The Goulstonian Lectures

ON

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

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LECTURE I.—[ABSTRACT.]

[AFTER some introductory remarks the lecturer said:]

It is the object of these lectures to consider the possible effects due to auto-intoxication when from any cause the organs and tissues of the body are made to disintegrate; to study the effects of the dissolution of cells of various organs and tissues as shown by the toxic effects of their products, restricting myself in the main to the consideration of the products of proteid and nucleo-proteid degradation, including not only the deep degradation products but those more vital agencies a study of which is only possible when we examine the effects produced by fresh tissues; that is, tissues which, though disintegrated by mechanical means, may be considered still living tissue in so far as the formation of their deep disintegration products has not yet begun.

BLOOD PRESSURE IN HEALTH AND DISEASE.

[Dr. Shaw then described observations on blood pressure in patients at different ages and in healthy youths, made with the Riva-Rocci sphygmomanometer, the details of which are contained in the subjoined tables.]

TABLE I.—Systolic Blood Pressure in Infirmary Patients
(Men in Recumbency).

Case.	Age in Years.	Systolic Pressure.	Clinical Association.
1	49	88 mm.	Tuberculosis; arterio-sclerosis; no albumin.
2	46	143 "	Ulcers of the legs; no arterio-sclerosis; no albumin.
3	55	138 "	Rheumatoid arthritis; slight albumin.
4	53	163 "	Sciatica; arterio-sclerosis; no albumin.
5	69	158 "	Ulcers of the legs; trace of albumin; very slight arterio-sclerosis.
6	67	170 "	Right hemiplegia; arterio-sclerosis; some albumin.
7	65	110 mm.	Arterio-sclerosis; (?) lymphadenoma; no albumin.
8	60+	160 "	Ununited fracture; no albumin.
9	65	160 "	Paralysis agitans; slight arterio-sclerosis; no albumin.
10	66	123 "	Bronchitis; moderate arterio-sclerosis; no albumin.
11	60+	210 "	Left hemiplegia; marked arterio-sclerosis; albumin present.
12	76	180 mm.	Diarrhoea; moderate arterio-sclerosis.
13	72	194 "	Partial right hemiplegia; trace of albumin.
14	78	155 mm.	Debility; arterio-sclerosis.
15	73	145 "	Ulcer of the leg; moderate arterio-sclerosis; albumin.
16	80+	155 "	Eczema; arterio-sclerosis.
17	82	144 "	"Senility"; albumin present; arterio-sclerosis.
18	88	130 "	Marked arterio-sclerosis; diarrhoea; "debility."
19	81	107 "	Marked arterio-sclerosis; (?) cystitis.
20	80	175 "	Debility; arterio-sclerosis; no albumin.
21	86	190 "	Bronchitis; marked arterio-sclerosis; albumin.
22	83	182 "	"Debility"; arterio-sclerosis.
23	83	160 "	Bronchitis; arterio-sclerosis; albumin.

These observations confirm the view that with increasing years there is generally a rise of arterial pressure.

[Observations on the systolic blood pressure of 42 apparently healthy schoolboys were described, and the following conclusions drawn:]

There were variations in the systolic blood pressure of different individuals of the same age; but there was no steady advance in pressure in accordance with the age of these youths.

Further observations, 68 in number, were made in various forms of disease in the wards at University

College Hospital; 48 were found to have systolic pressures within the limits of ordinary health, and these included under a clinical diagnosis: cirrhosis of the liver, 4 cases; valvular disease, 8 cases; diabetes mellitus, 4 cases; bronchitis and emphysema, 4 cases; aneurysm and arterio-sclerosis, 2 cases; tuberculosis of the lungs, 2 cases; and varia, 8 cases. Under the last category are included dyspepsia, ascites following removal of ovarian

of unusual character in which the only signs were pain about the root of the nose associated with a hard oedema of the neighbouring skin, independent of supuration of the frontal sinuses, etc. (See Charts 2 and 3.)

Chart 3.—A billiard-marker, aged 41; carcinoma ventriculi.

(2) Twelve cases in which the blood pressure was *higher* than normal.

In this case the right kidney weighed 4 oz. and the left

Chart 4.—Case II, a bricklayer, aged 41; acute Bright's disease

4 oz.; the capsules were adherent; the cortex was reduced to $\frac{1}{4}$ in.; the substance was tough, and cysts were present.

This patient was discharged at his own request, the albuminuria being still present; the oedema had disappeared. He was discharged feeling much better and the dropsy had disappeared.

