THE USE OF SODIUM CHLORIDE, POTASSIUM CHLORIDE, SODIUM BROMIDE, AND POTASSIUM BROMIDE IN CASES OF ARTERIAL HYPERTENSION WHICH ARE AMENABLE TO POTASSIUM CHLORIDE

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THIS paper is a further report of clinical experiments in arterial hypertension, commenced in 1923, and reported in *The Canadian Medical Association Journal* in 1924 and 1925.¹

J. B. S. Haldane² has shown that in an attempt to maintain the acid-alkali-balance of the tissues, the inorganic acidosis producing salts (calcium and ammonium chlorides), when administered in sufficient quantities, bring about a marked increase of ammonia and soda excretion as the acid phosphates.

Bunge,³ has shown, by experiments on himself, that potassium phosphate and potassium citrate increase the soda excretion by one-third of the potash taken.

Blume,⁴ of Paris, asserts that potassium chloride displaces sodium chloride, to cause a diuresis and an increase of soda excretion.

A large and increasing body of evidence tends to prove that the soda ion is a sensitizer of nerve and muscle function; a less, but increasing, body of evidence tends to show that the potassium ion, (while its action on the heart is in some ways similar to that of the soda ion) acts as a nerve depressor.

To summarize, calcium chloride produces an inorganic acidosis, with increased excretion of ammonia and soda; potassium chloride, without change of the acid-alkali ratio, gives an increase of soda excretion; potassium citrate produces an alkalosis, with an increased soda excretion; and all three, with proper dosage, reduce arterial pressure in the large majority of cases of hypertension.

In view of this summary, it was decided in 1925 to try the action of potassium and sodium chlorides in the same person, and, lest the chlorine be thought a party to the action, the experiments were repeated with the respective bromides. The tests with potassium citrate were added to Cases 4 and 5 as an after-thought in reviewing Case 1. The patients upon whom the experiments were carried out were on a salt-poor diet, from which meat, poultry, eggs, cheese, beans, peas, and nuts were excluded. They were allowed fish once daily; vegetables, fruits, cereals and milk freely. These patients, with the exception of the later period of Case 1, carried on under their ordinary living conditions. Cases 1 and 2 did not know of the experimental nature of their treatment. Cases 3, 4, and 5 knew of the purpose of the treatment.

In five cases the tests were made and are here reported :---

CASE 1

Mr. McA., aet. 64, was reported in 1924 as Case No. 13. The report, then, was as follows: Slight albuminuria, cedema of the ankles and lower eyelids.

Oct. 29, 1923—Blood pressure: systolic, 182; diastolic, 128. Urine: specific gravity, 1015. Gave calcium chloride, grs. 180 per diem.

Oct. 31st—Blood pressure: systolic, 162; diastolic, 110.

Nov. 5th-Blood pressure: systolic, 174; diastolic, 110.

Nov. 19th-Blood pressure: systolic, 168; diastolic, 112, Albumen and ædema were absent; treatment continued for three weeks, but the results were not reported.

May 3, 1924—Blood pressure: systolic, 134; diastolic, 80. (Urine: specific gravity, 1025. (Had been on a low meat diet, using milk freely).

1926-I saw him at his home. He had general ædema, dyspnæa, some cyanosis and vertigo, some delirium and delusions, no convulsions or coma, but ap-

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CHART I

parently he was in the early stages of uræmia. His urine varied from 1010 to 1014, and was scanty in quantity. The initial blood pressure was lower than in 1923, but the clinical symptoms were graver.

April 30th-Blood pressure: systolic, 164-166; diastolic, 116-118. Put on potassium citrate, grs. 120 per diem.

May 12th--Blood pressure: systolic, 154-142; diastolic, 102-92. Put on potassium bromide, grs. 90 per diem. May 25th-Blood pressure: systolic, 142-134; dias-

tolic, 96-98. Put on sodium bromide, grs. 90 per diem. June 2nd—Blood pressure: systolic, 168-162; dias-

tolic, 116-112. Put on potassium chloride, grs. 90 per diem.

June 6th-Blood pressure: systolic, 148-146; diastolic, 90-88. Put on sodium chloride, grs. 90 per diem.

June 14th—Blood pressure: systolic, 160-158; diastolic, 112-108.

July 27th-Off treatment for two weeks. Blood pressure: systolic, 160-158; diastolic, 104-100. Put on potassium eitrate, grs. 90 per diem.

