

**THE PHYSIOLOGICAL EFFECTS OF
INCREASED WATER INGESTION WITH SPECIAL
REFERENCE TO THE CIRCULATORY SYSTEM.**

A THESIS

by

JOHN BOYD ORR, D.S.O., M.C.,

M.A., B.Sc., M.D.(Hons).

ProQuest Number:27701193

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 27701193

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code
Microform Edition © ProQuest LLC.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

CONTENTS

Foreword -----	3
Introduction-----	4
Section I Blood pressure experiments-----	9
Elimination of excess water-----	20
Dilution of Blood-----	21
Section II Influence on protein metabolism----	34
Section III Excretion of Salts-----	53
General Discussion-----	58
Appendix - Tables of Results-----	66
Bibliography-----	88

FOREWORD.NOTE OF ACKNOWLEDGMENT.

In certain of the experiments, viz. those of Series A Section I where the writer was the subject of the experiments, it was necessary to have the sphygmomanometer readings of blood pressure taken by others who are named in the appropriate headings of the Tables. The analysis of Table 28 where the writer was again the subject of the experiment was done by Mr A.D.Husband, Assistant Biochemist, Craibstone Nutrition Institute. To these workers who were not interested in the research the writer is indebted for assistance given, often at the expense of considerable time and inconvenience to themselves.

Thanks are also due to Professor MacWilliam of the University Aberdeen, who kindly loaned apparatus and set aside a convenient room for the work on blood pressure.

Special acknowledgment is due to the Physiology Department of Glasgow University, where the first part of the work of Section II was done, and where the writer received the stimulus that led to this, and indeed to whatever other research work he has attempted.

THE INFLUENCE OF INCREASED WATER INGESTION
ON THE BLOOD PRESSURE.

INTRODUCTION.

The influence of water drinking has been dealt with in a voluminous literature which may be roughly divided into two sections, (1) that dealing with the therapeutic value of mineral waters, and (2) that dealing with the physiological effects of water either mineral or plain. The first section which may be termed the Spa literature is very extensive. Unfortunately much of it deals with theoretical assumption rather than precise fact. The most reliable data are the results of the analyses of the various waters and these afford little support for the rather extravagant claims sometimes put forward on behalf of the waters.

The therapeutic efficacy of mineral waters has been attributed to various salts or gases in solution, to the heat of the water itself or in recent years to the presence of radium. It is within the powers of the pharmacist to impart any of these physical characteristics to ordinary rain water. But there seems to be an impression not always confined to the layman that the special therapeutic value of mineral waters lies in something imponderable and elusive that escapes the analyst/

analyst.

In spite of the unsatisfactory nature of the literature, it must be admitted however that the value of "water cures" in many cases of disordered metabolism such as dyspepsia, gout, and "chronic rheumatism" and their frequent rejuvenescent effect on those past middle age appears to be a well established empirical fact. The influence of suggestion and of the various dietetic and hygienic measures which are included in Spa treatment undoubtedly play a part, probably the most important part in the "cure." But in addition there is evidently a definite curative effect due to the waters themselves Van Noorden (1907) and others.

The physiological effects of water drinking have frequently been investigated by exact methods. As this thesis deals only with certain changes produced in the blood pressure and with the metabolism of protein in so far as it throws light upon these changes, it is sufficient here to give a brief indication of the nature of previous work done with reference to the circulatory system and the metabolism of protein. Several investigations are referred to in greater detail later.

Most of the work done on the effect of water ingestion on the circulatory system has been to determine the effects of water ingestion on the molecular concentration and haemoglobin and red cell content of the blood.

Jones/

Jones (1887) found that the ingestion of water caused a fall in the specific gravity within a few minutes. After three or four hours it returned to the normal level. Continued copious water drinking appears to be without any permanent effect on the molecular concentration of the blood, Strauss (1904), though Graube (1904) found an increase in the dry residue, the ash and the osmotic tension after prolonged drinking of either plain or mineral water. There is no reference to any worker having found in a normal subject any permanent decrease in the molecular concentration of the blood to follow increased water ingestion.

The influence of chalybeate and arsenical waters in increasing the haemoglobin and erythrocytes in the blood has been the subject of frequent investigations. Both waters produce haemopoiesis Van Noorden (l.c.) 2.

Less attention has been paid to the effects of plain water. Leichtenstern (1878) however found that drinking large quantities of plain water on three successive days produced no marked change in the haemoglobin content of the blood.

Very little data is available on the effects of water drinking on the blood pressure. Glax (1897) noted an immediate rise in blood pressure on drinking cold water and a fall on drinking hot water. Hay (1882) by/

by strong saline cathartics removed water from the blood and found "contrary to expectations" a marked rise in blood pressure as shown by sphygmographic tracings.

Benedict and Carpenter (1918) in the course of an inquiry into the influence of water drinking on the energy exchange took a few readings of blood pressure and came to the conclusion that no significant change was produced by the ingestion of water. The time of the observations relative to the drinking of the water is not recorded. They were presumably taken on the day on which the water was drunk. Such fragmentary information is all that seems to be available on the influence of water drinking on the blood pressure.

With regard to the influence of water on the metabolism of protein many observations have been made on the effects of water in the output of nitrogen in the urine. There is almost unanimous agreement that if water be freely given to an animal in nitrogenous equilibrium, the consequent diuresis is accompanied by an increased excretion of nitrogen. As to whether this increased nitrogen signifies a mere mechanical flushing out of waste products or an accelerated catabolism of protein, opinion has been sharply divided. The former view is held by Von Noorden (l.c.)³ and the latter by Voit/

Voit (1860) and others.

Fowler and Hawke (1910) undertook an investigation and extended the field of observation to include creatinin and creatinine. They found that the addition of three litres of water per day led to the appearance in the urine of a considerable amount of creatine. This output of creatine was regarded as "evidence that the water had caused a partial muscular disintegration resulting in the release of creatine but not profound enough to yield the total nitrogen content of the muscles. Their general conclusion was that the drinking of large amounts of water with meals was attended by many desirable and by no undesirable features.

THE PRESENT RESEARCH.

The investigation recorded here originated in the Physiological Department of Glasgow University in a research undertaken by Dr. Burns and the writer at the suggestion of Professor Cathcart to ascertain whether as is held by Fowler and Hawke (l.c.) the drinking of water can cause the removal of creatine from muscular tissues without the total catabolism of the muscle. Thus started the investigations on the effects of water drinking were extended/

extended by the writer to the circulatory system.

This thesis deals with certain changes produced on blood pressure which appear to be of considerable importance in clinical medicine. Other work is dealt with here only in so far as it affords some explanation of the changes.

SECTION I.

INFLUENCE OF WATER INGESTION ON THE BLOOD PRESSURE

METHODS

In each experiment a number of readings of the systolic and diastolic blood pressure were taken in a preliminary control period of two or three days. During this period the subject neither curtailed nor increased his water consumption, so that the usual amount was taken and the readings obtained under these conditions may be regarded as normal readings for the subject. Then on one or more days a measured amount of water was taken. Sometimes the amount was all drunk within a limited period. At other times the drinking was spread over the day half a litre or so being drunk at intervals. On the following days on which the readings were continued the usual amount of water was taken as in the preliminary control period. Each experiment therefore consists of three/

three periods which are indicated in the text as " pre water ", " water ", and " post water ".

Throughout all the experiments ordinary tap water was used. In the last three experiments of Series A the water was heated to 30° to 35° before being drunk. In all the other experiments water was taken as drawn from the tap without previous heating. In experiments 1 to 6 of Series A a fixed diet was maintained throughout the experimental periods. In the other experiments, at corresponding meals which were taken at the same hour of the day, the nature of the food was kept constant but the amount was not weighed. The hours of taking the readings were adhered to throughout each experiment. This was considered of some importance as there appeared to be evidence of a diurnal variation in blood pressures. The subjects of the experiments were engaged in laboratory work. To eliminate the effects of previous exercise the subject was allowed to lie for 15 minutes before readings were taken. The readings were taken with the subject lying on a bed in a room which was reserved for the work and was conveniently situated in a part of the building little accessible to external noises.

The instrument used was a Riva-Rocci with an Oliver screw compressor which allows a fine adjustment. The auditory method first suggested by Korotkoff (1905) was/

was used throughout. The accuracy of this method has been conclusively demonstrated by MacWilliam, Melvin and Murray (1914).