CASE IV.—A man aged 69, with albuminuria; his systolic blood pressure was constantly above 160 mm., and reached 184. He was discharged.

CASE V.—A man, aged 21, with chronic Bright's disease. The blood pressure varied from 125 to 144 mm., and towards the end underwent rapid diminution, becoming before death subnormal. The heart was found to be greatly enlarged and dilated (it weighed 19 oz.), and the kidneys gave evidence of being in the early stage of sclerosis; they weighed 7 oz. each.

CASE VI.—A man, aged 43, with uraemia. Five blood-pressure observations showed 160 mm., 140 mm., 162 mm., 163 mm., and the last, taken an hour and a half before death, was 160 mm. The kidneys weighed 6 grams each; the capsule stripped off readily: the cortex was $\frac{1}{4}$ in. in depth; the renal arteries were thickened and atheromatous.

CASE VII.—A man, aged 32, admitted with uraemic dyspnoea and almost complete suppression of urine—only 4 oz. in two days. Four observations were made on the blood pressure. October 30th, evening, 187 mm.; October 31st, morning, 167 mm.; evening, 162 mm.; and November 1st, at 10 a.m., 88 mm. Death occurred seven hours later. The kidneys were found to be red, granular, and contracted, and contained cysts; the cortex was greatly reduced; each kidney weighed 4 oz.; the renal vessels were narrowed.

CASE VIII.—The symptoms gradually abated and he was discharged. The chart (7) shows the elevation and gradual fall of the blood pressure in acute Bright's disease.

CASE IX.—The blood pressure varied, falling during her stay in the hospital, but rising above normal again prior to her discharge.

CASE X.—The patient developed severe uraemia with convulsions, and was bled and infused. He left the hospital quite free from symptoms.

CASE XI.—The specific gravity of the urine was from 1015 to 1022; a slight trace of albumin was present. The patient was discharged relieved to a certain extent.

CASE XII.—The specific gravity of the urine was from 1012 to 1020, normal in amount, and no albumin was present. The patient was discharged relieved.

Chart 5.—Case IX, a married woman, aged 42; subacute Bright's disease.

The next case, one of chronic Bright's disease, is described at this stage, though she had at first normal and then subnormal blood pressure.

CASE XIII.—The right kidney weighed 5½ oz., and the left 6 oz. The cortex of the kidneys was reduced; the substance

of the organs was tough; the renal vessels showed no sign of thickening.

Consideration of the above 68 cases leads to the conclusion that in disease of various kinds the blood pressure

there remain 12 cases in which it is higher. It cannot be denied that possibly there are many causes of a quite different nature which may be responsible for the departures from the normal of the latter 26 cases. One feature stands out in great prominence. Of the 12 cases of hypertension all except one were associated with the occurrence of albuminuria.

As shown by *post-mortem* examination, grave renal disease was present in 4 of the cases, and, using purely clinical tests, a similar condition of renal disorder may be conjectured in the case of the remaining 7 or even 8. Remembering the close connexion existing between renal disease and intoxication by lead, it may even be thought highly probable that renal changes were present in Case XII, in whom hypertension was present but was not associated with albuminuria.

THE CREDITED CAUSES OF HYPERTENSION.

The problem, therefore, resolves itself into a solution of the difficult question, How is hypertension, such as is shown by the above 12 cases, to be explained?

The use of the sphygmomanometer shows that it is possible to establish clinically a group of cases in which there is maintained high blood pressure but

little or no signs of arterio-sclerosis or of renal disease; cardiac hypertrophy may be present to some extent. This group constitutes those cases of latent angio-sclerosis described by von Basch, or of pre-sclerosis as described by Huchard. Useful as may be this recognition, it cannot be said for certain that renal disease is absent in these cases; the absence of signs of arterial disease of cardiac hypertrophy or of albuminuria is not conclusive evidence that the

Chart 6.—Case III, a shop attendant, aged 17; chronic Bright's disease; (?) contracted kidney.

shows a great variation both in each individual and also comparing one case with another; 42 cases show a blood pressure which, so far as our knowledge goes at present, is well within the normal limits; 14 cases, however, show pressures which are distinctly lower than normal, and

Chart 7.—Case VIII, a fishmonger, aged 39; acute Bright's disease.