July 31st-Blood pressure: systolic, 146-140; diastolic, 98-92.

SUMMARY

He was put on potassium citrate, grs. 120 per diem, with a resultant rapid increase in the volume of urine, a decrease of the ædema and dyspnœa, and a slowly clearing mental condition. The potassium bromide improved his mental condition and lessened his vertigo. The sodium bromide produced nausea, caused a return of the ædema, and produced a rise of blood pressure. With the taking of potassium chloride the blood pressure receded, to rise again with the ingestion of sodium chloride. Associated with the rise of pressure there was a return of the dyspnea, and to a lesser degree an increase of the ædema. He was seven weeks without treatment, and returned approximately to his current blood pressure, but on potassium citrate had a recession to a systolic pressure of 140 and a diastolic of 88. This case is of special interest, in that it shows the response of a chronic nephritic to (a) an acidosis-producing saltcalcium chloride; (b) an alkalosis-producing salt --potassium citrate; (c) a neutral salt-potassium chloride. As far as our present knowledge goes, the common effect of these three substances is the increased elimination of the soda, and the lowering of blood pressure, followed by relief from the symptoms. This experiment gives a reasonable basis for hypothesis that the toxic agent in this case of nephritis was an excess of the blood-sodium content.

CASE 2

Female, aet. 46. When first appearing the patient had a blood pressure of systolic, 188, and diastolic. 94, with dyspnœa, vertigo, œdema of the ankles and slight cyanosis. Under potassium chloride, grs. 90 per diem, her condition had so improved that, during the warm season of 1926, her blood pressure approximated systolic, 130, diastolic, 80, after treatment had been dropped. With cold weather the hypertension returned.

Under experiment the following results were obtained:

Dec. 17, 1926-Current blood pressure: systolic, 170; diastolic, 98. Put on potassium chloride, grs. 120 per diem.

21st-Blood pressure: systolic, 160-140; diastolic, 94-82. Put on sodium chloride, grs. 120 per diem.

24th-Blood pressure: systolic, 182-172; diastolic, 98-94. Complained of basal and frontal headache. Put on potassium bromide, grs. 120 per diem.

28th-Blood pressure: systolic, 196-192; diastolic, 96-86. Had had a Christmas goose-dinner, with a headache following. Continued the bromide.

30th-Blood pressure: systolic, 152-138; diastolic, 86-82. Put on sodium bromide, grs. 120 per diem.

Jan. 3, 1927-Blood pressure: systolic, 180-176; diastolic, 90-86.

CHART II



Of further interest was an occurrence in 1925 when, for economy's sake in diet, she substituted beans for potatoes, with the result of a reversion to her previous blood pressure; a return to potatoes in her diet was accompanied by a remission of her blood pressure. The result of a goose dinner is seen on the chart. The recurrence of hypertension consequent on the taking of meat is frequently seen in our clinic.

CASE 3

Male, aet. about 65. This case, when first reporting, complained of vertigo, dyspnœa, and œdema of the legs. He had an initial blood pressure of systolic, 180-172; diastolic, 102-100.

During the warm weather, when on potassium chloride, grs. 120 *per diem*, his blood pressure approximated, systolic, 150; diastolic, 80.

The record of our experiments in this case is as follows:

Current pressure: systolic, 180-172; diastolic, 102-100. Put on sodium chloride, grs. 120 per diem.

Four days later-Blood pressure: systolic, 228-222; diastolic, 102-100. Put on potassium chloride, grs. 120 per diem.

Four days later--Blood pressure: systolic, 188-156; diastolic, 96-84. Put on sodium bromide, grs. 120 per diem.

Four days later.—Blood pressure: systolic, 210-196; diastolic, 102-100. Put on potassium bromide, grs. 120 per diem.

Four days later—Blood pressure: systolic, 186-154; diastolic, 92-82.



On being placed on the sodium chloride his face and body developed ædema, and he had headache, vertigo, dyspnæa, and a slight cyanosis. Though he did not know of the experimental nature of the treatment, he spoke of his well-being under the potassium chloride, of the drowsiness and comfort under the potassium bromide, and under the sodium bromide he complained of vertigo, dyspnæa, and of ''feeling silly.'' He was decidedly ill with the soda salts and comfortable with the potassium salts.