In a few of the experiments recorded there is a gap in the records. On these occasions for reasons not connected with the experimental work it was impossible for readings to be taken.

RESULTS.

To avoid encumbering the text with long tables the complete records of the readings are given in an appendix. The average readings of the pre water, water and post water days are given here. The figures indicate millimetres mercury.

S E R I E S A.

Subject J.B.O. age exper. 1. 33. exper. 2-6. 38.

Occupation prior to exper. 1 research worker. Between exper. 1 and 2 military service. Circulatory and renal systems normal.

EXPERIMENT 1 June 1914.

Readings were taken by Dr. Murray. The subject was on a constant low protein diet. On each of three days three litres of water were drunk throughout the course of the day between 9 a.m. and 4.30 p.m. Readings were taken/

taken at 9 a.m. and at 5 p.m. No readings were taken on second water day.

TABLE 1.

	No. of days.	No. of Readings.	Systolic.	Diastolic	Pulse Pressure.
Pre water	1	2	109	69	40
Water	3	4	106	66	40
Post water	1	1	102	68	34.

EXPERIMENT 2 April 1919.

Readings by J.R.Hewitt B.Sc. (Agr.) Research Student. On the one water day three litres were drunk between 10.25 a.m. and 12.5 p.m. Readings taken at 10 a.m., 12.30 p.m., 3 p.m., and 4.45 p.m.

TABLE 2.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	3	12	118.7	71.0	47.7	76.2
Water	1	4	116.0	73.0	43.0	73.0
Post water	1	4	115.5	72.75	42.75.	72.75

EXPERIMENT 3 April 1919.

Readings by A. Taylor. On each water day three litres were drunk throughout the course of the day from 9 a.m. to 4 p.m. Readings taken at 12 noon and 4 p.m.
Readings/

Readings were not taken at 4 p.m. on last water day. No readings were taken on first post water day. The two post water days referred to are the second and third days.

TABLE 3.

	No. of days	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	1	2	113	68.5	44.5	74
Water	3	5	114.8	67.2	47.6	75.5
Post water	2	4	99.5	62.5	37.0	71.25

EXPERIMENT 4. May 1919.

Readings as exper.3. The experiment was taken immediately after experiment 3 so that only five days elapsed between the water day of exper.3 and the water day of this experiment. $2\frac{1}{2}$ litres were taken between 10.30 a.m. and 12.15 p.m. Readings were taken at 10.30 a.m., 12 noon and 4 p.m. The 4 p.m. reading on the second post water day was not taken.

TABLE 4.

	No. of days.	No. of Readings.	Systolic.	Diastolic	Pulse Press.	Pulse
Pre water	2	6	109.5	63.2	46.3	75
Water	1	3	108.6	64.3	44.3	71
Post water	2	5	101.6	59.6	42.0	70

EXPERIMENT 5 June 1919.

Readings by Dr. Melvin. On each of the two water days two litres of water were taken on the first day between 3 p.m. and 5 p.m., on the second day between 10 a.m. and 12 noon. Readings were taken at 12.30 p.m. and 4 p.m. No readings were taken on the first and second post water days. The figures given for post water refer to the third and fourth post water days.

TABLE 5.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	3	3	110.2	62.8	47.4	72.75
Water	2	4	104.25	54.0	50.25	67.6
Post water	2	4	104.75	57.25	47.5	73

EXPERIMENT 6 August 1919.

Readings by Dr. Kinloch. Subject was on a constant high protein diet. On one water day three litres of water were taken between 1 p.m. and 5 p.m. Readings were taken at 9 a.m. before the first meal, at 1 p.m. and at 5 p.m. Readings were not taken at 5 p.m. on the first pre water day nor at 5 p.m. on the third post water day.

TABLE 6.

No. of
days /

TABLE 6.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	2	5	109.6	58.4	51.2	69.6
Water	1	3	109.3	60.0	49.3	68.3
Post water	3	8	107.5	56.4	51	72.0

S E R I E S B.

Subject J.R.H. age 31. Occupation prior to 1917
University Lecturer. 1917-19 military service. Circulatory
and renal systems normal.

EXPERIMENT 1 March 1919.

On each of three water days two litres of water
were taken between 11 a.m. and 3 p.m. Readings were taken
at 11 a.m. and 3.30 p.m. No readings were taken after the
11 a.m. reading on the third water day until the 3.30 p.m.
reading on the third post water day.

TABLE 7.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Pressure.
Pre water	2	4	111.5	70.75	40.75
Water	3	5	110.6	67.8	42.8
Post water	3	5	108.0	62.40	45.60

EXPERIMENT 2 April 1919.

On the water day three litres of water were taken between 12.30 p.m. and 3 p.m. Readings were taken at 10 a.m., 12.30 p.m., and 4.30 p.m.

TABLE 8.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Pressure.
Pre water	2	8	110.6	71.0	39.6
Water	1	4	112.25	73.50	38.75
Post water	1	4	108.5	70.0	38.50

EXPERIMENT 3 June 1919.

Readings by Dr. Melvin, Lecturer in Experimental Physiology University, Aberdeen. On the water day three litres were taken between 9 a.m. and 11.30 a.m. and 1.5 litres were taken on the previous evening between 6 p.m. and 7 p.m. Readings taken at 12 noon and 4.30 p.m. No readings were taken on the first and second post water days. The figures given refer to the third and fourth post water days.

TABLE 9.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Pre water	2	4	105	63.25	41.75	58.0
Water	1	2	106	65.50	40.50	58.0
Post water	2	4	102.5	61.25	41.25	51.5

S E R I E S C.

Subject J.I.M.I. age 21. Occupation prior to 1916 student. 1916-19 military service. No abnormality detected in circulatory or renal systems.

EXPERIMENT 1 May 1919.

On the water day three litres were taken between 10.40 a.m. and 2 p.m. Readings were taken at 10 a.m. 12 noon and 4 p.m.

TABLE 10.

	No.of days.	No.of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Pre water	2	6	124.3	74.2	50.10	62.2
Water	1	3	125.3	74.0	51.30	61.0
Post water	1	3	125.3	67.0	58.30	60.0

EXPERIMENT 2 June 1919.

On the water day four litres were taken between 10.45 a.m. and 3.40 p.m. Readings were taken at 12 noon and 4 p.m. No readings were taken at 4 p.m. on the second post water day.

TABLE 11.

	No.of days.	No.of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Pre water	3	6	121.3	68.1	53.2	62.0
Water/						

TABLE 11.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Water	1	2	120.5	69.0	51.5	66.0
Post water	2	3	117.7	65.3	52.4	60.0

EXPERIMENT 3 June 1919.

On the first water day four litres were taken between 10.20 a.m. and 3.15 p.m. On the second water day two litres were taken between 10.15 a.m. and 10.30 a.m. Readings were taken at 12 noon and 4 p.m. Only the 12 noon readings were taken on the first pre water days and no readings were taken on the second post water day. The three post water days referred to are therefore the third, fourth and fifth.

TABLE 12.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Pre water	3	6	120.9	67.8	53.1	60.2
Water	2	4	119.5	60.5	59.0	55.0
1st Post water	1	1	117.0	55.0	62.0	60.0
3, 4 & 5 " "	3	6	119.8	65.0	54.8	61.7

S E R I E S D.

Subject/

Subject F.W.L. (American soldier) age 30. Occupation prior to 1917 farmer. 1917-19 military service. This subject was powerfully built and inclined to corpulency. He was a very heavy meat eater. He had been rejected for whole life insurance in 1917 on account of high blood pressure but was accepted at ordinary rate for a 20 years' policy. He stated that his urine had been repeatedly examined for signs of renal disease but nothing abnormal had been detected. A clinical examination was being arranged but unfortunately the subject was recalled unexpectedly for embarkation before it took place.

EXPERIMENT 1. April 1919.

On the water day three litres of water were taken between 12.30 p.m. and 3.10 p.m. Readings were taken at 10a.m., 12.30 p.m., 3 p.m. and 4.30 p.m.

TABLE 13.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse.
Pre water	2	6	137.0	82.6	54.4	61.5
Water	1	3	136.3	88.0	48.3	58
Post water	1	3	137.3	84.0	53.3	60.3

EXPERIMENT 2 May 1919.

