common age of its occurrence, for the purpose of ordering presbyopic glasses.

Thus, a heavy responsibility is ours if in the ordinary routine examination of presbyopic subjects, we miss a case of hyperpiesia, and are content to order a pair of reading spectacles, without going

further into the case when the symptoms are suspicious, and the eyes insufficient to account for them. Is it possible, then, to diagnose from the condition of the retinal arteries whether hyperpiesia is present?

Bardsley⁶ states that in simple high tension the following manifestations may be found:

(1) The vessels have an appearance of uniform distension and fulness.

(2) The light streak is broadened out, it may be greatly increased, apparently reaching almost the whole breadth of the vessel.

(3) The light streak is very much brighter than normal, the brilliancy increasing with the increase of tension, until with very high tension it becomes like bright copper wire (not silver wire).

(4) The tight arteries indent the veins; with medium high tension they indent them slightly, with very high tension they indent them deeply, leading to back pressure and its consequences.

The following signs, he states, indicate actual sclerosis:

(1) Irregular tortuosity, especially of the smaller twigs.

(2) Increased brilliancy of the light streak, while at the same time the light streak appears narrower and more central.

(3) Irregularity of the calibre and beading of the arteries.

(4) General diminution in the size of the vessels and silver wire reflex show advanced sclerosis.

He confirmed his results, by the injection of solutions of adrenalin chloride on healthy adults, the difference in the vessels before and after injection being noted.

He goes so far as to say that it is possible to indicate roughly the actual height of the blood pressure in mm. of Hg. from the observation of the retinal vessels alone.

Where there are no signs of sclerosis, he says:

(a) Full arteries with broad light streak and very slight indentation of the veins indicate a blood pressure of 140-150 mm. of Hg.

(b) Very brilliant broad light streak with deeper indentation, and slight signs of obstruction indicates 150-160 mm. of Hg.

(c) Very brilliant broad light streak with apparent obliteration of the veins, indicates a pressure of 160-180 mm. of Hg.

But where the signs of advanced sclerosis are present, the veins may be indented and nipped at lower tensions.

Bardsley also emphasizes the pitfalls that may arise; namely (1) High error of refraction. (2) Acute toxæmia. (3) Failing heart.

Keeping these three liabilities to mistake in mind, Bardsley thinks it is possible for the ophthalmic surgeon to distinguish by means of the ophthalmoscope the signs of increased blood pressure and to differentiate between that and arterio-sclerosis.

Personally, whilst recognizing the value of Bardsley's observations

According to Oliver⁷, the average normal pressures
between 40 and 60 = 125 to 135 mm. of Hg.
between 60 and 80 = 135 to 165 mm. of Hg.

adding or subtracting 15 mm. to get the outside limits of normal variation.

So the two cases of 59 and 56 with a blood pressure of 170 and the doubtful case of the woman of 49 with a blood pressure of 170, are the only cases that were badly outside possible normal limits, yet whom one passed as normal as regards their retinal circulation.

Probably every man practised in the examination of retinal blood vessels looks out for some particular sign more than another, and comes to lay more stress on this than any other, and I must admit that the sign of heightened pressure which has impressed me most, is the small size and pale colour of the arteries, quite apart from thickening or exaggeration of the light reflex, and I believe you can safely say that you never see a nice fat artery with an ordinary light reflex or even an exaggerated light reflex in high blood pressure. This is rather what one would expect, remembering Russell's observation on arterial hypertonic contraction.

Again, where an artery crosses a vein in a normal patient, the light reflex of the latter is continuous practically up to the artery, but if the pressure is raised, before one sees obvious pinching or indentation at the crossing, there is an absence of light reflex for some short distance up and down the vein, due I suppose to some flattening of the curvature with consequent alteration of the reflex.

It is these two symptoms, then, which to me show the earliest indications of an elevation of the blood pressure pure and simple, before the onset of any signs of actual sclerosis.

Williamson⁸ in his lecture says that it is necessary to emphasize the importance of persons of middle age having their blood pressure measured at intervals in order that the early development of hyperpiesia may be detected and that arterio-sclerosis may be prevented. I rather think that the ophthalmoscope is in many ways a more accurate instrument than the manometer, and certainly will give more information as to the exact condition of the smaller blood-vessels, considering the fact that the retinal arteries can be examined in their natural condition during life under a magnification of 15 diameters by direct ophthalmoscopy.

Group II

Arterio-sclerosis with associated high tension, renal and heart changes.

