The Goulstonian Lectures

ON

AUTO-INTOXICATION: ITS RELATION TO CERTAIN CARDIO-VASCULAR DISORDERS.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON ON MARCH 13TH, 15TH, AND 20TH, 1906.

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LECTURE III.—[ABSTRACT.]

[At the beginning of the third lecture Dr. Batty Shaw continued the discussion of the subject of intracellular ferments, and especially hydrolytic ferments, quoting the results of earlier and later investigations by others. He proceeded as follows:]

From these observations it is obvious that we have to deal with numerous ferments acting in the various organs of the body, and we can accept it as a fact that these ferments are not simply escaped digestive ferments but are ferments peculiar to various organs.

Fig. 1.—Experimental atheroma produced in the aorta of rabbits by intravenous injection of adrenalin. (After Külbs.)

One of the most common experiences is to find that an organ, the artery to which has become occluded, undergoes atrophy. We are forced to believe that intracellular ferments have been the agents by which such disappearance of tissue has been brought about. The products of such autolysis will be absorbed into the system: if not simplified rapidly or excreted it is reasonable to suspect that they will exert disturbances in the rest of the economy.

[The lecturer then described experiments he had made to test the effect on the blood pressure of extracts of autolyzed organs, with the following results:]

The autolyzed liver produced a much greater fall of blood pressure than an equal amount of fresh liver substance. A change had taken place which resulted in the production of a more powerful depressor substance or substances.

Turning to the effect of autolysis upon kidney substance we find the almost immediate pressor effect of fresh kidney extract replaced by an immediate depressor effect of autolyzed kidney substance or the immediate depressor effect occasionally met with in fresh extract is made more prolonged.

[Dr. Shaw then detailed the more important evidence to

show that the depressor effect of substances derived from the disintegration of proteid and nucleo-proteid was due to proteoses, but not peptones, histones, etc.; also the effect of injecting fresh extracts of organs in producing intravascular clotting, an effect not produced by the extracts of autolyzed organs; after which he described the results obtained by Josué in producing aortic atheroma, calcification, and even aneurysms by injecting suprarenal extract into rabbits. He proceeded:]

Fig. 2.—Experimental adrenalin atheroma. Section of part of vessel involved in the change, showing disappearance of muscular tissue between elastic fibres, loss of waviness of the latter as well as disintegration between *a* and *b*, which marks the site of one of the slight diverticula produced: *i*, Inner coat. *m*, Middle coat. Specimen specially stained to show elastic fibre. (After Erb.)

Much as one is impressed with the close similarity of this experimental arterial disease with that met with in man, more close than the effects produced in any other experiments dealing with this subject, I do not bring forward these observations as proof of auto-intoxication for the very simple reason that I cannot correlate experimental adrenalin atheroma with any clinical condition in which it can be shown that arterial disease is due to disturbed function of the suprarenal gland. If adrenalin is injected with an amount of amyl nitrite which is just capable of neutralizing its pressor effects, arterial disease identical with that produced by adrenalin alone is manifested—in other words, adrenalin produces its effects, not because of its pressor tendency, but from some other much more subtle influence.

Fig. 3.—Experimental adrenalin atheroma. Section of an artery. *m*, Middle coat. *l*, Weakened and dilated elastic lamina. *i*, Proliferative change in inner coat. *p*, Calcareous deposit in middle coat. *z*, Areas of round-celled infiltration. *b*, Blood clot. (After Erb.)

We have no experimental grounds for believing that persistence of any stimulus should at length lead to degeneration instead of hypertrophy of the middle coat,

Auto-intoxication by the tissues of various organs, or by derivatives of these tissues, is very probable. We know clinically a group of cases in which the kidney has undergone reduction in size. This reduction of size affects mainly the cortex. In a large proportion of these cases we know that the blood pressure has been raised and certain signs and symptoms spoken of as uraemia were present. We have been quite ignorant of the agency which was responsible for both the raised blood pressure and the uraemia. The discovery has been made by Tigerstedt and Bergman that the kidney substance, especially the cortex, when fresh, is capable of causing experimentally a rise of blood pressure. The actual substance responsible for this effect has not been isolated. It is not a crystalline body, but is of a colloid nature, or is so closely associated with colloid substances that it cannot be dialysed. It is very labile and appears to be destroyed when the kidney tissue has lost its freshness. Clinical and experimental observations therefore support the view that maintained hypertension may be due to the entrance of kidney substance into the circulation.

Fig. 4.—Experimental adrenalin atheroma. Section of vessel affected, stained to show elastic tissue. Rupture has taken place in the internal and middle coats, leading to the formation of an aneurysmal dilatation. (After Külbs.)