Chart 8.—Case XII, an engineer, aged 36; debility; lead poisoning.

kidneys are healthy. I venture to insist upon this point, for the evidence drawn from the above list of clinical cases of raised arterial pressure tends to show, with one exception, that all the cases of hypertension found by me are associated with renal disease, as shown by albumin, etc. The fact that one case (Case XII, Chart 8) revealed no signs of renal disease, and yet had high pressure, was explained on the ground that he was a labouring man, and that the rest in bed had very shortly been followed by a fall to normal; as already stated, the view that effort is capable of producing maintained arterial tension has been denied, so that this explanation of the case is not assured. Early sclerotic changes in the splanchnic vessels are said to be the cause of these cases of presclerosis, but the fact that this patient with ordinary rest in bed and no special treatment got rid of his high pressure suggests that there is still some other explanation for a rise of pressure which, as in this case, was found to fall, not at once, but by the end of two days to normal.

To sum up, there is a general admission that the explanation of increased arterial tension of cardiac hypertrophy independent of valvular disease and obstruction of the pulmonary circuit is not satisfactory. We do not possess any clear ideas of the nature, origin, and mode of action of the hypothetical irritant substance which has been invoked to explain hypertension and which may have been the operative factor in Case XII above described, as well as in the cases of hypertension associated with albuminuria. During the last few months I have set myself the task of making a direct appeal to biological tests for an answer to the various differences of tension as shown by sphygmomanometer observations at the bedside. The idea was that it was possible for certain substances to be extracted from the organs in different diseases, which acting on the circulation of the patient would be capable of producing those rises or falls of blood pressure which con-

stitute the abnormalities of the above list of 68 cases. For this purpose four cases were selected in the wards, in whom there were differences of blood pressure (Table II).

Twenty c.cm. of blood were removed from a vein of the forearm by puncture with a needle. The blood was at once placed in ice, and within three hours after preparation by grinding up with sand, when clotting had taken place, and after diluting with 1 in 3 sterilized salt solution (86 per cent.),

Chart 10.—Case X, a capmaker, aged 43; chronic Bright's disease; (?) exacerbation.

it was injected in 4 c.cm. doses into the femoral vein of a cat weighing 3,100 grams. The blood pressure was taken from the carotid artery; anaesthesia was secured by means of ether and the respiration was spontaneous; the vagi were intact.

The changes above recorded were very brief, and, as will be seen, do not give any support to the view that in hypertension of the arterial system (Cases III and IV) such small quantities of blood of patients with high tension contain a pressor substance capable of exerting its influence on the cat.

TISSUE EXTRACTS AND THEIR PRESSOR OR DEPRESSOR EFFECTS.

[The lecturer gave an historical account of observations on this subject, and then proceeded as follows:]

The perusal of a paper by Swale Vincent and Sheen¹ on the effect of intramuscular injections of extracts of animal tissues has aroused my interest in connexion with the subject of auto-intoxication, as I have defined it for the purpose of these lectures, because the writers appeared to have procured some evidence which favoured the idea that when once the parenchyma of any particular organ as a result of various pathological processes reached the circulation it was to be expected that changes would take place in the degree of vascular tension.

In the perusal of this paper one is struck by the observation that these workers have frequently to refer to the fact that the results obtained were not uniform, and notably is this the case with their observations on pressor effects, so that they say the pressor effect seems to be less marked and of a more fleeting character, and consequently more difficult to obtain, than the depressor effect; the pressor effect may be easily missed unless the extracts are made in various ways and a long series of experiments undertaken.

In connexion with the subject of hypertension Swale Vincent and Sheen's results:

TABLE II.

Case.	Age Injury.	Disease.	Blood Pressure.	Effect on Experimental Intravenous Injection.	
				Before.	After.
1	21	Lymphadenoma	117 mm.	168 mm.	176 mm.
2	78	Empyema	127 mm.	172 mm.	160 mm.
3	80	Uræmic hemiplegia, albuminuria, etc.	165 mm.	164 mm.	160 mm.
4	69	Aphasia without paralysis of arm or legs; albuminuria	175 mm.	160 mm.	156 mm.

Chart 9.—Case XI, a painter, aged 55; lead palsy.

are most important in those particulars in which they are able to state that they have established a pressor effect of tissues when injected into the circulation. My own efforts at attempting to discover variations in the effects following the injection of tissues in various pathological conditions were followed merely by the observation that in practically all cases there was but one effect—namely, a depressor one; occasionally the injection of a preparation would produce a brief rise, much as does the simple injection of saline solution in some cases, though as a rule this latter solution generally causes a slight fall. However, a careful perusal of Swale Vincent and Sheen's paper impressed me that the organs removed from individuals dying from

Chart 11.—Case XIII, a widow, aged 49; chronic Bright's disease.

different diseases were not fresh tissues, although keeping the bodies in an ice chamber had prevented their putrefaction. Moreover, suspicions were aroused that possibly *post-mortem* softening might have so affected the reactions of the fresh tissues that, supposing any pressor substances had been present in the organs of the patients who had died, such active agent would have disappeared. At this time I was very materially helped by Dr. Schryder, who pointed out to me a certain period subsequent to the removal of tissues from animals in which the tissues do not undergo chemical change. An appeal, therefore, was made to the effects of fresh tissues removed from a cat and after preparation injected into another.