Hitherto we have been considering the pre-sclerotic stage of arterio-sclerosis, *i.e.*, before the disease has persisted sufficiently long or progressed so far as to cause permanent damage to the

blood-vessels. We must now consider the more advanced changes that we meet with, when actual and permanent damage has occurred.

Here it is necessary to refer to the classical work of Marcus Gunn.⁸ He was the first in this country to draw attention to the importance of and to describe accurately the changes in the blood-vessels met with in this condition.

His work is so well known to you and has been quoted so often that it is not necessary here to do anything more than enumerate the various signs that he described. These observations have been universally confirmed, and their extreme value recognized again and again.

They were as follows :

- (1) Irregularity of the lumen of the retinal vessels.
- (2) Tortuosity of the arteries.
- (3) A very narrow and bright central light streak which may show a series of brighter points at intervals. These changes being of chief importance, when they involve the secondary and tertiary branches of the retinal artery.
- (4) Loss of translucency of the arterial walls.
- (5) Obstruction of the blood flow in the veins where they are crossed by arteries.
- (6) Oedema of the retina.

The importance of some of these signs has proved to be greater than others and a few more have been added, but they still remain the fundamental and classical signs of arterio-sclerosis.

de Schweinitz,⁹ another authority on this subject, divides the signs of persistent high tension into those that are suggestive, and those which are pathognomonic:

The suggestive signs are : A. Uneven calibre and undue tortuosity of the retinal arteries ; B. Increased distinctness of the central light streak ; C. An unusually light colour of the breadth of the artery and alterations in the course and calibre of the veins.

The pathognomonic signs : A. Changes in size and breadth of the retinal arteries of such character that a beaded appearance is produced ; B. Distinct loss of translucency ; C. Decided lesions of the arterial walls and white stripes of perivasculitis ; D. Alternate contractions and dilatations of the veins : indentations of the veins by stiffened arteries in such a way as a solid rod would indent a rubber tube when lying across it. The vein may be :

(a) flattened slightly, (b) pushed aside, (c) its calibre contracted, so that beyond the point of crossing there is an ampulliform dilatation.

In addition there are changes in the venous walls, white stripes, oedema of retina, linear extravasations, and haemorrhages.

de Schweinitz⁹ also lays stress on the fact that these changes may occur at any age, provided the raised blood pressure is persistent.

According to him, the earliest signs are :

(a) Corkscrew appearance of certain twigs, either round the macula or small branches of larger vessels, especially single vertical twigs from a transverse branch.

(b) When a vein crosses over an artery, it is like a strap over a solid tube, and when the vein passes under an artery it is like a solid tube over a strap. The changes are first noticed in the inferior temporal artery, but personally I have found them as often in the superior temporal artery.

(c) A congested appearance of the optic disc, giving it a dull red appearance,

Foster Moore¹⁰ lays most stress on Gunn's fifth sign, i.e., obstruction of the blood flow in the veins where they are crossed by arteries, but with emphasis more on the course of the vein rather than on any obvious sign of damming up of the blood, which is found very rarely.

The more marked the sclerosis, he states, the greater is the displacement of the vein. Normally, where an artery crosses a vein, at whatever angle, the line of vein at, and on each side of the crossing, is not even slightly diverted. In the earliest stages of sclerosis of the artery, the vein will remain unaltered, but will be hidden under the artery and for a narrow margin on each side, owing to the loss of translucency of the arterial wall. As the thickening of the arterial wall progresses the line of the vein comes to be diverted.

In a case of marked arterio-sclerosis, in which the vessels approach each other obliquely, the vein is at first diverted so as to lie alongside the artery, it then passes under it, and having reached the other side, again lies alongside the artery for a very short distance before continuing the former line.

In a case of very severe sclerosis, the vein though meeting the artery at an angle of say 15° , and leaving it at a similar angle, passes under it at right angles.

The same phenomenon may be observed where a vein crosses over an artery.

Evidence of obstruction of the venous flow.

One would expect that where a hard and thickened artery crosses a vein, obstruction to the blood in the latter would be caused, with consequent dilatation of the vein, a condition which has been described as "banking." As a matter of fact, Foster Moore says this is rarely seen, and my own experience as regards this is the same, though every now and then it is present beyond doubt, and is very striking when seen, though of all the cases I have examined in the past year, I can only recall three in which it was unmistakable.

The most marked case I ever remember was in a woman, aged

60, with a blood pressure of 240. The superior temporal artery crossed the superior temporal vein about one disc's breadth away from the disc. From the crossing to the disc the vein and artery were the same size, but beyond it the vein was quite twice the size of the artery, and very dark in colour. Elsewhere in the retina, where the arteries crossed the veins, there was pinching of them, but no evidence of interference with the circulation.

