the subendothelial layer. Dr. Byrom Bramwell holds that syphilis attacks the vasa vasorum, and so impairs the nutrition of the aorta and other large vessels. Dr. George Oliver² has noted that "in cases of acquired syphilis the radial calibre is commonly reduced with loss of postural variation." His "observations point to a general arteritis as the ordinary effect of the syphilitic infection, the intima of the whole arterial tract being involved."

It would seem that there is a hyaline degeneration with cell proliferation of the subendothelial layer which leads to rigidity of the vessel wall, and loss of its physiological variation in calibre. In most cases the blood pressure is somewhat raised, though never to such a degree as occurs in chronic Bright's disease; but in some cases the nutrition of the heart is impaired and the arterial tension low. In these latter, mercury, which is a sheet-anchor with some men for every patient with a syphilitic taint, plays havoc.

Heredity has an important influence in determining disease of the arteries, but personally I would very much rather inherit a tendency to gout than one to phthisis. The vigorous man has very little reason to find fault with his progenitors for his gouty tendency, for he has largely in his own hands the power to modify his ancestral tendencies. Not so, however, the poor hypotonic individual with feeble digestion, who is a prey to tuberculous disease and every depressing influence. Those who cannot produce healthy offspring had better leave that duty to others.

TREATMENT.

I have no time on this occasion to enter on the wide subject of treatment by diet, exercise, and drugs, but I can commend to your serious consideration the pioneer work of George Oliver. I am convinced that he is working on right lines, and he has made some valuable additions to our stock of vasomotor tonics and depressants. He lowered my mean blood pressure by 20 mm. of mercury for twenty-four hours with a single dose of ammonium hippurate. Personally I am very fond of agents which increase metabolism, as life itself implies change; hence I prescribe freely the iodine compounds and thyroid. Just as I frequently order a cardiac tonic with a vasomotor relaxant, such as a combination of digitalis and nitroglycerine, so I frequently combine a vasomotor tonic such as adrenalin with an agent like iodine to increase the metabolic changes. Sir Hermann Weber recently delivered an admirable lecture on "On means for the prolongation of life," which is worthy of careful study.

Prevention is always better than cure, and if you clearly recognize how these arterial changes are produced you will have no difficulty in preventing their appearance, or at least in delaying their development. The medicine of the future will be largely one of prevention of disease and preservation of health, and even in the present day there are very many individuals willing to pay—and pay well—for the maintenance of their health. I am confident that a great many more would go to the medical man to get overhauled—just as they go to the dentist—if medical men would deal with physiological conditions as well as pathological, and tell patients not merely how to get well but how to keep well. You must clearly understand that I am advocating not merely the prolongation of life, but also the vigour and manhood of the nation. God forbid that I should ever advocate any means which would sacrifice the latter for the former. There are already far too many weaklings—mentally and physically—in these degenerate days, when sentiment rather than reason rules the world.

Ill fares the land, to hastening ills a prey,
Where wealth accumulates and men decay.

Whatsoever thine hand findeth to do, do it with thy might; for there is no work, nor device, nor knowledge, nor wisdom, in the grave, whither thou goest.

REFERENCES.

¹ *The American Journal of the Medical Sciences*, March, 1904. ² *Blood and Blood Pressure*, 1901.

INTERNATIONAL CONGRESS OF OBSTETRICS AND GYNAECOLOGY.

—The fourth International Congress of Obstetrics and Gynaecology will be held at St. Petersburg, September 11th to 18th, 1905. Professor von Ott of St. Petersburg is the chairman of the Organizing Committee.

FEMALE MEDICAL STUDENTS IN AMERICA.—There are at present forty-three women pursuing the study of medicine and surgery in the University of Michigan. In the department of law of the same university there are only four female students.

THE EFFECT OF SALTS OF POTASSIUM, AMMONIUM, AND BILE SALTS UPON BLOOD PRESSURE.