On the first water day one litre was taken between 10 a.m. and 12 noon. On the second water day three litres/

litres were taken between 10 a.m. and 1 p.m. and on the third day three litres were taken between 12 noon and 1.15 p.m. Readings were taken at 10 a.m., 12.30 p.m. and 4 p.m. The 4 p.m. reading on the second post water day was not taken.

TABLE 14.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	3	8	135.1	73.5	61.6	66.6
Water	3	9	133.9	77.8	56.1	69.6
Post water	2	5	131.0	75.8	55.2	67.2

EXPERIMENT 3. May 1919.

On the water day six litres were taken between 12 noon and 5 p.m. Readings were taken at 12.30 p.m. and 4 p.m.

TABLE 15.

	No. of days.	No. of Readings.	Systolic.	Diastolic.	Pulse Press.	Pulse
Pre water	2	4	130.7	77	53.7	64.5
Water	1	2	131.0	77	54.0	60.5
Post water	2	4	126.0	72.25	53.75	64.5

As the volume of the blood is a physical factor increasing the blood pressure it is necessary before discussing/

discussing the results obtained, to ascertain to what extent the volume of the blood is increased by the increased ingestion of water. To that end several experiments were done to determine (1) how long the additional water takes to pass through the system, and (2) to what extent dilution of the blood occurs during the passage of the water through the circulatory system.

EXPERIMENTS TO DETERMINE HOW LONG THE WATER TAKES
TO PASS THROUGH THE SYSTEM.

Several observations were made. As the results are fairly uniform it is sufficient to give the data of one experiment. The subject was J.B.O. that of series A. On three pre water days during which the water intake was uncontrolled two hourly collections of urine were made between 9 a.m. and 5 p.m. and a single collection from 5 p.m. to 9 a.m. On the last pre water day a further two hourly collection 5 p.m. to 7 p.m. was made. On the water day three litres of water were taken between 10.30 a.m. and 12 noon and the two hourly collection was continued. The results are given in Table 16.

TABLE/

TABLE 16.Rate of excretion of urine after water drinking.

	a.m.a.m.	a.m.p.m.	p.m.p.m.	p.m.p.m.	p.m.p.m.	p.m.a.m.	Total
	9 - 11	11 - 1	1 - 3	3 - 5	5 - 7	7 - 9	
	521		350		1380		2231
Water	75	175	205	105	805		1360
	95	131	202	202	240	830	1700
Water	155	1347	1607	640	128	915	4855 3 litres
Hot water	75	75	220	-	-	-	-- water

Average

On the water day there was no increased diuresis after 5 p.m. by which time all the extra water taken between 10.35 a.m. and 12 noon had been recovered in the urine.

Diuresis is evidently prompt and efficient. The excess water is eliminated within four or five hours of its ingestion.

EXPERIMENTS TO DETERMINE THE DEGREE OF DILUTION OF THE BLOOD AS SHOWN BY THE HAEMOGLOBIN AND ERYTHROCYTE CONTENT.

Several experiments were done on J.B.O. subject of Series A., and J.R.H. subject of Series B.

EXPERIMENT 1.

Subject J.R.H. Three litres of water were taken during the course of the day.

TABLE 17.

	11 a.m.		3.30 p.m.	
	Hb.	Red cells	Hb.	Red cells
Pre water day	95	5,000,000	95	5,277,000
1st water day	90	4,966,000	90	4,828,000
2nd " "	100(?)	4,260,000	90	4,200,000
3rd " "	90	4,933,000	-----	-----

EXPERIMENT 2 June 1914.

Subject J.B.O. Three litres of water were drunk during the course of the day.

TABLE 18.

	11 a.m.		3 p.m.	
	Hb.	Red cells	Hb.	Red cells
Pre water day	92	5,240,000	92	5,080,000
1st water day	94	5,100,000	92	4,200,000
3rd " "	86	3,430,000	86	3,980,000
1st Post water day	88	4,600,000	--	-----

EXPERIMENT 3 August 1919.

Subject J.B.O. Three litres of water were drunk between 1 p.m. and 5 p.m. on water day.

TABLE/

TABLE 19.

	10.45 a.m.			5 p.m.	
	Hb.	Red cells	Hb.	Red cells.	
Pre water day	105	4,750,000	110	5,300,000	
Water day	110	5,010,000	97	4,780,000	
1st post water day	97	4,850,000	110	5,600,000	
2nd " " "	--	-----	113	5,010,000	

There is evidently a definite dilution of the blood which follows the increased water ingestion and passes off as the water is eliminated. The irregularity shown in the red cell count is probably a reflection of fluctuations in the dilution of the blood on the water days. While excretion would tend to be regular, absorption would be most rapid a few minutes after the drinking of the water.

The results are in accordance with those obtained by Jones (l.c.) who found the Specific Gravity of the blood to alter within a few minutes of drinking water and to return to normal within four hours.

The following records of experiments are given by him:-

Before drinking water -----S.G. 1060.5
 5 minutes after 24 oz. were drunk.-----S.G. 1059.9
 40 " " " " " -----S.G. 1057.0
 65 " " " " " -----S.G. 1056.7

On the same subject after a meal with water the results were/

were:-

Before meal-----S.G. 1060.0

$\frac{3}{4}$ hour after-----S.G. 1058.5

4 hours after-----S.G. 1060.0

It would appear to be safe to assume that following the ingestion of a large quantity of water the volume of the blood may be temporarily increased but if no further water be taken the period of increased volume does not last beyond four or five hours. Starling (1912) states that an increase in volume due to injected fluid disappeared within two or three hours.

DISCUSSION OF BLOOD PRESSURE RESULTS.

As it is doubtful whether the subject F.W.L. can be regarded as normal the results of series D are discussed separately.

Water days. Of the Series A, B and C the readings on the water days show on the average comparatively little change from the preliminary control period. Of eleven averages of the systolic pressure seven show a decrease and four an increase. Of the diastolic averages six show a decrease and five an increase.

On these days it is evident from the above experiments that there occurred a temporary increase in the volume of the blood which would of itself tend to raise the systemic blood pressure/

pressure and more especially the diastolic as the increase would be more marked in the venous than in the arterial system. Bayliss and Starling (1894). This is evidently what occurs. The rises are more frequent and more marked in the diastolic than in the systolic pressure. The distention of the gut by the bulk of water would also probably tend to raise the systemic pressure. On the other hand the dilution of the blood would cause a diminution of viscosity which would tend to less resistance to the flow and therefore to a decrease in the pressure. A prolonged discussion of the results obtained on the water days when the issue is complicated by various physical factors would be unprofitable.

Post water days. On the post water days the volume of the blood has returned to normal and the effects of passing the water through the system are uncomplicated by the physical factors noted above. Table 20 shows the difference between the averages of the preliminary control period and the post water period.

TABLE 20.

SERIES A.

Differences in pressure between pre water and post water
days

Experiment.	1	2	3	4	5	6
Systolic	-7.0	-3.2	-13.5	-7.9	-5.45	-2.1
Diastolic	-1.0	-1.75	-6	-3.6	-7.55	-2.0

SERIES B.

Experiment	1	2	3
Systolic	-3.5	-2.1	-2.5
Diastolic	-8.35	-1.0	-2.0

SERIES C.

Experiment	1	2	3
Systolic	+ 1.0	-3.6	-3.9 (1.1)
Diastolic	-7.2	-2.8	-.2,8 (-2.8)

In experiment 3 "-3.2 and -12.9" refer to the first post water day; "-1 and -2.9" are averages for 3rd. 4th. and 5th days.

With the exception of a small rise in the diastolic pressure in experiment 2 Series A and a small rise in the systolic in experiment 1 Series C there is a more or less distinct fall in every case.

Series D. In Series D on the water days of the first and second experiments there is a marked rise in the diastolic pressure; the systolic is little effected. In the post water days of experiments 1 and 2 the rise in the diastolic has not entirely disappeared though exper.2 shows a decrease in the systolic. The third experiment is in keeping with Series A,B and C in showing a distinct fall in both the systolic and diastolic pressures.

