An Address ON HYPERPIESIA AND ARTERIO- SCLEROSIS.

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SIR CLIFFORD ALLBUTT says that hyperpiesia is a malady in which at, or towards, middle life the blood pressure rises excessively—a malady having a course of its own and deserving the name of a disease, without any organic association other than cardiac hypertrophy and altered blood vessels, the raised blood pressure or hyperpiesis being a sign of the disease hyperpiesia.

It is clear that this disease may be missed by the clinician because raised blood pressure may be undetected by the finger, the cardiac hypertrophy may not be observed because coincident emphysema may obscure the maximum impulse of the heart, and alteration of the arteries in the beginning of the malady may be but slightly developed, or if well advanced may be obscured by the presence of much subcutaneous fat. It follows that the only certain way to detect the disease is by the use of the sphygmomanometer as a routine; an isolated observation or two made at any moment is useless; the blood pressure must be found to be raised whenever observation is made for at least four days—not only after a day's work, but, most important, just after a night's rest.

Extended pathological studies have shown that Sir Clifford Allbutt's contention that, if hyperpiesis is not transient—that is to say, if it is persistent—though it is a serious menace to decadent structures such as weakened arteries, it does not follow the clinical course of Bright's disease in any of its modes, must be modified. There can be no doubt that hyperpiesis, or raised blood pressure, may be shown at the bedside as well as at *post-mortem* examination to be coexistent with all the signs of grave kidney disease, even including hyperuraemia. Hyperpiesis has also that other feature possessed by many diseases of being able to cause the death of a patient apparently unaided by any other disease so far as present-day methods of *post-mortem* examination can show. Lastly, hyperpiesis may exist in a patient and be accompanied even to fatal issue by manifestations of so-called uraemia, and even retinitis, without the kidneys being diseased at all, or so slightly as to exclude the possibility that renal disease could have been responsible for the uraemia or retinitis.

It may be difficult to grasp the bearings of the terms "hyperpiesia" and "hyperpiesis" (that is, high tension); they may be compared with the terms "infection" and "fever." Hyperpiesis is the clinical sign of a diseased condition—hyperpiesia—just as fever is the clinical expression of infections, and in the course of time it may transpire that just as fever is the common clinical expression of different infections caused by different micro-organisms, so hyperpiesis may be shown to be the common clinical expression of different hyperpiesias caused by different pressor agencies. At the present moment it is not known what is the nature of the agent which causes hyperpiesis, so that medicine is in much the same position with regard to hyperpiesia as it was when the micro-organismal causes of fever were unknown.

This discovery of hyperpiesia is most momentous, because there is good reason to believe that several conceptions held by physicians and pathologists in the past must be discarded, or at least considered from quite fresh points of view, and be quite differently assessed. Already it is clear that the medical student of the near future will be no longer harassed by attempting to fit clinical pictures into the frames of the various forms of anatomically altered kidneys. The use of the term "uraemia," long known to be independent of an excess of urea in the blood, will probably give place to the use of the term "hyperuraemia" (*sensu stricto*), which, though unassociated with

any clinical manifestations, has become a most invaluable means of detecting whether the kidneys, whatever their anatomical configuration may be, are functionally incapable of discharging the duty of adequately excreting urea. Albuminuria and retinitis, so long held to be proofs of disease of the kidneys or of the retinal arteries, are probably rather tokens or signs that there is something circulating in the blood which, if removed or neutralized, would lead to the disappearance of albuminuria and retinitis. Hyperpiesis, which is shown to vary so quickly and so markedly and so frequently, can no longer be regarded as being due merely to occlusive intimal disease of the arteries, since such intimal change could not possibly undergo such quick parallel change. Hyperpiesis must be due to chemical or chemico-physical agencies circulating in the blood which vary in amount at different times according to the supply, and which are capable of being neutralized for short or long periods by equally variable supplies of other chemical or chemico-physical agencies which are depressor in type. There is no need any longer to look upon eclampsia as a disease peculiar to women and pregnancy—it is but a variety of hyperpiesia. Puerperal hyperpiesia is peculiar to women in pregnancy, in whom the blood poisons can be got rid of by emptying the womb, so that the hyperpiesis, the albuminuria, the convulsions, and the retinal changes may be entirely cured—only to recur, maybe, during subsequent pregnancies. Eclampsia may occur independently of disease of the kidneys and independently of arterio-sclerosis.