CASE 4

L. S. is a professional man of scientific training, who volunteered for experiment, knowing the risk and discomfort he would incur. May we not refer to him as of "the honourable company of gentlemen adventurers?" The records of the case are as follows:

Dec. 9, 1926—Current blood pressure: systolic, 188-162; diastolic, 110-98. Put on potassium chloride, grs. 120 per diem, which was taken with difficulty.

13th—Blood pressure: systolic, 166-150; diastolic, 90-82. Slept well when sleeping, but slept less time than usual. 14th—Blood pressure: systolic, 168-158; diastolic, 112-92. Put on sodium chloride, grs. 120 per diem.

17th—Blood pressure: systolic, 194-186; diastolic, 126-118. Was ill and had dyspnœa and vertigo. Put on potassium bromide, grs. 120 per diem.

19th—Blood pressure: systolic, 148-144; diastolic, 110-104. Was comfortable and drowsy. Put on sodium bromide, grs. 120 per diem.

21st-Blood pressure: systolic, 176-172; diastolic, 118-116. Was ill of vertigo and dyspnœa.

21st—Put on potassium citrate, grs. 120 per diem. 24th—Blood pressure: systolic, 134; diastolic, 78.





His chart is here given, and it is seen that his hypertension is of a moderate degree, and the spread between the higher and lower readings would indicate a nervous temperament not obvious to his friends.

The potassium chloride produced a good recession in both systolic and diastolic pressures. The sodium chloride gave a marked rise in excess of his current hypertension, with irritability, dyspnœa, and vertigo, and he was quite ill. The potassium bromide, as is seen, gave the greatest recession of systole, though not so great a recession in diastole, as did the potassium chloride. The sodium gave a notable rise in systole with little spread in the readings, with a marked rise in diastole and marked vertigo, moderate dyspnœa, difficult enunciation of words, and an illness more profound than with the sodium With potassium citrate the drop in chloride. blood pressure was greater than with the chloride, and produced less gastric distress.

CASE 5

This is my own, which I had hoped to work out at an earlier date, but any hypertension during the warm weather was of so transient a sort as to form a poor basis for experiment. That one had the experiment under one's own observation robbed it of risk, but one must own to an unhappy time when taking the soda salts. The experiments, as here carried on with frequent observations, are possible only under circumstances, or in a hospital, and should one carry them farther, the rising dose at frequent intervals and under constant supervision would be the method used. The preliminary tests with the chlorides were interrupted and the bromides of this set only given. To avoid interruption, a Saturday and Sunday were selected to complete the test with the chlorides and the citrate, and the increasing dose used, and these were worked out in 36 hours. To obtain a hypertension a substantial meat diet was taken for two days. The results are given below:

Dec. 19, 1926, 7 a.m.—Current blood pressure: systolic, 202-198; diastolic, 128-118. Put on potassium bromide, grs. 120 per diem. 1 p.m.—Systolic, 192-188; diastolic, 118-108. 9 p.m.—Systolic, 180-170; diastolic, 108-102.

20th, 6.30 a.m.—Blood pressure: systolic, 180-180; diastolic, 118-112. 1 p.m.—Systolic, 184-176; diastolic, 118-108.

21st, 6 a.m.—Blood pressure: systolic, 174-162; diastolic, 112-100. 7 p.m.—Systolic, 198-168; diastolic, 118-104.

22nd, 6 a.m.—Blood pressure: systolic, 164-152; diastolic, 110-102. 9 p.m.—Systolic, 178-152; diastolic, 112-106. Commenced soda bromide, grs. 120 per diem. Taking grs. 80 on retiring.

23rd, 6 a.m.—Blood pressure: systolic, 186-178; diastolic, 124-120. 9 p.m.—Systolic, 208-194: diastolic, 146-130.

24th, 7 a.m.—Blood pressure: systolic, 212-208; diastolic, 150-140.

Jan., 1926, 6 p.m.—Current blood pressure: systolic, 196-186; diastolic, 128-116. Took potassium chloride, grs. 40. 9 p.m.—Systolic, 188-186; diastolic, 114-106. Tock potassium chloride, grs. 50. 3 a.m.—Systolic, 172-152; diastolic, 106-104. 10 a.m.—Took 40 grs. of sodium



CHART VI



chloride. Noon—Systolic, 168-162; diastolic, 118-108. Took 50 grs. sodium chloride. \$ p.m.—Systolic, 218-198; diastolic, 138-134. 5 p.m.—Took potassium citrate grs. 40. 7 p.m.—Systolic, 181-168; diastolic, 128-114. Took potassium citrate grs. 50. 9 p.m.—Systolic, 176-160; diastolic, 116-104. 6 a.m.—Systolic, 168-154; diastolic, 104-96.