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[*Prefatory Note by Professor W. D. Halliburton.*—The detection of choline in the cerebro-spinal fluid and blood of animals, and human beings suffering from various forms of degenerative disease in the central or peripheral nervous system, was first shown to be practicable by Mott and myself. Our results have been confirmed by Gumprecht, Donath, Allen, O. Grünbaum, S. A. K. Wilson, Dana and Hastings, Rosenfeld, and others. The test is becoming widely recognized as an important one in the differential diagnosis of organic nervous lesions from cases of functional neurosis. On the other hand, certain investigators like Vincent and Cramer, and Mansfield, have questioned these results, and allege that the methods employed do not exclude contamination with chloride of potassium and ammonium. Even if we admit the slight solubility of these inorganic chlorides in perfectly absolute alcohol, it is difficult to see how the minute quantity of these substances which would be present could affect our general results. Some of the criticisms which have been passed on our methods appear to take it for granted that we considered a single test—that with platinum chloride—to be sufficient to establish the presence of choline in a solution. If our original papers are consulted, it will be seen that, where sufficient material was at our disposal, the chemical tests we employed were numerous, and the possibility of confusing inorganic chlorides with choline is discussed. We further considered it to be essential that chemical methods should be combined with physiological experiments. The most marked physiological result which follows the intravenous injection of choline is a large temporary fall of arterial blood pressure, but, if the animal is previously atropinized, this fall is not produced, and is usually replaced by a rise. We still hold that a combination of such tests is necessary; the platinum test, with or without Donath's modification, or the iodine test as modified by Allen, may be used from the chemical point of view; and, if either or both of these are positive, and if they are confirmed by the physiological reaction just mentioned, there can be no doubt as to the presence of choline.

Before any of the criticisms alluded to appeared I had become convinced of some gaps in our observations, and had set to work to remedy these. For instance, while Dr. Otto Grünbaum was working at the test in the wards of King's College Hospital, he pointed out to me that the bile salts give a platino-chloride very similar in crystalline form to that given by choline, and as Croftau¹ showed that small quantities of bile salts are present in normal blood, it was necessary to eliminate this possible source of error. I therefore suggested to Mr. Edmunds that he should investigate the physiological action of intravenously-injected bile salts, with which he has combined a similar investigation of the effect of small doses of potassium and ammonium chlorides. The following paper is the result of this work, and it is there shown that though cursory inspection of crystals of the platino-chlorides may lead to confusion between these various substances and choline, there can be no confusion if the simple physiological test is performed also. I am at present engaged in a systematic reinvestigation of the chemical tests for choline, and hope to present my results shortly. In the meanwhile I have been largely relieved of this task by the researches of Donath.²]

The present series of experiments was undertaken, as explained in Professor Halliburton's note, in view of possible confusion that may arise between choline and other substances. The substances investigated have been bile salts, potassium chloride, and ammonium chloride. I have not dealt with their chemical reactions, but with the results upon blood pressure that occur when they are injected intravenously. All, it is true, produce a fall of arterial pressure, but in no case is this fall neutralized or replaced by a rise of pressure after the previous administration of atropine. There can therefore be no confusion between such substances and choline if this reaction is investigated.

The experiments have been performed on cats and rabbits,

fully anaesthetized in all cases with either ether or A.C.E. mixture. The blood pressure in the carotid artery was registered in the usual way by a mercurial manometer. The injections were made into the external jugular vein. In some cases tracings were simultaneously taken of the intestinal volume by the oncometric method. The substances in question have often been injected consecutively in the same animal, but abundant controls have been performed to eliminate all possible error from this source. The effect produced by the mere volume of fluid injected has been checked throughout by the injection of similar quantities of normal saline solution.

Potassium Chloride.

The poisonous action of potassium salts is well known, and since my work commenced two papers on the subject have appeared. In one of these, by L. Braun,³ very full references to the previous literature is given from Blake⁴ onwards.

Fig. 1.—Effect on the arterial blood pressure of a rabbit produced by the injection into the external jugular vein of 2.5 c.cm. of a 1 per cent. solution of potassium chloride. This and all subsequent tracings read from left to right. The time tracing marks seconds. The raising of the signal line indicates the period of injection. The height of the blood-pressure tracing is indicated by the scale at the side, which marks in centimetres the distance from the abscissa. At A the injection was made slowly, at B rapidly.