The subject of the experiments of this Series had an initial high blood pressure. It is probable that the renal efficiency was impaired and that diuresis was less effective than in the other three subjects in keeping pace with the absorption of water from the intestine. A delay in the excretion of the excess water would cause an increased volume of blood with a consequent rise in the systemic pressure which would be more marked in increasing the diastolic pressure, where in fact the rise occurs.

The changes in Series D are shown in Table 21.

TABLE 21.

Changes in pressure in Series D.

Experiment	1	2	3
Systolic	+ 0.3	-4.1	-4.7
Diastolic	+ 1.4	+2.31	-4.75

Cumulative Effect. In Series C and D in both of which the subjects had a relatively high blood pressure there is evidence of a cumulative effect. Table 22 gives the average readings of the post water days of the experiments which are in chronological order and are separated by an intervening period of ten to fifteen days.

TABLE 22.

Cumulative effect: - Average pressure for post water days.

SERIES C.

Experiment	1	2	3
Systolic	125.3	117.7	117 (119.8)
Diastolic	67.0	65.3	55 (65)

In experiment 3 "117 and 55" refer to 1st post water day; "119.8 and 65" are averages for 3rd., 4th. and 5th. days.

SERIES D.

Experiment	1	2	3
Systolic	137.2	131.0	126.0
Diastolic	84.0	75.8	72.25

In the Series A and B the experiments were done at more irregular intervals. Thus in A five years intervene between experiment 1 and experiment 2 and two months between experiment 5 and experiment 6. Even in these series however though the same regularity is not shown the results suggest that the effects of the one experiment had not passed off when the following one was begun.

Pulse rate and pulse pressure. The pulse records are unsatisfactory. Usually several counts of one minute duration were taken before readings of the blood pressure to ensure that any effects of previous exercise had passed off/

off and that the rate had reached a constant. As the writer was frequently the subject of experiment the keeping of these and other certain data not dealt with here were entrusted to an assistant and are not now available. The counts given are controls taken after the pulse pressure readings before the subject rose from the bed. These were fortunately noted with the sphygmomanometer readings. Table 23 shows the average difference between the post water and the pre water periods.

TABLE 23.

Change in pulse rate produced by water ingestion.

Experiment	1	2	3	4	5	6
Series A		-3.45	-2.75	-5.0	+0.25	+2.4
Series B			-6.5			
Series C	-2.2	-2.0	-0.2		+(1.5)	
Series D	-1.2	+0.6	nil			

In experiment 3 Series C "0.2" refers to the first post water day; 1.5 refers to 3rd., 4th. and 5th. post water days.

The tendency throughout is to a diminution rather than to an increase in the rate.

The pulse pressure shows a decrease in eleven experiments and an increase in four.

While the results are not uniform the evidence is against/

against any attempts on the part of the organism to counteract the fall in the systemic pressure by an accelerated pulse rate or a more powerful heart beat.

The regulatory nerves of the circulatory system are normally efficient in preventing a fall in blood pressure below the required level. A fall below that level is quickly counteracted by the heart beat being altered to give either increased frequency in accordance with Marey's law or increased force as occurs for example to counteract the fall due to vascular dilution in the intestinal area after meals. Howell (1908). The fact that diminution in pressure following water ingestion is not accompanied by any increase in the rate or force of the heart beat seems to indicate that the lower level established on the post water days does not embarrass the organism or necessitate the calling into action of the regulating nervous mechanism. If this view be correct the post water systemic pressure is nearer the optimum than the pre water and the effect of the increased water ingestion has been to remove a cause of an unnecessarily augmented blood pressure. The nature of the probable cause will be discussed later in the light of the results obtained on the influence of increased water ingestion on the protein metabolism.

There is very little work with which the results obtained here can be compared. Glax (l.c.) found an immediate/

immediate increase in blood pressure to follow drinking cold water and the opposite effect to be produced by hot water. These results are doubtless to be explained as due to thermal influences causing contraction or relaxation of the vessels of the intestinal area. That the heat of the water has no lasting influence is shown in Series A where the water taken in experiments 1-3 was cold and that taken in experiments 4-6 was at nearly blood heat. There is no marked difference in the results obtained. The findings of Glax however may account for some of the increases of pressure recorded on the water days. In several instances the drinking of cold water occurred immediately before the taking of the blood pressure.

Benedict and Carpenter (l.c.) took some sphygmomanometer readings of the systolic pressure before and after the ingestion of 500 c.c. water at a temperature of 22° to 35°. Their readings which are few in number are given here in full:-

	<u>Before Water</u>	<u>After Water</u>
V.G.	102, 107, 105.	103, 100
J.J.C.	108, 111, 120.	102, 105, 102
C.H.H.	119, 122, 120, 120.	119, 115, 104.
A.S.E.	117, 116.	126, 128, 119, 117.

The/

The average readings are:-

	<u>Before Water.</u>	<u>After Water.</u>	<u>Difference.</u>
V.C.	104.67	101.5	-3.17
J.J.C.	113.0	103.0	-10.0
C.H.H.	120.25	106.7	-13.55
A.S.E.	116.5	122.5	+6.00

The conclusion of these workers is that "a general inspection of the results shows nothing significant in the change of either pulse or blood pressure as a result of the ingestion of water."

No indication is given of the time relationship of the drinking of the water and the taking of the blood pressure readings. If the readings were taken on the water day as is most probable the records are confirmatory of the results shown here. A fall occurs in every case except A.S.E. and the after water readings show a distinct tendency to fall. A record of the blood pressure of A.S.E. on the following day would have been of interest. It is unfortunate that the records are so scanty and lack any reference to the diastolic pressures.

Summary of Results on Blood Pressure.

- (1). In the normal person increased ingestion of water is followed by a decrease in both systolic and diastolic/

diastolic blood pressure.

- (2). The decrease in pressure is not accompanied by an increase in either rate or force of heart beat.
- (3). There is evidence of a cumulative effect of periods of increased water ingestion in reducing blood pressure.

It is suggested that the increased water intake operates by removing some cause which produces an unnecessarily augmented arterial pressure.

SECTION II.INFLUENCE OF WATER INGESTION ON PROTEIN METABOLISM.

A number of observations have been made on the effects of increased water ingestion on the output of nitrogen. That the subsequent diuresis is accompanied by an increased output of nitrogen in the urine is now well established. The point in dispute is whether the increase in urinary nitrogen signifies a mere flushing out of waste products or an increased catabolism of protein. It was thought that further information might be gained by making a more complete urinary analysis and by doing several experiments each with a different amount of protein in the diet the total caloric value of which however would be in each case sufficient to cover the energy exchange of the subject.

METHODS.

The subjects of the experiments, normal healthy males, were given a fixed creatine-free diet for several days, until the daily excretion of the various nitrogenous constituents of the urine had become approximately constant. Thereupon, in addition to the diet, a given quantity of water was drunk each day for three days, whereafter, the diet/

diet was continued for several days more without the extra water. Some of the water was taken with the meals and the rest in the intervals between. The protein content of the food was varied in the different experiments from 27 to 319 grams per. day. The urine was collected in 24 hour samples, the collection being completed at 9 a.m. before either food or water had been taken for the day.

In one of the experiments, No. 4, the water taken during the preliminary period was fixed in amount. The daily requirements however, as indicated by the inclination of the subject to drink, were not uniform. In all the others therefore, to ensure that the conditions on the "pre water" days would be as natural as possible, the amount taken was not restricted. It was considered that this procedure would give a more perfectly normal period for comparison with the period of excessive consumption and that the volume of the urine would indicate the average daily intake, with sufficient accuracy for the purposes of the research.

The methods of analysis adopted were: total nitrogen-- Kjeldahl: ammonia-- Folin: urea Experiments 2, 3 and 4,-- Folin, 1 and 5,-- the urease method described by Plimmer and Skelton (1914): amino acids-- Sorensen's formalin titration method: creatine and creatinine-- Folin.

EXPERIMENTS/

EXPERIMENTS.

A series of four experiments was done. In the first the protein in the diet was very low 27 grams. In the second moderately low 48 grams. In the third moderately high 160 grams. In the fourth very high 319 grams. A fifth control experiment with a normal diet containing 110 grams of protein was done. In it nitrogenous equilibrium had not been attained before the increased water intake. Its results are omitted in discussing the effects of water on the excretion of total nitrogen.

To avoid burdening the text with long tables the details of the diets and the records of the urinary analysis are given in the appendix.