To discuss for a moment the importance of these various signs:

(1) Irregularity of calibre of the arteries. To me this is one of the commoner and more important signs of definite sclerosis, especially if one adds general diminution in the size of the artery as well. The normal ratio of artery to vein, according to Leber, is 2 to 3. In arterio-sclerosis I should put it at 2 to 4.

In following the course of the artery towards the periphery it can be seen to be narrowed for a short distance, and then to return to its original size; the variations are not gross, but quite unmistakable, and may be repeated several times in the course of the vessel.

One case I came across illustrates the importance of this sign. He was a man of 63, and his blood pressure was 210, and there was some albumen in the urine. There was no sheathing, no bright reflex, and no pinching of the veins, yet the arteries were small and showed definite variations in calibre.

This irregularity is not always present, but it is a most certain and valuable sign of high pressure when it is.

(2) Tortuosity of the arteries is one of the rarer and less valuable signs, and is one that is often seen as a physiological condition. When the small "corkscrew" vessels running towards the macular region are present, it is a corroborative sign, but I believe by no means so common as many of the others.

(3) Central light reflex exaggerated.

It is not only a bright reflex in the artery which is important; this is often seen physiologically. It is the hard sharply defined bright streak that indicates high blood pressure, and is a very important sign of this. At the same time I have been struck by several cases of very high blood pressure that showed practically no exaggeration of the reflex at all, other signs being present in abundance, as for instance in the case quoted above.

(4) Loss of translucency of the arterial wall.

This, when present, is again a very characteristic sign of severe sclerosis. You all know how the vein looks as if a gap had been taken right out of it, the artery apparently running through the middle of the gap, the explanation being that the vein is hidden by the thickened arterial wall which itself is not visible.

With one sign or another then, a hard artery is, as a rule, unmistakable. It looks hard. It is small in size and gives one the

impression of a round solid rod. I believe this to be due to a slight shadow, as it were, cast on the retina behind it, making it stand up in relief, and its reflex is usually, though not invariably, thin and bright, and its general colour pale.

(5) Where the artery crosses a vein.

1st. The vein is frequently pushed out of its direct course.

2nd. There is the appearance described by Foster Moore and quoted above. I have seen this, but must confess it had not impressed itself on my notice as very common.

3rd. There is loss of light reflex from the vein for a varying distance up and down from the arterial crossing.

4th. The vein appears to be pinched or indented; it is different from the gap appearance described above and there is no evidence of "banking;" it more resembles the condition of a rubber tube with a piece of string tied round it.

6th. Oedema of the retina—generalised oedema of the retina have not seen, but localized areas of oedema I have come across on two occasions only.

The congested appearance of the disc emphasized by de Schweinitz is seen in some cases, but is hardly as striking as the changes enumerated above.

In addition to these signs of arterio-sclerosis in the retina, Foster Moore¹⁰ describes a condition to which he ascribes the title of arterio-sclerotic retinitis, and differentiates it from renal retinitis. In addition to the ordinary signs of sclerosis, retinal exudate is present in the form of small scattered white spots, irregularly circular in outline and variable in size, with no oedema or pigmentary disturbance, and the spots are usually scanty. Between the macula and disc is a common site for their occurrence, and sometimes a partial star figure is present at the macula. The white dots are slow to develop and slow to undergo changes, the dots may become confluent and may completely disappear and leave no trace. In addition, larger areas or small white plaques may be seen, usually in the central region. Pipe stem sheathing of the arteries may also develop. The changes occur very frequently in one eye only, though the ordinary signs of sclerosis are present in both eyes.

Pathology

Before passing to the consideration of the pathological changes that occur in the retinal vessels as a result of arterio-sclerosis, a few words must be said about their normal structure.

The central artery of the retina¹¹ from its entrance into the nerve until it reaches the lamina cribrosa has the structure of an ordinary small arterial twig. The intima consists of 3 layers: (1) elastic membrane; (2) a thin layer of subendothelial tissue; (3) endothelium.

When the lamina cribrosa is reached, the lumen becomes narrower, which must tend to cause eddies and so favour the occurrence of endarteritis and it may also tend to arrest foreign bodies circulating in the blood.

In addition certain structural alterations are observed.

The surrounding connective tissue becomes much denser, the elastic membrane is replaced by a feltwork of fine fibres, which separate the endothelium from the outer layers, and the subendothelial tissue seems to disappear. Therefore a retinal artery appears to consist of an endothelial lining and a connective tissue wall in which elastic and muscular fibres are present, but in the smallest twigs both elastic and muscular fibres disappear.