Blake was the earliest to point out the condition of standstill of the heart which potassium chloride produces. Braun states that vaso-constriction is another result of non-lethal doses; he never observed vaso-dilatation. Among other things he finds that previous atropinization makes no difference to the effect of potassium on the heart; and I fully agree with him that the therapeutic use of potassium as a

cardiac stimulant is contraindicated. The other paper is by E. G. Martin.⁵ He also has directed particular attention to the heart, and finds that the inhibition produced by vagus stimulation is in many points similar to the effect of potassium on the terrapin's heart.

I employed solutions of potassium chloride varying in strength from 0.1 to 1 per cent. The effect of from 5 to 10 c.cm. of the weaker solutions was a slight fall of blood pressure, but it was not until a 1 per cent. solution was employed that the results became marked. The rate of injection makes a considerable difference. Thus in Fig. 1 it will be seen that the injection of 2.5 c.cm. of a 1 per cent. solution caused a fall of only a few millimetres of mercury, but a few minutes later the same amount injected rapidly stopped the heart and killed the animal.

Choline never produces this immediate fatal result, and in the methods employed by Mott and Halliburton there can never have been the possibility of as much potassium chloride being present as to make a 1 per cent. solution. The effect of injecting atropine establishes an even more marked difference of physiological effect (Fig. 2), the fall of blood pressure being as well marked as before, whilst the injection of choline produces a rise, as shown in Fig. 3.

Fig. 2 also illustrates how the fall of blood pressure is mainly of cardiac origin; the primary heart failure is followed by a well-marked "vagus pulse." Choline, on the other hand, produces a fall of pressure, mainly by dilating peripheral vessels. The tracing of the intestinal oncometer above the blood pressure tracing in Fig. 2 shows no evidence of vascular engorgement.

I further tested upon rabbits the effect of injections of similar doses of potassium chloride after the animal had received sufficient nicotine intravenously to abolish any reflex elevation of blood pressure on stimulation of the central end of the sciatic nerve. Owing to the lowering of general blood pressure produced by the nicotine, the effect of potassium chloride was not so marked, but still a good fall of blood pressure was obtained of the same character as before, and in some cases this was sufficient to kill the animal.

Ammonium Chloride.

If solutions weaker than 0.5 per cent. strength are employed the effect of injecting doses of from 5 to 10 c.cm. is practically negative. The same dose of a 0.5 per cent. solution produces a temporary fall of arterial blood pressure without any marked effect on the rate or regularity of the heart. The effect of 1 per cent. solutions is similar, but rather more intense. Fatal results were never obtained. Accompanying the fall of blood pressure is a dilatation of the splanchnic vessels, as

Fig. 2.

Fig. 3.

Figs. 2 and 3.—These show the effect in an atropinized animal (cat) of an injection of potassium chloride (5 c.cm. of a 1 per cent. solution) in contrast with that of choline hydrochloride (5 c.cm. of a 0.2 per cent. solution). The uppermost line in each case is a tracing of the intestinal oncometer. The fall of blood pressure produced by the potassium chloride (Fig. 2) contrasts very markedly with the rise produced by choline (Fig. 3).

shown by the intestinal oncometer. As in the case of the potassium salt, the previous administration of atropine has no effect on the action of ammonium chloride. The tracing in Fig. 4 shows the effect of an injection in an animal under the influence of atropine. The previous administration of nicotine has also no effect on the results.

Fig. 4.—This shows the effect in a cat of the injection of 5 c.c.m. of a 1 per cent. solution of ammonium chloride. The general character of the fall of pressure is very like that produced by choline, but differs from it in occurring after atropinization. The above tracing was taken in an animal under the influence of atropine: in the same animal in this condition the injection of choline produced a rise of pressure exactly similar to that shown in Fig. 3.

Bile Salts.