One of the facts which stamp medicine as an unscientific study is that false theories of the causation of disease when once launched float so long, often as useless hulks—the power of floating being dependent upon the conservatism, so marked in medical studies, which would prefer to hold on to names and theories when their falseness and uselessness have been completely demonstrated. Harmful as the retention of the word "uraemia" and all it denotes are to progressive medicine, still more disastrous is the use of the word "arterio-sclerosis." The doom of this term and of all it has been held to mean in the explanation of certain clinical signs has come, for already at least one recently published textbook of medicine has, through one of its collaborators, expressed the view that it should be abolished, and medical students will learn this in the future. In order to realize that the term should be abolished it is only necessary to take other textbooks in which the term still stands to note how each may contradict another with regard to the pathology and clinical manifestations of arterio-sclerosis, and even may contradict itself within its own pages. One recent paper dealing with the subject shows such hesitation to get rid of the term that by its partial retention really important results of investigation by the author are rendered confused.

It is impossible to define arterio-sclerosis—or arterio-capillary fibrosis, as it is also known—and no two authorities agree as to what is the meaning of arterio-sclerosis. Included in the term are various pathological conditions of the arteries which are quite distinct from one another, and the clinical manifestations which are supposed to be dependent upon arterio-sclerosis are found in the same book to be identical with those met with in hyperpiesia and in "uraemia."

The present occasion is not at all suited to a detailed review of what different authors consider to be arterio-sclerosis. All that can be said is that it is possible at the bedside to recognize certain states of the arteries which are departures from the normal, but it is impossible in most cases to tell what is the pathological anatomy underlying such changes. The most manifest changes are few in number. It is possible to detect by sight that an artery is more tortuous than it should be; it appears to be longer than it should be, and it is a good clinical guess that such lengthened artery owes its peculiarity to the fact that its walls have become lengthened owing either to increase of the length of the walls from increased pressure from within, or to the walls having become weakened and stretched axially by a normal intravascular pressure. It is also possible to detect *de visu* that an artery is dilated locally, as in the case of an aneurysm; and again it is a safe clinical guess to say that such dilatation is

due to local weakening of the vessel wall. It is also possible to tell that the walls of an artery have become more rigid; but it is impossible to tell clinically whether such an increased rigidity is due to increase of the muscular tissues of the media or to fibrosis of the media or to proliferation of the intima, or to functional increased action of the tissues of the middle coat—that is, the spasm of the muscle fibres. It is possible also to guess that the walls of the arteries may have become rigid from calcareous deposits in the middle coat, and this observation can be confirmed by x-ray examination. It is possible, finally, to tell that pulsation has ceased to take place in an artery; but it may be difficult to say whether such absence of pulsation in the smaller arteries is due to occlusion locally or at a spot nearer the heart unless it is possible also to demonstrate a tender swelling indicating the lodgement of an embolus. In larger arteries, however, it is quite possible to find that the loss of pulsation is directly due to local thrombosis; as is the thrombo-angitis obliterans of Buerger. It is possible by direct and indirect observation to detect that an artery is becoming occluded, as in intermittent claudication and in angina pectoris.

There does not appear to be any justification for bunching together all the above changes in the arteries under the title of "arterio-sclerosis," or "arterio-capillary fibrosis," which, strictly speaking, is not a clinical term, but a permissible pathological one to be used to describe particular conditions in which fibrosis affects the walls of an artery *in toto*, or only in part.

So valuable is the presence of hyperpiesis as a distinctive feature accompanying evidence of functional renal inadequacy that, during the war, persons showing albumin and hyperpiesis were looked upon as being much less fit to return to any form of military duty than were those in whom renal insufficiency was unaccompanied by hyperpiesis; this knowledge has been made use of by insurance companies, who are not disposed to accept at all cases of hyperpiesis and albuminuria, whereas cases of albuminuria without hyperpiesis are accepted with a load. Recent work has shown also that cases of albuminuria and dropsy without hyperpiesis are less likely to be accompanied by hyperuraemia than are cases of less marked albuminuria and dropsy accompanied by hyperpiesis.