The central vein has a more delicate wall, consisting of connective tissue with curly elastic fibres, muscle cells are scanty, there is no true elastic membrane or subendothelial tissue, so that the endothelium rests directly on the connective tissue wall.

Within the eye there are no elastic elements in the walls of the retinal veins, which consist of endothelial lining and a connective tissue wall. Any or all of the structures may be diseased in arteriosclerosis, and the difference in structure between the retinal and central vessels produce differences in the microscopical lesions which are found.

In the central artery the intima is usually chiefly affected, and in the majority of cases all the lesions are inside the elastic membrane. The membrane may be thickened and itself split into two or more layers. Inside are layers of cells among which small curly elastic fibres are evident. These are often of some size and may form small elastic membranes within the true one, but they never reach all the way round. The lumen is usually lined by a single layer of well-formed endothelial cells, even when the layers beneath are extremely degenerate, which suggests that the essential lesion is not a proliferation of the endothelium, but of the subendothelial layers.

Changes in the retinal vessels.—Disease of the intima takes the form of cellular proliferation but no elastic fibres are found.

Therefore, Coats concludes, the endothelium of arteries is incapable of forming elastic fibres, but that the subendothelial tissue, under pathological stimulation, is capable of laying down new deposits.

This subendothelial tissue being absent in the retinal vessels, no elastic membrane is normally laid down, and under pathological stimulation no new fibres are found in the intima.

In the retina the connective tissue wall is often greatly thickened and results in hyalin degeneration, and when the connective tissue wall thickens it encroaches more or less concentrically on the lumen, but when the intima is affected narrowing is always eccentric, the lumen being displaced to one side.

Coats concluded that white lines along the vessels are probably due to thickening of the connective tissue coat, whilst a simple narrowing of the lumen is due to endothelial proliferation. Disease of the intima is most probably due to a circulating toxin, whereas thickening of the connective tissue wall is probably compensatory for raised blood pressure.

The significance of changes in the retinal arteries

The retinal arteries, being end arteries, resemble the blood-vessels which supply the large ganglia of the brain, lesions of which lead to apoplexies (Knapp).¹²

Coats,¹¹ however, states that the ocular circulation must not be looked on as a mere expansion of the cerebral circulation, in the same sense as the nerve is of the brain. He states that it by no means always shares in disease of the brain, the angio-sclerotic processes being exceedingly irregular in their distribution, one region may be affected whilst another is normal.

Thus at the lamina cribrosa, which, as shown above, is a favourite site for endarteritic processes, the artery may be almost obliterated by a knob-like nodule and yet be practically normal a millimeter or two up the nerve. He says, therefore, that whilst disease of the retinal vessels is not a proof of disease of the cerebral circulation, it furnishes a presumption in favour of its existence. Conversely, absence of retinal change is no positive proof that other vascular areas are intact.

Again, fairly extensive disease of the retinal vessels may exist without ophthalmoscopic evidence ; but in spite of this, he concludes that they are the best indicator we possess as to the general state of the vessels.

Raehlman¹³ in 210 cases of arterio-sclerosis found nearly half showed changes in the retinal vessels.

Hertel¹² says that a positive finding of sclerosis of retinal vessels assumes a similar condition of the cerebral vessels, but that the reverse does not apply.

Foster Moore¹⁰, out of 44 cases of cerebral haemorrhage or thrombosis, found that 30 per cent. showed no evidence of disease in the retina ; 27 per cent. mild or moderately severe disease ; 43 per cent. severe disease and arterio-sclerotic retinitis.

Gunn quotes 17 cases of sudden onset of hemiplegia ; out of which, 7 had definite retinal vascular disease, 3 slight vascular changes, and 7 showed no decided retinal changes.

Again, taking 46 cases of arterio-sclerosis Foster Moore found gross vascular lesions occurred in 21. In 25 cases there was no evidence of this ; 18 of them were still alive. As a result he concludes that the relation between the condition of the retinal arteries and the arteries of the brain is both striking and close.

Finally, of the 156 cases of various retinal vascular lesions which¹⁴ I attempted to trace to the end, out of 49 in whom the cause of death was definitely known, 22 died of cerebral haemorrhage or stroke, and possibly more, though the death certificates were too vague to be certain in all cases.

Group III

Chronic nephritis with secondary high pressure—arterio-sclerosis and heart changes.