Sodium glycocholate and sodium taurocholate both produce a fall of blood pressure; but this fall is an insignificant one, even if the solutions used are of 1 per cent. strength, a concentration far beyond physiological limits. The effect of the taurocholate is rather more marked than that of the glycocholate. (See Figs. 5 and 6.) Any effect noted on intestinal

Fig. 5.—This shows the effect in a rabbit of the injection of 5 c.c.m. of a 1 per cent. solution of sodium glycocholate.

Fig. 6.—This shows the effect in a cat of the injection of 5 c.c.m. of a 1 per cent. solution of sodium taurocholate.

volume was in the direction of dilatation, but this was, as a rule, too slight to be measurable. These results are unaltered by the previous injection of atropine or of nicotine.

Some years ago in this laboratory Dr. R. A. Young, who was at the time interested in the question of jaundice, commenced an investigation of the influence of bile salts on the circulatory system. The results he obtained were never published, and the reason why he did not continue the work was that the effect on blood pressure was found to be so slight; even with 5 per cent. solutions the fall presented was hardly greater than that shown in the accompanying figures. (Figs. 5 and 6.)

CONCLUSION.

From these experiments it will be seen that the physiological actions of potassium chloride, ammonium chloride, and bile salts are in many points fundamentally different from those of choline.

REFERENCES.

- ¹ *American Journ. of Med. Science*, 1902, p. 150. ² Donath's latest paper dealing with Mansfeld's criticisms appeared in *Zeitsch. f. Physiol. Chem.*, xlii, p. 563. 1904. ³ *Pflüger's Archiv*, clii, p. 476. 1904. ⁴ *Edin. Med. and Surg. Journ.*, 1839. ⁵ *American Journ. of Physiology*, xi, p. 370. 1904.

THE SANATORIUM TREATMENT OF PHTHISIS. IS IT WORTH WHILE? *

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It is now six years since, at a meeting held at Marlborough House, the mind of the people of England was first strongly drawn to the prevalence and possible prevention of consumption, and especially to its treatment by the so-called "open-air" method in sanatoriums. At that meeting the leaders of medicine of Great Britain and Ireland testified to the gravity of the plague and to their faith in the new principles. These views, though well known to a limited number of English medical men, came as a complete novelty to the general public and a considerable section of our profession, but in the course of the next two years spread widely and obtained many converts both medical and lay.

Since then sanatoriums for the well-to-do have multiplied abundantly; a few for the poor have been at work for two or three years, while others are being projected. But, as the wave of enthusiasm was great and expectations were lifted high, it is useless to deny that some depression has followed, that we are now in a vale of criticism which asks, Were these expectations justified and is this costly movement worth the cost?

These are questions which cannot be shirked and which we who advise the public in matters medical are bound to do our best to answer. Is the "sanatorium," or "open-air," treatment of phthisis markedly superior to older methods? If so, can it be carried on in this country as well as abroad, and, even if it can, is it equally applicable to the poor as to the rich?

That abundance of fresh air makes for strength and that the atmosphere of close, crowded, though comfortably warm, rooms makes for weakness, is a belief now generally professed (though rarely practised) by doctors and all men. But it must be clearly understood that life in the open air is not "sanatorium treatment." It is too commonly one's lot to meet an unfortunate consumptive who has been told to get plenty of fresh air, and who in spite of hectic, dyspnoea and loss of flesh, struggles along road, meadow, or seashore, panting for the breath of life, which to him is but a will-o'-the-wisp luring soul from body, when it should be a gentle spirit permeating a peaceful mind and quiet body. The medical man who casually orders fresh air without thoroughly insisting on the need of rest to the feverish patient has much to answer for. Abundance of the purest air, good food, and a careful regulation of rest and exercise, are the three essentials of sanatorium treatment as advised by Brehmer exactly fifty years ago (1854), and fifty years' experience of this triple rule has convinced impartial judges all over the world that in this way, with time and patience, phthisis can be more often arrested than by any other known method, and that whatever further therapeutic agent may be hereafter adopted this mode of life will always be a basis.

That a doctor should take his own physis is rightly considered a proof of his belief in it, and nothing is more striking

* A paper read before the Midland Branch of the British Medical Association, June 9th, 1904.