RESULTS.

Total Nitrogen. In all the experiments except No. 4 the increased ingestion of water causes a distinct rise in the excretion of total nitrogen. There is, however, in the degree of the increase a lack of uniformity, which corresponds to the divergent results obtained by different workers. Thus Forster (1878) found an increase of 90%, Heilner (1906) 40%, Voit (1860) 25%, Mayer (1880) 9%, Gruber (1901) 7%, Frankel (1877) 6-12%, and Salkowski and Munk (1877) about 3%. Dubelir (1891), Seegen (1871) and Straub (1899) found no distinct increase./

increase. Heilner (1906) suggests that the results vary with the amount of food. Voit and Forster worked with fasting dogs, while Dubefir and others used dogs on an ample diet of flesh. In the present series of experiments the greatest increase was obtained in exper. 1, where the protein was abnormally low, whereas in experiment 4 with the high protein intake there was no increase. In table 24 the whole series is compared.

TABLE 24

Exper.	No. of in diet Protein approx. g	Excretion of Tot. N. on last pre- water day, g.	Excretion of Tot. N. on first water day, g.	Increase in Tot. N. g	Increase per cent
1	27	6.30	8.6	2.3	36.5
2	48	8.77	9.83	1.06	12.1
3	160	17.47	19.04	1.57	8.9
4	319	40.22	40.19	nil	nil

It is thus seen that the percentage of total nitrogen excreted on excessive water ingestion tends to vary inversely with the amount of protein fed.

In experiment 4 there is evidence of a marked retention of nitrogen on the cessation of the excessive water intake. After the single water-drinking day the amount excreted fell from 40.19 to 34.69 grams. After the three-day period of increased water intake it fell from 39.24 to 34.16, /

34.16, and only returned to its former level on the fourth day.

There would appear to be two distinct factors involved, one, whose action is immediate and whose influence is most manifest in protein deficiency, tending to cause a flushing out of nitrogenous end products, and another, whose influence is more prolonged, tending to cause a retention of nitrogen.

Ammonia. There is in every instance a distinct rise in the ammonia output which coincides exactly with the increased water intake. This is in keeping with the results of Fowler and Hawk (1910), who argued that the water stimulated gastric secretion and the increased ammonia represented the amount necessary to neutralise the excess of HCl thereby produced. If this argument were well founded the increase in ammonia output should be more or less parallel with the increase in water drunk. As appears in Table 25, there is no evidence of such parallelism.

The increase of water passing through the system must accelerate the flow of blood through the liver and of lymph through the tissues. In the process of deamination as the NH_2 moiety is detached it would tend to be carried off by the accelerated flow of blood and lymph and excreted as ammonia instead of being converted to urea. If this supposition be correct, the increase in ammonia would be in some degree proportional to the extent of deamination taking/

taking place in the tissues, which in turn would be influenced by the amount of protein in the food. The following table shows that the increase in ammonia more or less corresponds to the amount of food protein being catabolised.

TABLE 25.

No. of exper.	Protein in diet g.	NH_3N Aver. excret. on non-water days, g.	NH_3N Aver. excret. on water days, g.	Increase g.	Percentage increase.
1	27	0.222	0.259	0.037	16.6
2	48	0.345	0.461	0.116	33.6
5	110	0.301	0.392	0.091	30.2
3	160	0.430	0.575	0.145	33.7
4	319	0.273	0.529	0.256	93.8

The increase in ammonia evidently represents a mere flushing-out process, and the amount of the increase depends upon the amount of ammonia being liberated in the liver and other tissues.

Urea. The rise in the urea output is most marked, both in absolute amount and in percentage of total nitrogen excreted as urea, the increase is maintained throughout the water and the post water periods. Thus, in Exper. 1 on the third water day the total nitrogen falls from 6.3 grams on the pre/

pre water days to 6.125, while the urea rises from 4.154 to 4.388. In experiment 2 the average urea output of the post water days is 6.52 as against 6.03 on the pre-days. In exper. 3 the figures are: pre water 14 g., post water 16.46 g. In experiment 4, on the last day of the records, i.e. the fourth day after the period of increased water intake, the total nitrogen output is 40 g., as compared with an average of 41.53 g. in the preliminary period, while the urea, instead of decreasing with the total nitrogen, rises from 34.09 to 37.184 g. The prolongation of the increased excretion of urea beyond the period of increased diuresis is evidence that the increase cannot be accounted for by a mere mechanical flushing-out of urea accumulated in the tissues.

Table 26 shows the percentage of total nitrogen excreted as urea in the preliminary period and in the period following the beginning of the increased consumption of water including both the water and post water days.

TABLE

TABLE 26.

No. of Exper.	Average daily excretion in preliminary period.			Average daily excretion on water and post water days.			
	Tot. N. G	Urea G.	Per. cent. of Tot. N. as urea	Tot. N.G.	Urea G.	Per Cent of Tot. N. as urea	In- crease Per. cent.
1	6.3	4.154	65.9	7.02	5.184	73.8	7.9
2	8.92	6.025	67.5	9.374	6.492	69.3	1.8
3	17.50	14.005	80.0	19.286	15.666	81.2	1.2
4	41.53	34.09	82.8	38.27	35.07	91.6	8.8
5	11.848	9.199	77.6	13.30	10.779	81.0	3.4

It will be seen that the greatest increase in the excretion of urea occurs in exper. 1 where there is a protein deficiency, and in exper. 4, where the protein intake is excessive.

Amino acids. In experiments 1 and 2 on the low protein diets there is an immediate rise in the excretion of amino acids on the first day of increased water ingestion. In exper. 3 with a moderately high protein intake there is a slight drop, and in exper. 4, where the protein intake is higher, the drop is marked. Table 27 compares the series.

TABLE/

TABLE 27

No. of Exper.	Prot. Intake G.	Amino acid N. Average in prelim. period.	Amino acid N. First water day.	Difference.
1	27	0.128	0.163	+ .035
2	48	0.181	0.363	+ .182
5	110	0.255	0.257	+ .002
3	160	0.117	0.100	-.017
4	319	0.270	0.103	-.168

While there is an absence of uniformity in the results, they are such as suggest, that with a deficiency of protein in the food the stimulated diuresis due to increased water intake causes an initial washing out of the amino acids, while with an excess of protein the increased water intake causes an initial retention of these. As these results are not maintained, they would appear to be due to the sudden alteration in the amount of fluid passing through the system.

Faecal nitrogen. Only in experiment 1 was the collection and analysis of faeces made. The daily evacuation was fairly regular, taking place in the forenoon. The first day's collection was discarded, as they belonged more properly to the preceding period. Those of the first water day were regarded as belonging to the preliminary period and those/

those of the first post water day as belonging to the water period. The results obtained were:

Preliminary period.		Increased water period.	
Dried Weight	Total nitrogen	Dried Weight	Total nitrogen
19.42 g.	0.927 g.	12.9 g.	0.542 g.

These results are in agreement with those of Fowler and Hawk (1910). Too much importance should not be attached to the results of a single experiment, but even keeping in view the fact that the faecal nitrogen is not all derived from food residues, the results seem to suggest that the increased consumption of water is productive of a more complete utilisation of the ingested protein.

Creatine and creatinine. In expts. 2, 3 and 4 there is on the water days an apparent decrease in the excretion of creatinine. On these days however, the bulk of the urine was enormously increased and the concentration of the creatinine correspondingly decreased. It was necessary, therefore, to depart from the routine mode of analysis on the water days. In some instances 30 c.c. of urine were taken for analysis instead of 10 c.c., and in other instances, after development of the colour, dilution was carried only to 250 c.c. instead of to 500 c.c. Both of these deviations, which are recommended by Folin (1904) in such cases, in his original description/

description of the calometric method are productive of error, showing a reduction in the amount of creatinine found which is quite fictitious. In experiments 1 and 5 the urine from the beginning was diluted to 5,000 c.c. and the dilution and method of analysis rigidly adhered to throughout the experiment. In these, on the water days there appears no decrease in the amount of creatinine excreted. It may be concluded, therefore, that the decrease found in the earlier experiments should be ascribed to faulty methods of analysis. On no occasion was the increased consumption of water followed by the appearance of creatine in the urine.