In this group the primary lesion is in the kidney, associated with fibrosis, which leads secondarily to high blood pressure, sclerosis of the arteries and hypertrophy of the heart, as opposed to those cases which we have already discussed in Group II, which start with hyperpiesia, then develop arterio-sclerosis, eventually leading to sclerosis of the kidneys.

There are two important divisions of chronic nephritis, that of the infections and that of the intoxications, e.g., gout, lead, and alcohol.

(4) To diagnose between the primary nephritic and the primary arterio-sclerotic cases is not often difficult.

In the infectious group the history is generally distinct, the patients are younger and have not the vigour of the arterio-sclerotic cases, whilst lead and gout toxæmia when present is generally manifest.

The urinary changes differ from the arterio-sclerotic form in the persistent low specific gravity, lower nitrogen output, the more constant presence of albumen, and the persistence of granular casts.

The symptoms are more renal and cerebral in the nephritic, cardiac in the arterio-sclerotic.

Osler says that marked ocular changes are more common in the primary nephritic form and the retinal changes are degenerative, not simply haemorrhagic.

In the nephritic class remarkable variations are found in the arterial tension, persistently high in some cases, in others quite moderate, although associated with extreme arterio-sclerosis and hypertrophy of the left ventricle.

With regard to the changes found in the retina in these cases, two factors are responsible, the one vascular and the other toxic, and according as one or other of these predominates, so the retinal changes vary.¹⁰

In chronic parenchymatous nephritis, the vascular factor is much less prominent than the toxic. The blood pressure may or may not be much raised and the retinal changes are indicative of a toxic element. The picture one gets is as follows:

Numerous "cotton wool" patches scattered about, and associated with these much oedema, which may lead to retinal detachment. Retinal haemorrhages are not very plentiful, but may form a fringe

round the areas of exudate. The well known star shaped figure at the macula is not often seen.

A case that I saw recently of this type showed numerous cotton wool patches, much albumen in the urine, blood pressure of 200 mm. of Hg. and yet the arteries were only very slightly affected.

In chronic interstitial nephritis with which high blood pressure is always associated, the vascular factor predominates over the toxic, and the retinal vessels show signs of sclerosis, haemorrhages are more plentiful, and the star figure at the macula is frequently present. "Cotton wool" patches are much less plentiful and not so extensive as in the former variety.

In arterio-sclerosis, the retinitis which develops is probably, as Foster Moore¹⁰ states, due to disease of the retinal vessels and corresponds with the vascular moiety of renal retinitis, but as the disease progresses the vascular disease in the kidney may so seriously involve the kidney substance, as to lead to renal insufficiency; so "cotton wool" patches, indications of this insufficiency, may appear in the retina.

Prognosis

The important question in these cases is not the prognosis of the eye condition; this is of secondary importance when compared with the prognosis as regards life.

Allbutt in speaking of hyperpiesia states that it may be cured or at any rate recur with less persistence, but if neglected ultimately leads to arterio-sclerosis, thus emphasizing the importance of early recognition of the condition if one is to be able to give a good prognosis.

Looking at it from the side of the general physician, Osler, with all other authorities, emphasizes the fact that the high pressure is not the disease, but a compensatory and salutary state, and in his experience the pressure may be kept at a reasonable height by treatment but that it never falls to normal again. In spite of this, however, a man may enjoy good health and do hard work with high pressure, whipcord arteries, and a hypertrophied heart.

Mackenzie⁹ again found that some arterio-sclerotic patients lived for years, whilst others died of heart failure and apoplexy. These latter were always associated with gross evidence of disease of the heart, kidneys, and blood-vessels. In those who survived an ordinary life, there was no lesion of these organs more than one would expect from the age of the patients.

Therefore, in giving a prognosis, it is necessary to enquire into the condition of the kidneys, the state of the arteries, and the condition of the heart, with especial reference to its size and its functional efficiency.

James Taylor¹⁵ also agrees that the prognosis depends, not so much on the actual appearance of the vessels as on the associated visceral changes, especially renal and cardiac.

In 1916¹⁴ I undertook an inquiry into the prognosis *re* life of cases of vascular disease of the retina and found, as other observers have done, that the expectation of life varied enormously. To obtain a more accurate idea as to the prognosis, the cases were divided up according to their ages into decades and it was found that the age of onset made a great difference to the prognosis, it being much more serious in young subjects than in older ones, but the factor which made the greatest difference was the presence or absence of albumen in the urine, i.e., renal involvement.