In the same way tortuous and hardened arteries may be present in some cases without hyperpiesis and in others with this change; the outlook in the two sets of cases is quite different: in the former the tortuosity may be simply due to muscular effort, which, oft repeated, has led to temporary oft-repeated rise of blood pressure; whereas in the other the blood pressure is constantly raised and is dependent upon the circulation of pressor agencies—in fact, is due to hyperpiesia. It is not to be wondered at that with increasing age, especially in manual workers, the arteries are tortuous and thickened, but the prognosis is much more favourable than in hyperpiesia. The changes met with histologically in the arteries of the last two groups of cases may be strictly limited to the media which in the early stages show a true hypertrophy of the muscle fibres of the middle coat, and in late stages show an increase of fibrous tissue as well—a conservative process which *per se* is no menace to the individual, indeed is an insurance against rupture.

But arteries may appear to be tortuous and yet not feel thickened, and if hyperpiesis, temporary or permanent, is absent, such tortuosity may be referred to weakening of the middle, and even internal, coat of the artery. In such cases rupture is possible. It is almost certain that such cases are due to infection, as has been proved in the case of syphilis and typhoid infection; but such weakening has been demonstrated to be the result also of other infections, such as streptococci and other pyogenic infections, in which even the inflammatory arterial change may be acute (rarely) or chronic (frequently).

So far, two forms of arterial disease which may be recognized clinically have been discussed: (a) hyperpiesic and occupational tortuosity and hardening due to hypertrophy of the media, and (b) tortuosity and maybe hardening independent of hyperpiesia and occupation, but due to infection which causes formative inflammation of the coats

of the artery, as shown by cellular proliferation and by cellular exudation.

There remain other forms of arterial changes which may defy clinical detection—these are arterial degeneration affecting the intima (atheroma) and degeneration affecting the media. There can be little doubt that such degenerations are toxic in character, maybe from lead, but in many other cases the toxic material is, judging by analogy, due to bacterial infection, which instead of being formative and protective is destructive and menacing.

It is not to be wondered at that, in certain cases, histological examination may prove that arteries which show hypertrophy resulting from rise of blood pressure within the vessels—permanently as in hyperpiesia, or occasionally only as in manual workers—also show evidence of inflammation with new formation or degeneration; but these latter changes are not due to the hyperpiesis but to bacterial infection acting directly on the walls of the arteries, or indirectly through their toxins. The outlook in such cases is very grave, for the presence of the hyperpiesis is a menace, as Sir Clifford Allbutt says, to decadent structures, and rupture of arteries is very possible if they are degenerated.

It is thus clear, I hope, that as clinicians we can get on quite well without the use of the term "arterio-sclerosis"; arterio-sclerosis is not the cause of the hyperpiesis of hyperpiesia. Hyperpiesis causes hypertrophy of the media, and infection causes the new formations and degenerations of the media and of the intima. We do not know how calcification of the media is caused, but the only other infiltrations of arteries—namely, lardaceous and hyaline—are almost certainly micro-organismal in origin.

Thus I hope that in trying to make you familiar with a new conception—hyperpiesia—I have also helped you to other views of the significance of arterial changes, and to the relegation of arterio-sclerosis to the background, so that it need no longer cause difficulties.

THE TREATMENT OF GENERAL PARALYSIS.

BY

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THE action of the Board of Control in issuing the circular letter to which attention was called in the *BRITISH MEDICAL JOURNAL* of March 15th (p. 479) and the rules there printed in full will be welcomed by all medical practitioners who have to deal with this particularly tragic class of mental case. The moment seems, therefore, appropriate to call attention to one or two additional points which have become evident to me during the course of observations on this method of treatment during the past few years.

The beneficial effects of intercurrent fevers, such as erysipelas or enteric fever, in patients suffering from general paralysis have long been recognized. They have led to the introduction, for therapeutical purposes, of innocuous artificial pyrexia. This has been achieved by various methods, notably by injections of tuberculin, of sodium nucleinate, etc. Malarial inoculation, introduced by von Jauregg in 1917, seems rather more convenient, because not only is pyrexia induced by a single inoculation, but a whole series of resulting febrile reactions can be allowed to recur for days or weeks and then terminated by the exhibition of quinine. As a result of such pyrexial treatment remissions in the course of general paralysis have been obtained, sometimes lasting months or years, and in many recorded cases the mental symptoms have cleared up, so that the individual has been able, for a time at least, to resume his normal occupation. It is especially noteworthy, however, that in no case treated by von Jauregg or by any of his followers is it stated that the cerebro-spinal fluid has returned to normal. On the contrary, its characteristic pleocytosis and positive Wassermann reaction are observed to persist, practically unchanged, despite the improvement in the clinical symptoms. So long as this is so, it is evident that the patient is not really cured of his disease,