The influence of excessive water ingestion on the excretion of creatine and creatinine was dealt with in a separate research (Burns and Orr, 1914) and need not be further discussed here.

DISCUSSION OF RESULTS

The source of the increased excretion of nitrogen on excessive consumption of water has been much discussed. V. Koorden (1907, 13) after a review of the literature says: "It all turns on the flushing of nitrogenous end products out of the system." He bases his conclusion largely on the work of Neumann (1899), who found that, as the consumption of water rose, the urinary nitrogen rose, the rise being most/

most marked on the first day and rapidly disappearing, and that on a return to a normal consumption of water there occurred a retention of nitrogen. This view is supported by Abderhalden and Bloch (1907). These workers used as a subject of a water drinking experiment a person suffering from alkaptonuria. On the administration of 5 litres of water there occurred a distinct increase in the amount of nitrogen in the urine. The output of homogentisic acid however showed a slight decrease. The amounts were: pre water 10.51, water 10.18 and post water 10.27. They concluded that the constancy of output of homogentisic acid indicated a constancy of protein metabolism, and that the increase in the excreted nitrogen represented a washing out of nitrogenous end products.

The initial increased output of nitrogen in the urine and subsequent retention have been here verified, but the compared results obtained on the varying protein intakes do not support the view that the increase represents a mere flushing out of end products. If that view were correct, the greatest increase would appear where there existed the greatest amount of end products, which one would expect to be during the period of highest protein intake. We have seen however that it is just in this case that no increase takes place, a result which is in/

in agreement with the findings of those who worked with dogs on a heavy flesh diet Dubelir (1891) and others. On the contrary, the highest increase is found in experiment 1, where the protein was abnormally low, viz. 27 grams per. day, the diet consisting mostly of carbohydrate and fat, in which case one would expect the minimum accumulation of nitrogenous end products liable to be flushed out.

While it is not to be doubted that there occurs a flushing out process, to which the increase of ammonia appears entirely due, the whole of the influence exerted by the water cannot be ascribed to this mechanical cause. The results obtained on the varying protein intakes, together with the fact that the increased percentage of urea continues on the post water days, after the mechanical flushing-out process has ceased, indicate that the water has a direct influence on the protein metabolism.

Voit (1860) believed that the influence of the water is to produce an increased protein catabolism, a view supported by Forster (1878) and others. In conditions of protein deficiency as in fasting dogs with which Voit worked, such a conclusion appears reasonable. In experiment 4, however, where the protein of the food is excessive in amount, there appears on the addition of the extra water no increase in the urinary nitrogen, but there occurs a most marked rise both in the absolute amount of urea and in the percentage/

percentage of total nitrogen excreted as urea, a result obtained in all the experiments. While it is doubtful, therefore, whether in conditions of protein sufficiency excessive consumption of water causes an increase in the amount of protein catabolised, as indicated by the urinary nitrogen, there appears to result in every case a stimulation of the catabolic processes, leading to a more complete disintegration of the protein molecule and the production of those end products whose immediate destination is excretion.

The subsequent marked retention of nitrogen in experiment 4 is in agreement with the results obtained by Neumann (1899) and Fowler and Hawk (1910). In view of the fact that the retention takes place on the highest protein diet (319 grams per day), when there would be a surplus of circulating protein and non-protein nitrogenous material within the economy, it is improbable that the amount retained, viz. about 8 grams after the one day's water drinking, and in addition to that about 14 grams after the three day's period, would represent an addition to either of these bodies. It is more probable that the retained nitrogen represents an increase in tissue protein.

A possible explanation is available for the mode of action of increased passage of fluid through the tissues in accelerating catabolism. In enzyme action the accumulation of/

of end products paralyses the enzyme and the action slows down Kronecker (1874). An increased flow of fluid in the environment of the cell and probably a resulting increased interchange of both water and substances in solution between the cell and its fluid environments would conduce to a more rapid removal of the end products of catabolism and thus allow the reaction to continue without any reduction of velocity.

To afford an explanation for the suggested acceleration in the synthetic phase of protein metabolism is more difficult, if, as is probable synthetic processes within the living cell are determined by the action of enzymes. Synthesis occurs in a concentrated solution more readily than in a dilute one. It is highly improbable however that any marked degree of dilution occurs within the cell. It has been seen in the section dealing with the changes produced in blood pressure that the excess water is eliminated almost as fast as it is absorbed from the intestine and that even in the blood, dilution is slight and only temporary. There is no stagnant concentration of water. The marked feature is not dilution but increased velocity of the flow of the body fluid with presumably increased mobility of the products of metabolism. It is quite conceivable that the accelerated/

accelerated movement of the fluid may afford a means of removing the products of synthesis from the sphere of the reaction either by washing them away to a different part of the organism or by removing them to another part of the cell. This would allow the synthetic action to proceed with undiminished velocity. In the pre water period when the products of the reaction were not so efficiently removed their accumulation would tend to slow down the reaction. Consequently the water days would show an increased synthesis as compared with the pre water days.

It is noteworthy that in privation of water a loss of nitrogen takes place both during the privation and for several days afterwards Dennig (1901). The loss is not associated with increased consumption of oxygen Salmon (1905). It looks as though the loss were associated with a failure to synthesise rather than with increased catabolism. Reference has been made to the fact that the percentage of total nitrogen excreted as urea increases on the water days. The increased percentage persists on the post water day. In exper. 4, with the very high protein diet it is even higher on the post water than on the water days. In those of the preliminary period the average percentage is 82.175. on the first (single) water day it rises to 90.6. On the three/

three water days it rises further to 91.63. On the four post water days it reaches 91.95. In the post water period diuresis is practically the same as in the preliminary period so that the increased excretion of urea can not be attributed to urea being washed out. Nor indeed even on the water days can the increased percentage of urea be wholly accounted for by a flushing out process for in that case on the cessation of the increased diuresis there would tend to be an accumulation of urea in the fluid and tissues of the body until the level of the preliminary period had been reached. The results which are uniform in all the experiments rather indicate that the influence of the water has been to produce a more complete disintegration of the protein molecule resulting in a higher percentage of the final products. This is well shown in exper. 4 the very high protein diet. On the four pre water days the amount of undetermined nitrogen including purin bodies is in grams:

4.07	4.44	6.217	6.666
------	------	-------	-------

On the four post water days after the double flushing out the amounts are:

0.503	0.663	0.681	0.854
-------	-------	-------	-------

Howe, Mattill and Hawk (1911) obtained a reduction in the excretion of purin bodies following increased water ingestion in a dog.

Evidently what appeared as undetermined nitrogen

in the preliminary period became converted to urea after the ingestion of the water. The fact that this more complete conversion to urea persists after the increased diuresis has ceased suggests that it is not due to the mechanical effects of the increased flow but to the influence of the flushing out process either by producing a stimulus to metabolism or, what is more probable in removing some substances that interfere with catabolism. It seems highly probable that the water flushes out certain deleterious waste products and that the removal of these permits the metabolic processes to proceed with greater vigour.

If the views put forward here be correct what occurs on water drinking is firstly a preliminary clearing out of the tissues of certain nitrogenous metabolites probably after their conversion to urea. This produces the initial increase in excretion of nitrogen in the urine which has been observed by most workers. Following the removal of these substances there is an acceleration of both the catabolic and synthetic phases of metabolism resulting in the one case in final products which are excreted and in the other in completely synthesised protein built into the tissues. The amount of protein metabolised is not necessarily increased but both catabolism and synthesis are more complete.

SUMMARY/

SUMMARY OF THE RESULTS OF SECTION 2.

The excessive ingestion of water produces:

(1) An increased excretion of urinary nitrogen which is most marked on a low protein diet.

(2) A retention of nitrogen on the return to normal consumption of water in the case of abundant protein intake.

(3) An increase which persists on the post water days in the percentage of total nitrogen excreted as urea.

(4) A ~~marked increase in the excretion of ammonia~~

(5) ~~No~~ excretion of creatine and no decrease in the excretion of creatinine.

(6) A decrease in the faecal nitrogen which is interpreted as indicating a more complete utilisation of the food protein.

It is suggested that the results indicate that the influence of the increased water consumption is to accelerate both the catabolic and the anabolic phases of protein metabolism and that this is accomplished by the flushing out from the tissues of certain nitrogenous waste products which retard metabolic processes.