The conclusions I drew from the study of these cases were, that retinal lesions were considerably more common in women than men, and that the cases were most numerous between the ages of 60 and 70, and next between 50 and 60. That the older the patient, the better the prognosis, as regards life, irrespective of the presence of albumen in the urine to a large extent. Whilst the younger the patient, the worse the prognosis, and especially so if albumen was present in the urine.

As regards the prognosis *re* vision. In many cases with haemorrhages the sight is not perceptibly affected as long as the macular region remains clear. In the grosser lesions, however, such as venous thrombosis, if the lesion is in the central vein, very little recovery is to be expected, and the eye may become glaucomatous. When only a branch is involved, it is often surprising how the sight will improve, but as the temporal vessels are almost always the ones involved, the macular usually suffers, but the sight may clear up eventually, leaving a vision of about 6/18 to 6/12, but the sight is patchy and uneven.

Treatment

This, I feel, hardly comes within my province to talk about; at the same time there are certain general lines which it is important for us, as ophthalmic surgeons, to know, as we are expected at times to indicate lines of treatment and give general advice to our patients.

The first and most important thing is to dispel anxiety and apprehension, as worry, nervousness, and mental strain increase the trouble.

Then, Osler's recommendations are worth remembering: A. A thorough study of each case is required; B. Determine the nature of the case, whether one of simple hypertension, arterio-sclerosis, chronic nephritis, or all combined; C. Reduce speed; D. Lessen intake, ordering a diet of low proteid content with large quantities of fluid; E. Elimination should be promoted in every way, by kidneys, bowels, and skin.

Next, it is important to remember that the high tension is not the disease, as Lauder Brunton, Mackenzie, and others have emphasized, nor is it a bad thing to be got rid of at all costs. As in most other diseases, it is most important to look round for possible sources of infection and toxæmia, the teeth should be carefully examined for pyorrhœa, and if present, proper treatment should be adopted.

Indigestion and the possibility of toxic absorption from the bowels must be most carefully gone into and constipation rigorously dealt with, if present, not only on account of the toxæmia caused, but also to avoid the harmful effects which may be produced by straining. This, I believe, is of the utmost importance.

Speaking generally, you want to place the patient under conditions giving the heart less work to do. After attending to the above, the question of diet next arises :

- (1) Reduce the bulk of each meal.
- (2) Reduce the proportions of those constituents of the foodstuffs which more particularly stimulate the cardio-vascular apparatus, e.g., various salts, soluble extractives, alcohol, etc.
- (3) Encourage proper mastication¹⁶ and insalivation, especially of soft amylaceous foodstuffs.
- (4) Substitute as much as possible, boiled for roasted forms of fish, fowl, beef, and mutton.
- (5) Reduce the proportion of animal and increase the amount of vegetable foodstuffs.
- (6) Tea, coffee, and tobacco should be reduced.

Such exercise as the patient can undertake without distress should be encouraged, at the same time remembering that some of these arterio-sclerotic patients are extremely vigorous and need cautioning against undue exertion.

As regards the eyes, avoidance of stooping, straining, bending, and lifting is of importance, as such tend to increase extravasation of blood into the retina and cause fresh hæmorrhages.

Ordinary care should be taken with light and print, but I see no reason for forbidding all close work, as is sometimes done.

Elsworth Smith¹⁷ gives sound advice, I think, when he says: "If the conditions in the eye are so grave as to threaten the integrity of the organ, the patient should be placed in bed, but if the condition is not urgent enough to demand complete rest in bed, then the patient shall be urged to pursue the even tenor of his way, free as possible from all sources of worry and strain."

Such then are a few broad rules for the general management of the arterio-sclerotic patients that we meet. For further details of treatment, I must refer you to such works as Lauder Brunton, "Therapeutics of the Circulation"; Oliver, on "Blood Pressure"; Bodley Scott, on "Some Modern Remedies," etc.

Before leaving the subject of arterio-sclerosis and the retina, I must refer to the work of Thomson Henderson,¹⁸ who devised an instrument for the purpose of measuring directly the height of the arterial diastolic pressure in the eye. His instrument is like the familiar Geneva lens measure, and is applied to the eye, usually through the lid, at its upper outer angle. He first showed that the intra-ocular fluid contents must lie at venous exit pressure, because this is the lowest attainable pressure of the intra-ocular circulation. The important point is, that the two pressures, venous exit and intra-ocular are in perfect equilibrium, so that if the intra-ocular pressure is raised by pressure of the fingers, the veins at their point of exit are constricted and the venous exit pressure is raised to the same level. The two thus rise together, and as the pressure is increased, it rises first to arterial diastolic pressure, and finally to arterial systolic pressure; when this point is reached the circulation ceases altogether.