[Dr. Shaw then described the method of his experiment, and gave a summary of his results as follows:]

The first series of experiments carried out in the above way include those animals in which several different tissue extracts were injected into the same animal; it consisted of eight experiments carried out on eight animals. There are six experiments left for consideration [after he had excluded two for accidental reasons]. Injection of spleen gave a rise of pressure on three occasions of 18 mm., 2 mm., 8 mm., lasting respectively 45 seconds, 10 minutes, 30 seconds; a fall occurred in 2 cases of 4 mm., lasting 1 to 2 seconds, and of 6 mm. lasting 4 seconds. Injection of muscle extract was practised twice; in one there was a marked fall of 38 mm. lasting

4 minutes 28 seconds, and in the other a fall of only 4 mm. lasting 1 minute 55 seconds.

[The observations on the kidney, liver, and brain were more numerous, and the lecturer referred to tables which showed that these organs sometimes caused a rise and sometimes a fall. He then proceeded in conclusion as follows:]

It is obvious that though other organs than the kidney occasionally show a rise of pressure on injection, yet this rise is small and of short duration, whereas the kidney effect of a rise, though varying within considerable limits, is a striking feature, and the same may be said of the duration in which such rise takes place; no other organ has been noticed to have such an effect so frequently. The liver and brain show a much greater tendency to cause a fall of blood pressure, and even then such fall is generally of very brief duration. One point to which it is necessary to draw attention is that in none of these experiments was the kidney extract injected first; the injection always succeeded that of some other organ, and it may be objected that it is possible that the rise of pressure following the injection of renal extract is due to some interaction of renal extract with some previous extract. Moreover, it may be thought that the renal extract is of a different physical character, and likely to cause a rise of pressure from some mechanical effort dependent upon the granules contained in the emulsion. As will be seen later, there is no reason to believe that either of these objections holds good. It is to be observed that the animals were simply under the influence of ether; this was so carefully administered that the respiration was maintained regularly. In one experiment with ether anaesthesia and artificial respiration the vagi were cut; an injection of renal extract then produced the exceedingly small rise of only 4 or 1 millimetre, lasting one minute, forty seconds, and twenty-five seconds respectively. So far as this one experiment is concerned, it must be stated that the second injection of an extract has on other occasions shown a less marked reaction than the first one. The slight rise, such as it is, merely suggests that the rise of pressure on injecting renal extract is due to a peripheral effect whereby the arterial pressure is raised.

REFERENCE.

¹ *Journal of Physiology*, 1903, vol. xxix.

EUCALYPTUS POISONING.

By J. ORR, L.R.C.P. AND S. EDIN.,
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HAVING recently noticed a record of a case of poisoning by eucalyptus oil, I forward notes of a similar case which occurred in my practice on April 16th, 1901. An urgent message was sent to me asking me to visit a little boy aged 2 years and 9 months, who had swallowed 2 drachms of eucalyptus oil. As I was suffering from influenza I could not leave the house, and my *locum tenens* was out on duty; I therefore ordered the child to be brought to me as quickly as possible. This was done, and I saw him about fifteen minutes after he had swallowed the poison. He was unconscious, and collapsed, with a quick pulse, stertorous breathing, and pupils contracted almost to a pin-point, just as in opium poisoning. This pupil contraction, indeed, was the most striking feature in the symptoms. The child had vomited immediately after taking the oil, and purging quickly set in. I gave 10 gr. of sulphate of zinc, and the child having again vomited, I followed this up with a teaspoonful of whisky. The patient still remained in a state of collapse, and as no improvement took place, I thought I would try the effects of strong coffee. A fair amount of this was swallowed by the child, and in a short time the effect was very marked; the pupils began to dilate, and consciousness returned quickly. He was fit to be removed to his home comparatively well an hour after I had first seen him, and made a speedy recovery.

At the sixty-first anniversary dinner of the German Hospital, Dalston, on May 7th, it was announced by the Chairman, Count Maternich, German Ambassador, that a new convalescent home combined with an open-air sanatorium was about to be presented to the institution by certain of its supporters. The necessary land had been acquired near Hitchin, and some £14,000 contributed for the erection and fitting of the buildings.