SECTION 3.THE INFLUENCE OF WATER INGESTION ON THE EXCRETION OF SALTS

It is well known that certain salts play an essential part in the production of the heart beat. Sodium ions are necessary to maintain the contractability and irritability of the cardiac muscles. Potassium induces a relaxative of the muscles. Calcium promotes tonic contraction. It was thought that in the excessive diuresis produced by the quantities of water used in the experiments a possible washing out of certain of these salts might occur and the alteration in the relative proportions be responsible to some extent for the change noted in the blood pressures. The excretion of salts in water drinking has been neglected. No data could be found to give information as to whether a flushing out of salts takes place. It was thought desirable to obtain some definite data. The following experiment was therefore carried out.

The subject (J. B. O.) was given the following constant diet with no salts except what was contained in the food stuffs.

Oatmeal	75 g.	Plasmon	150 g.	Cocoa	10 g.
Haricot Beans	100 g.	Margarine	50 g.	Cheese	100 g.
Biscuits	100 g.				

The routine of the experiment was as has been described

in/

in Section II. On the fourth day of the constant diet 3 litres of water were drunk, analysis for the first day of the diet are not given. The diet was continued on two post water days. Urine was collected in four-hourly periods from 7 a.m. to 7 p.m. during the day and in a single period 7 p.m. to 7 a.m. overnight.

The methods of analysis adopted were:

Chloride - Volhard; Phosphates - Uranium acetate.

For Calcium, Magnesium, Sodium and Potassium, the methods as described by Plimmer (1915) were adhered to.

The excretions for each of the periods are recorded in page 87 of the appendix. The following table gives the amounts for the full day.

TABLE 28.
EXCRETION OF SALTS.

Day	Calcium	Magnesium	Potassium as K.Cl.	Sodium as NaCl.	Chlorides as NaCl.	Phosphates as P_2O_5	
	g	g	g	g	g	g	
2	0.2430	0.1174	2.950	6.186	6.177	1.610	
3	0.2472	0.0455	1.5168	6.0372	3.6772	1.500	
4	0.2182	0.0827	1.2808	4.8112	2.1924	3.130	3 litre
5	0.2491	0.0411	0.9672	5.2378	2.449	2.910	H_2O
6	0.3029	0.0431	0.9155	6.3545	3.480	2.175	

DISCUSSION/

DISCUSSION OF RESULTS

Calcium. The excretion of calcium is a function of the intestine rather than of the kidney. The amounts appearing in the urine without reference to the amounts excreted in the faeces give no indication of the total loss to the body or of any change in the metabolism. The small decrease of calcium in the urine on the water day is probably without any special significance except that it indicates that no loss of calcium takes place through the kidney as the result of increased diuresis.

Magnesium. About 50% of the excreted magnesium is eliminated through the kidney. Starling (l.c.). There is a marked increase in the amount excreted which is confined to the water day. It is probably due to a flushing out process.

Sodium and Potassium. The excretion of potassium shows a uniform diminution which is not affected on the water day. A marked decrease takes place in the excretion of sodium. The difference in behaviour of these two bases is probably dependent upon their different association in the blood. Potassium is contained in the corpuscles and is only present in the plasma in very small amounts. Sodium on the other hand is present in the plasma to the extent of 4 or 5 parts per 1000. In the dilution of the blood following increased water /

water ingestion the percentage of sodium would tend to be lowered below the threshold limit of elimination and the excretion would consequently tend to be diminished. The potassium on the other hand being within the corpuscles would not be affected.

Chlorides. The decrease in the excretion of chlorides is probably related to the diminished excretion of sodium with which it is chiefly associated in the blood plasma. There is a parallelism in the diminution in the two cases.

Phosphates. In the excretion of phosphates there occurs a marked decrease which has not disappeared on the third post water day. As the diet is fixed there is a constancy in the intake of calcium and alkaline metals. There is no reason therefore to suppose that any reduction has taken place in the amount of phosphates excreted by the bowel. The increase therefore suggests an increased catabolism of phosphorous containing substance and is analogous to the continued increase in the urea on the post water days.

SUMMARY OF RESULTS OF SECTION 3.

The increased ingestion of water produces the following changes in the urinary excretion of the substances named:-

(1) Calcium. A small decrease which is probably without/

without significance.

(2) Magnesium. An increase which is attributed to a mechanical flushing out.

(3) Potassium. No change.

(4) Sodium. A decrease, the reason for which is suggested to be the decreased concentration of sodium in the blood due to dilution.

(5) Chlorides. A decrease which is parallel to and probably associated with the decreased eliminations of sodium.

(6) Phosphates. An increase which persists on the post water days and which is taken as an indication of increased catabolism of phosphoreous containing substances.

A general inspection of the results seems to justify the conclusion that the ingestion of water causes no increased excretion of salts that can account for the post water decrease in blood pressure.

GENERAL DISCUSSION.

The general conclusion arrived at in Section I was that increased water ingestion produces a definite fall in blood pressure. The results of Section II suggest that the same cause promotes the more efficient elimination of waste products and give a stimulus to the processes of metabolism of protein resulting in a more rapid elaboration of the end products of both catabolism and synthesis. The question arises as to whether these results are related. It has long been known that the products of cell activity affect blood pressure. Gaskell (1880) showed that the acid end products of metabolism produced a local dilatation. Hooker (1911) found that a like effect is produced by certain nitrogenous catabolic products. The central effect is the opposite of the local. Acid metabolites promote greater efficiency in cardiac muscle by increasing diastolic relaxation as well as increased systolic contraction Jerusalem and Starling (1910). This occurs in extreme degree in asphyxia. A like stimulating effect is produced by urea and certain other nitrogenous catabolic products (xanthin, hypo xanthin, creatine, ammonium carbamate, sodium hippurate). Hooker (l.c.)

In the literature of clinical medicine there is abundant evidence of a strongly held belief that increased peripheral/

peripheral resistance due to contraction of arterioles is brought about by excess of nitrogenous waste products, by the products of incomplete or perverted metabolism, and by decomposition products of protein which originate in bacterial action in the intestine and are absorbed to the blood stream Huchard (1893), Senator (1907), Russell (1907) and others. These beliefs however are in general, opinions rather than conclusions based on experimental data.

In recent years there has been an accumulation of definite evidence of the influence of nitrogenous metabolites in raising blood pressure. Mott and Halliburton (1899) showed that neurine a substance closely related to cholin produced a fall in blood pressure chiefly due to direct action on the heart. This is followed by a rise of pressure due to contraction of arterioles. Abelous Ribaut, Soulié and Troujan (1906) found an extract of putrid meat that markedly raised blood pressure. Dixon and Taylor (1907) found in extract of placental tissue an active principle that caused a like result. Barger and Dale (1909) showed that the most active pressor substance of putrid meat was p-hydroxyphenylethylamine which is derived from tyrosine in anaerobic disintegration by the splitting off of carbon dioxide. Rosenheim (1909) showed that the same amine was the active principle of placental extract which caused the rise of blood/

blood pressure noted by Dixon and Taylor (l.c.). This derivative of tyrosine seems to be of frequent occurrence in protein disintegration in the presence of bacteria. Van Slyke and Hart (1903) and Winterstein and Kunz (1909) found it in different kinds of cheese. Dale and Laidlaw (1910) showed that *b*-iminazolyethylamine, an amine derived in the same way from histidine promotes contraction of the arterioles and rise of blood pressure in rodents though in carnivora the direct action on the muscle of the systemic arterioles is overcome by some antagonistic peripheral action the nature of which is not understood. Another substance of this class is agmatine isolated from herring roe by Kessel (1910). It is derived from aginine by the loss of carbon dioxide. A number of the primary fatty amines that promote arterial constriction and rise of blood pressure have been enumerated and their relationships shown by Barger and Dale (1910). Dale and Dixon (1909) showed that isocamylamine and hydroxyphenylethylamine derived by bacterial action from leucine and tyrosine respectively are absorbed from the alimentary canal and produce pressor effects when so administered. These results make it clear that certain products of putrefaction which may arise in the intestine can be absorbed in the blood and exercise a pressor influence/

influence by promoting arterial constriction.