By means of this instrument, we can obtain the exact index of the height that the diastolic pressure is above the intra-ocular pressure, or what is the same thing, the venous exit pressure. He puts it at 15 to 25 mm. of Hg.; that is to say, that the arterial diastolic pressure is only 15 to 25 mm. of Hg. above the intra-ocular or venous exit pressure. He has found it as high as 35 to 40 mm. of Hg.

Using the instrument, I have measured the diastolic pressure in several cases of normal and heightened general blood pressure, but I have not yet taken enough observations to come to very definite conclusions.

The pressure readings obtained with the instrument in eyes normal as regards tension, have varied from 9 m.m. of Hg. up to 17 mm., but to my surprise I have not found them vary appreciably with the height of the general blood pressure.

According to my results, the cases of highest general blood pressure, have not shown a corresponding rise in the pressure one obtains in the direct reading from the eye. I do not believe it is due to faulty technique, as this is not difficult if ordinary care is taken to see that the instrument is applied at right angles to the eye and besides, the results have been the same throughout. Nor is it due to an increased tension of the eyes, some were controlled by the tonometer and all the rest with the fingers, and they were normal as far as it was possible to judge. It is possible that a more direct relationship would have been found if the arterial diastolic pressure had been measured as well.

More recently Bailliart has introduced a new instrument, but, as far as I can see, the principle is the same as T. Henderson's, though the shape is different.

The method he recommends is as follows:

(1) Apply pressure until well marked pulsation is seen in the artery, then read off the force that has been employed, this gives the diastolic reading.

(2) Increase the pressure until the arterial pulsation is arrested. This gives the systolic reading.

(3) With the tonometer, take the height of the tension, whilst similar force is applied to the eye as in (1) and (2).

This gives the actual diastolic and systolic pressure in the retinal artery of that eye.

In normal eyes Bailliart found that the arterial blood pressure usually exceeds the chamber pressure by 5 to 10 mm. of Hg. during diastole, and by 30 to 35 mm. of Hg. during systole.

Assuming the normal tension of the eye to be 18 mm., this gives an average diastolic pressure of 25 mm. of Hg., and an average systolic of 50 mm.

Priestley Smith,¹⁹ as the result of many experiments, places the average chamber pressure at 24 mm. of Hg. The central vein pressure, he states, is slightly higher than this as a rule, and he concludes that the exit pressure in the central vein is on the average not less than 25 mm. of Hg. The pressure in the central artery of the retina, at the point of entrance, he states to be probably from 90 to 100 mm. of Hg. The pressure in the retinal capillaries calculated from the relative cross sections of the arteries and veins, he concludes, is not far removed from 40 mm. of Hg.

These observations on the direct blood pressure in the eye should prove of great value when a little more is known about them, and their normal ratio to the general blood pressure understood, and I believe there is here a great field for further investigation.

We must now leave the subject of blood pressure and the retina and pass on to another question of some importance. That is the relation between glaucoma and blood pressure. Is there any connection between the two, or is high blood pressure a causative condition of glaucoma? At first sight it would seem natural to suppose that the higher the blood pressure the higher would the ocular tension be. Recent researches have, however, not borne out this supposition.

Craggs and Taylor²⁰ conducted a research into the relation between systemic blood pressure and raised intra-ocular pressure.

They compared the blood pressure readings in patients of the same age, with and without glaucoma. They found normal tension with very high blood pressure, and conversely high tension eyes with normal blood pressure.

In their glaucoma cases, the average systemic tension was not raised above the normal, and they came to the conclusion that arterial tension was very far from being a necessary factor in the causation of glaucoma.

Again, A. MacRae²¹, after comparative measurements in glaucoma patients and controls, came to the conclusion that an altogether exaggerated importance had been given to the blood pressure as a factor in maintaining or increasing eye tension. He found that the blood pressure might alter greatly without any corresponding effect on the ocular tension being observable, and it was very doubtful if blood pressure was of any importance in the causation of glaucoma.

Foster Moore²² in his paper on intra-ocular tension with especial reference to its variations in general and local vascular disease, says, "It is clear that such variations as do occur in the tension of the globe, are not caused by or associated with a like variation in general blood pressure," and he came to the conclusion that a rise in blood pressure, as a result of arterio-sclerosis, does not lead to a corresponding rise in intra-ocular pressure.

My own observations lead me to the same conclusion as the above. At the same time, everyone is familiar with the appearance of retinal vascular disease, that is sometimes seen after an acute glaucoma, which has been relieved by operation. Then, again, I have three cases, all occurring in painters, whose cases I would like to mention.