Seeing that raised blood pressure occurs so often in uraemia, it is reasonable to think that the latter also may be due, in part at least, to the entrance into the system of toxic material derived from the same source—namely, the kidney. That the cerebral manifestations of uraemia are due to arterial spasm in conformity with Traube's theory may be accepted in view of the fact that the toxic substance derived from the kidney acts upon the peripheral centres of the vasomotor nerves, and we know that the cerebral arteries, although formerly alleged to be devoid of vasomotor nerves, possess a nervous supply. The pressor effect of the kidney substance may be lost when the organ has undergone autolysis. Seeing that autolysis is an accepted physiological agency by which the chemical changes of the body are carried on, it is reasonable to believe that autolysis has a new significance for pathology. It is known that when tissues are cut off from the circulation experimentally autolysis after a certain period of

time takes place. If, then, the blood-supply to various organs is cut off by arterial disease there is reason to believe also that after a certain period of time the organs undergo atrophy by a process of autolysis. Autolysis is a process allied to digestion, and is due to the existence of intracellular proteolytic enzymes. No derivative of autolysis is known which is capable of causing a rise of blood pressure. Therefore kidney substance can alone be the cause of the rise of blood pressure met with in renal disease; it must enter the circulation before autolysis has occurred during the period of maintained vitality which Miss Lane-Claypon and Dr. Schryver have shown to exist before autolytic degradation takes place.

All organs which have undergone the initial process of autolysis may yield such substances as proteoses, histones, nucleinic acids, and choline. In this stage they can yield to the circulation material which is capable of exerting a fall in the blood pressure. If autolysis of organs has proceeded further the derivatives are, so far as the blood pressure is concerned, quite without effect. Although the existence of proteosis in the circulation is a physiological impossibility it is probable enough in pathology. Proteosuria is well recognized and is probably not dependent only on the presence of digestive ferments in the urine, but more probably depends in part upon autolysis of kidney substance, or even of the tissues of other organs. It is known that in certain cases of granular kidney proteose and heteroproteose may occur. Moreover, in

Fig. 5.—Section of the aorta in the neighbourhood of a rupture which occurred in a child aged 9 years: showing cloudy degenerated areas in the media. (After Oppenheimer.)

uraemia with suppression of urine it is well known that proteosuria is apt to occur. The fall of blood pressure, which is a feature of some cases of renal disease or which may supervene after a period of high blood pressure, may be adequately explained by the entrance into the system of derivatives of kidney tissue which have undergone the early stages of autolysis. The experimental observation that kidney substance can produce different effects according as to whether it has or has not undergone autolysis is not only of importance in the consideration of various clinical problems connected with the elevation or depression of blood pressure, but has other important bearings. The extracts made from fresh highly-cellular organs when injected into the circulation experimentally are capable of producing widespread coagulation. There has, however, been one insuperable difficulty in accepting such an explanation—namely, that it was difficult to believe that the cells of any organ could liberate their contents in such a fresh and unaltered condition into the circulation as to produce in disease the effects produced experimentally. The view that fresh kidney substance can enter the circulation and produce results quite the reverse of those produced when the kidney substance has undergone autolytic degradation gives us much more reason for adopting Wooldridge's explanation of certain cases of *ante-mortem* thrombosis, and to accept the view that certain conditions is due to the entrance into the

circulation of nucleo-proteids derived from various organs.

Possibly the occurrence of various cerebral palsies in uraemia independent of haemorrhage is due not to vascular cramp effected by the entrance of renal substance into the circulation but is due to the coagulating properties of this fresh tissue or of some other organ involved in the disease. The action of kidney substance when once it has reached the circulation and produced a rise in pressure provides us with an explanation of the common occurrence of hypertrophy of the middle coat of the arteries and of the heart. There is no experimental evidence which would lead us to believe that mere elevation of blood pressure can cause degenerative change in the blood-vessels. Adrenalin, however, can cause widespread degeneration of the middle coat, development of atheroma, and even aneurysm. Though it is not possible to recognize any clinical correlative to the experimental production of atheroma in the blood-vessels by means of the injection of adrenalin or other suprarenal products, yet the fact that a substance derived from an organ like the suprarenal body can produce a disease so much like atheroma and so much like the earliest changes met with in the media in human pathology cannot fail to arouse our interest and stimulate further research on problems which have remained unsolved for so many years.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL.