The results in Case 5 are very similar to those in Case 4, except in the heavy rise of the diastolic pressure on the use of sodium bromide. The sodium bromide produced more dyspnœa than did the sodium chloride and there was a decided vertigo and difficult enunciation of words.

DISCUSSION

For the past year I have been giving in my clinic a mixture of potash salts, as follows:

The above formula is used as the potassium bromide has shown itself one of the most efficient of the potash salts in reducing arterial hypertension, and in certain cases other than those quoted in this paper, where the chloride acted indifferently, this formula has been quite effi-To balance the salt privation in the cient. routine, the potassium chloride is included, in that the chlorine plays so large a part in stomach and kidney function. The citrate is one of the normal methods of potassium ingestion, and in the cases in which it was used and reported here it was the most potent salt in reducing the hypertension. The bicarbonate of potassium is now under experiment and its action will be reported later.

Bunge estimates the potash in the food of some classes as 50 to 100 grammes, *i.e.*, 850 to 1700 grains *per diem*, and deems the absence of any toxic action of the potash to be due to its rapid excretion in the urine.

In Bulgaria it has been pointed out byMetchnikoff that more than 1/10 of 1 per cent of the people reach 100 years of age, while in Great Britain less than 1/10000 of 1 per cent of people attain the century mark. This occurrence he ascribes to the large volume of milk taken in an acid or fermented condition and so influencing intestinal flora. Milk contains 90 grains of potash per quart. In addition the Bulgarians make use of sour wine, which has a heavy potash content as the tartarate. They also use vegetables and fruits, these also being rich in potash. Meat forms a small portion of their diet, and, while meat *per se* has a considerable potash content, its sparing use calls for a less amount of sodium chloride as a seasoning, thus lessening the tendency to excessive salt consumption.

One has forced on one the concept that the prevalence of arterial hypertension on this continent is in large part due to a potash poor diet, and an excessive use of salt (sodium chloride) as a condiment, and as a preservative of meat.

There has been a curious fear of the use of potash salts. This fear probably has been based on experiments done on heart muscle, with modified Ringer's solution, in which potash is in excess. The conditions *in vitro* do not obtain in the living animal, and this traditional dread is one of the myths consequent on the incompleteness of laboratory experiment. Cushney in his *Pharmacology and Therapeutics*, p. 521, quotes some work by Held, as follows: "In nephrectomized dogs, absorption of potash by the tissues proceeds so rapidly that it is only by intravenous injection or subcutaneous injections of very large quantities that the toxic threshold is reached. This does not occur if given by the mouch. In mammals 1 gramme per kilogram has a toxic action, if given subcutaneously. No danger arises to man unless given intravenously."

SUMMARY

1. That in these cases the giving of potassium chloride, bromide and citrate is associated with a drop in blood pressure below the current one with a decrease in the symptoms of hypertension, and that the giving of sodium chloride and bromide is associated with a rise of blood pressure above the current one and an increase of the symptoms of hypertension.

2. That in Case 1 the potassium citrate was as efficient a salt in the reduction of blood pressure as the chloride, and in Cases 4 and 5 it was more efficient than the chloride.

3. That in Case 1 the soda apparently acted as the toxic agent in the nephritis.

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THE TREATMENT OF FIBROIDS*

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UNTIL further research reveals something more definite as to the causative factors underlying the development of fibro-myomata of the uterus, it is unlikely that efficient preventive measures will be devised. In the meantime, we are confronted with the problem of dealing with a condition where our treatment at its very best is directed toward protection of the patient against the injurious effects of these tumours. By no means are all fibroids of the uterus injurious, but a certain proportion of them sooner or later bring about a distinct disturbance of function, while a small percentage will actually end fatally. The autopsy statistics of Hoffman show that 27.9 per cent of all women over 35 years of age have fibroids. It is thus very evident that this is a condition always to be considered, and frequently to be dealt with.

In the symptomless fibroids we are not particularly interested, except to say that we do not believe that radical measures should be adopted just because a fibroid is accidently discovered. There is an exception to this statement, to be found in the nervous type of patient, who has come to learn that she possesses a fibroid, and whose intelligence is such that she will be un-

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