1. Iridocyclitis with secondary subacute glaucoma, haemorrhage in retina. Blood pressure 160, aged 46 years. Both eyes operated on.

2. Aged 48 years, subacute glaucoma right eye and left eye. Blood pressure 200, arteries thick in both. Retinal haemorrhages right eye. Both eyes operated on.

3. Aged 49 years, Haemorrhages in right eye. No albumen or sugar in urine, May, 1916. Still haemorrhages in retina and tension full, March, 1917. Tension higher October, 1917. Trephined January, 1918.

All these men were painters. They had no albumen and no signs of lead poisoning and yet they had definite signs of arterio-sclerosis and sub-acute glaucoma associated with disease of the retinal vessels.

In a different category and quite a different type of glaucoma associated with vascular disease, is the glaucoma which is so liable to follow on cases of venous thrombosis. As a rule, the cases of this type that I have observed, have been rather acute with vascular engorgement, but recently I have had two cases absolutely quiet and free from all signs of congestion, but with a steamy cornea, T.+2, and the sight abolished.

Finally, I believe there are some cases of apparently a low degree of chronic glaucoma with tensions about 30 mm. Hg. (Schiötz) in whom one finds high blood pressure and signs of arterio-sclerosis. Their glaucomatous symptoms and tension are to a certain extent relieved by attention to their general health and treatment directed

to the reduction of their blood pressure. Cridland has drawn attention to this point.

Thus there do seem to be certain cases in which there is a definite connection between intra-ocular pressure and intra-ocular vascular disease and raised blood pressure, but in the large majority of cases, there is, I believe, no direct relation between the two.

There is yet one other eye disease which in some cases is definitely associated with arterio-sclerosis and that is, a chronic form of iridocyclitis. I do not mean to say that it is caused by the actual height of the blood pressure, but whatever the toxin may be that is causing this, it probably also accounts for the iridocyclitis. I have seen several cases of this type and one of them, typical of the others, I will now quote :

Patient is a lady aged 56. Teeth clean, no gastro-intestinal symptoms or constipation; some rheumatic pains in joints, and knuckles of fingers are slightly enlarged. She developed a quiet iridocyclitis in August, 1918, first in one eye, followed by the other. The pupils have always dilated fully, but there was much "K.P." and fibrinous vitreous opacities which clear up and then recur for no apparent cause. In the course of examination, I found the arteries small, hard, and pale, no gross obstruction of veins, but slight indentation of them, and on measuring the blood pressure I found that it was 200 mm. of Hg. Since then, she has had occasionally a small striate retinal haemorrhage and a white spot or two of retinal exudate which slowly clear up. The inflammation obviously falls chiefly on the ciliary body as she has had no definite adhesions, but what she has had on several occasions, are the small cysts just on the free margin of the iris, which Doyné²³ described under the name of "Guttate Iritis" and which he attributed to gout, and these I have found in other cases of this type. At the same time none of these patients had any symptoms that one could say were definitely "gouty" and there was no albumen in the urine.

So called "central senile choroiditis" is another condition which is sometimes associated with high blood pressure, though it is a fact that one does not find sclerosis of the choroidal vessels associated with retinal or cerebral arterio-sclerosis, a fact pointed out by Russ Wood.²⁴

The two following cases of this disease are rather striking :

(1) Blood pressure 270, arteries not grossly thickened but well marked central senile choroiditis; aged 79.

(2) Blood pressure 230, central choroiditis, no albumen or sugar, retinal arteries very small, variable in calibre, reflex not bright; aged 68. The condition closely resembled that known as "hole in the macula."

Nettleship²⁵ believed that central senile choroiditis resulted from

disease of the posterior ciliary arteries, and the two cases that I have quoted might well have been caused by this.

In now bringing my lecture to an end I do not wish you to think that I have exhausted the whole subject of the relation of arteriosclerosis to the eye. There is the question of optic atrophy and retrobulbar neuritis caused by pressure of the thickened wall of the carotid artery, and probably other complications that will occur to you. What I have endeavoured to do is to set forth the results of my own observations, at the same time quoting largely from recognized authorities on the subject, but what I did not wish to do was to copy out of a book all the facts that I could find and retail them to you.

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COLOUR BLINDNESS AND YOUNG'S HYPOTHESIS

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IT has been pointed out frequently as an objection to Young's hypothesis of vision that individuals who confuse red and green, and who, therefore, should be classed as either red blind or green blind, when they are told to describe a pure prismatic or diffraction spectrum, do not state that the end occupied by colours of long