TREATMENT OF COLIC.¹

IN May, 1905, I attended a Mussulman, aged 33, during the latter part of an attack of renal colic on the right side. It lasted, from beginning to end, seven days, and ended in the passage per urethram of two small, smooth, uric acid calculi. An interval of two months passed, during which he was quite well, and then a second attack began; it occurred to me, when I was called seven hours later, that its duration might be shortened by manipulation of the abdomen. Accordingly, having anaesthetized the patient deeply with chloroform, I put one hand behind and the other in front of the right kidney, and went through movements as if I were trying to roll it between my hands. This procedure was followed by the passage of the calculus and cessation of all pain within twenty-four hours. Two months later again he had a third attack, this time on the left side. I saw him within ten hours of its onset, and went through the already described procedure. When I called the next day he was still in pain, so I again manipulated, and less than five hours later, and within forty-eight hours of pain commencing, the stone was passed. Since then he has been taking lithon- triptics, and up to the date of writing, some ten weeks afterwards, he has remained quite well. I have never seen manipulation advocated in this condition, and it seems a plan of treatment worthy of more extended trial. For it will be noted that whereas during the first attack the calculi took seven days in passing from the kidney to the bladder and urethra, the second and third attacks—those in which manipulation was used—lasted respectively only one and two days. I do not think we need fear damage to the renal tissues of the ureter, because (1) the stones are generally small; (2) they are invariably smooth or finely tuberculated, (3) several structures intervene between the surgeon's hands and the calculus and thus disseminate the pressure applied by the hands without materially diminishing the rolling movement which is exercised and intended to dislodge the calculus from the sinus of the kidney.

The rapid passage of a calculus under manipulation can probably be ascribed partly to the rolling movements liberating it from recesses and partly to the chloroform counteracting spasm of the ureter.

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Raichur, India. Senior Plague Medical Officer, Raichur.

¹ Condensed.

SUCCESSFUL VACCINATION.—Dr. Henry J. F. Badcock, Public Vaccinator for the Gillingham District of the Medway Union, has received the Government grant for successful vaccination.

REPORTS

ON

MEDICAL AND SURGICAL PRACTICE IN THE HOSPITALS AND ASYLUMS OF THE BRITISH EMPIRE.

DUNDEE DISTRICT ASYLUM.

(By HENRY C. MARTIN, M.B., Resident Medical Officer.)

As an example of abnormally small viscera in the adult, I send you a few particulars of a case which recently came under my notice.

A woman, J. W., aged 28 years, died in this institution from exhaustion following acute mania on May 22nd. She was well developed, 5 ft. 3 in. in height, with no external deformity or malformation, and, although emaciated at the time of her death, was well nourished when admitted. She had enjoyed good health previously.

At the *post-mortem* examination the following facts were ascertained: The lungs, which were normal as regards the number of lobes, etc., were in size those of a child, the left weighing 7 oz. and the right 6 oz. The heart weighed 7 oz.; the lumen of the aorta was small, scarcely admitting the little finger.

The liver weighed 39 oz.; it showed no pathological change except some venous congestion. The spleen weighed 2 oz.; it was very distinctly divided into an upper and lower lobe; the small weight may partly have been due to the exhaustion. Each kidney weighed 3½ oz.—slightly below normal. The lumen of the small intestine was very small—not larger than the index finger.

The brain weighed 44 oz., thus being about the normal for the female.

According to *Gray's Anatomy*, the average weights of these viscera are:

Lung (right), 22 oz.; (left), 20 oz.
Heart (female), 8 to 10 oz.
Brain (female), 44 oz.
Liver, 50 to 60 oz.
Spleen, 7 oz.
Kidney (right), 4 to 5½ oz.; (left), 4 to 5½ oz.

British Medical Association.

CLINICAL AND SCIENTIFIC PROCEEDINGS.

NORTH OF ENGLAND BRANCH.

Stockton-on-Tees, April 25th, 1906.

Dr. FULTON in the Chair.

The Treatment of Heart Disease.—Dr. GEORGE MURRAY (Newcastle-on-Tyne) read a paper on some points in the treatment of acute and chronic heart disease. He emphasized the importance of (1) administering salicylate of sodium in acute rheumatism—10 gr. every hour until the urgent symptoms subsided—and the continuance of administration for six weeks; (2) the careful examination for pericarditis and endocarditis; and (3) for nodules. He drew attention to the frequent absence of joint lesions in children. For endocarditis he recommended the administration of iodide of sodium for four to six weeks and the application of a series of small blisters. In mitral stenosis digitalis not only did no good, but often did harm; experiments on dogs showed that digitalis dilated the left auricle; sodium nitrite sometimes did good. He related the case of a man who had mitral regurgitation at 20 years of age and lived until he was 90 years old, his condition being greatly relieved, when his heart became embarrassed, by taking blue pills. In order of merit for the treatment of rheumatic heart affections he would place, first, digitalis—fresh infusion, combination of tincture (m.v) with fresh infusion (3ij) or liquid extract (Parke, Davis), persevered with for a week, as the full effect is very often not produced until that time has elapsed; secondly, apocynum cannabinum 5 to 10 minims of the tincture (cannot be given for long periods as it produces vomiting); and, thirdly, tinct. strophanthus, 10 minim doses. Tincture of convallaria is more especially useful in the heart troubles of exophthalmic goitre; nux vomica