The possibility of these pressor constituents of protein disintegration arising by means other than bacterial action has been shown by Emerson (1902) who obtained p-hydroxyphenylethylamine (derived from tyrosine) in the autolysis of pancreas under conditions that excluded putrefaction. Langstein (1902) obtained the same body in prolonged peptic digestion of egg albumin.

Though the primary object of the researches referred to above was to determine the chemical structures and relationships rather than the physiological effects of certain amines, they have incidentally shown that certain amines which exert a pressor influence on the circulatory system, can originate in the intestine and be absorbed to the blood stream. They also suggest the possibility of certain nitrogenous substances with a pressor influence arising in the tissues as a result of a perverted or incomplete metabolism.

In section 2 it has been shown that the increased water ingestion produced a marked decrease in faecal nitrogen, a result which is merely a confirmation of that obtained by Fowler and Hawk (l.c.). These workers found further that there was a decrease in the bacteria of the faeces. The explanation offered by them is that "the water has brought about/

about conditions which have caused a more rapid digestion and absorption of the protein constituents of the blood," and "there being less nitrogenous material present in the intestine during the water period, naturally the bacteria could not develop so satisfactorily as in the preliminary period."

It is probable that the greater dilution of the gastric contents as discharged into the duodenum would facilitate a more rapid hydrolytic cleavage of the protein to amino acids (see page 47). The rapid absorption of water from the upper part of the intestine would tend to the more rapid absorption of the soluble products of digestion. There would thus be less residual nitrogenous material available for anaerobic disintegration in the lower part of the intestine, with a consequent reduction in the formation and absorption of these amines noted above and probably also of other bodies not yet identified which cause arterial constriction. This may afford a partial explanation for the reduction of blood pressure noted in Section I.

Evidence was brought forward in Section II to support the view that the passage of the water through the system promotes an acceleration of both catabolic and synthetic processes. If this be correct there would result a/

a reduction of intermediate products of metabolism. The great reduction in the amount of undetermined nitrogen including purin bodies in the water and post water days (page) lends support to this view. It is noteworthy that the reduction in blood pressure and the decrease in the amount of undetermined nitrogen in the urine persist concurrently for two or three days after the water drinking has ceased. It has been shown that substances which produce arterial constriction can originate from protein by means other than bacterial action. Emerson (l.c.) Langstein (l.c.) It may well be that these do rise in cases of sluggish or perverted metabolism or under conditions of protein surfeit. If this were established one could attribute the fall in blood pressure to the flushing out of these bodies or to their change to inert final products.

An explanation is afforded to the results obtained by Hay (l.c.) who reduced the volume of the blood by concentrated saline cathartics and "contrary to expectations" found an increased blood pressure due to "a contraction of the smaller arteries and capillaries." He attributed the result to the salt "stimulating the tunica intima of the vessels as it circulates in the blood." He used sodium sulphate and magnesium sulphate. MacWilliam, Mackie and Murray (1904) found that magnesium sulphate produces a fall in/

in blood pressure whether injected to artery or vein and that sodium sulphate produces no change. The explanation offered by Hay is evidently invalid. The cathartics in reducing the volume of the blood would reduce diuresis and the flow of fluid through the tissues which condition of affairs according to the view put forward here would facilitate the production and accumulation of these metabolic products which have been suggested as a cause of arterial constriction. Hay produced conditions which are exactly opposite of those induced in the experiments recorded here, and obtained an opposite result.

GENERAL CONCLUSIONS.

Increased water ingestion produces:-

(1) A fall of blood pressure both systolic and diastolic, which is not accompanied by an increase of either rate or force of heart beat.

(2) An acceleration of both the catabolic and synthetic phases of protein metabolism, with elimination of intermediate products of metabolism and probably also the products of perverted metabolism.

Reasons are advanced in support of the view that the fall in blood pressure is brought about by the removal of/

of these metabolic products which by promoting arterial constriction produce an unnecessarily augmented blood pressure.

APPENDIX.

Detailed Tabulated Results.

DETAILED RESULTS OF SECTION 1.SERIES A. SUBJECT J.B.O.EXPERIMENT 1. June 1914. (Table 1.)

Readings by Dr. Murray, Physiological Department,
Aberdeen University.

Subject was on a constant low protein diet.
On each of three days three litres of water were drunk
throughout the course of the day between 9 a.m. and
4.30 p.m. Readings were taken at 9 a.m. and at 5 p.m.
No readings were taken on the second water day.

TABLE (See page 12.)

<u>9 a.m. Reading</u>				<u>5 p.m. Reading.</u>		
	Syst.	Diast.	Pulse Press.	Syst.	Diast.	Pulse Press.
Pre water	108	70	36	110	68	42
Water	108	65	43	108	68	40
	-	-	-	-	-	-
	104	66	38	104	65	39
Post water	102	68	34	-	-	-

EXPERIMENT 2. April 1919. (Table 2).

Readings by J.R.Hewitt, B.Sc., (Agr.) Research Student. On the one water day three litres were drunk between 10.25 a.m. and 12.5 p.m. Readings were taken at 10 a.m., 12.30 p.m., 3 p.m. and 4.45 p.m.

TABLE 2 (See page 13.)

<u>9.45-10 a.m. Reading.</u>				<u>12.30 p.m. Reading.</u>				
Pulse				Pulse				
	Syst.	Diast.	Press.	Pulse	Syst.	Diast.	Press.	Pulse
Pre water	125	69	56	78	110	69	41	72
	120	69	51	84	118	73	45	72
	125	75	50	64	120	75	45	72
Water	122	73	49	79	111	73	38	80
Post water	116	73	43	-	128	72	46	-

<u>3 p.m. Reading.</u>				<u>4.45 p.m. Reading.</u>				
Pulse				Pulse				
	Syst.	Diast.	Press.	Pulse	Syst.	Diast.	Press.	Pulse
Pre water	118	68	50	80	124	70	54	72
	113	69	44	-	119	74	45	-
	116	69	47	72	116	72	44	-
Water	120	73	47	72	111	73	38	78
Post water	117	72	45	-	111	74	37	-

EXPERIMENT 3April 1919. (Table 3).

Readings by A. Taylor, Senior Attendant, Physiological Department, University Aberdeen.

On each water day three litres were drunk throughout the course of the day from 9 a.m. to 4 p.m. Readings taken at 12 noon and 4 p.m. Readings were not taken at 4 p.m. on last water day. No readings were taken on first post water day.

TABLE 3 (See page 13.)12-12.30 p.m.4 p.m.

	Pulse			Pulse	Pulse			Pulse
	Syst.	Diast.	Press.		Syst.	Diast.	Press.	
Pre water	110	68	42	70	116	69	47	78
Water	116	70	46	72	115	67	48	72
	119	64	55	74	112	65	47	84
	112	70	42	-	-	-	-	-
Post water	102	60	42	70	102	58	44	72
	100	66	34	74	94	66	28	69

Reading as experiment 3.

The experiment was taken immediately after experiment 3 so that only five days elapsed between the water day of experiment 3 and the water day of this experiment. $2\frac{1}{2}$ litres were taken between 10.30 a.m. and 12.15 p.m.

Readings were taken at 10.30 a.m. 12 noon and 4 p.m. The 4 p.m. reading on the second post water day was not taken.

TABLE 4 (See page 13.)

	<u>10.30 a.m. Reading.</u>				<u>12 noon Reading.</u>			
	Pulse				Pulse			
	Syst.	Diast.	Press.	Pulse	Syst.	Diast.	Press.	Pulse
Pre water	109	58	51	78	101	57	44	76
	116	67	49	78	115	70	45	74
Water	114	56	48	76	114	68	46	66
Post Water	97	58	39	72	97	63	34	70
	102	53	49	70	108	61	47	70

4 p.m. Reading.

	Syst.	Diast.	Pulse Pressure	Pulse.
Pre water	110	63	47	72
	106	64	42	72
Water	98	59	39	70
Post water	104	63	41	68
	-	-	-	-

EXPERIMENT 5 June 1919 (Table 5)

Readings by Dr. Melvin, Lecturer in Experimental Physiology, University, Aberdeen.

On each of the two water days 2 litres of water were taken on the first day between 3 p.m. and 5 p.m., on the second day between 10 a.m. and 12 noon. Readings were taken at 12.30 p.m. and 4 p.m. No readings were taken on the first and second post water days.

TABLE 5 (See page 14.)

	<u>12.30 p.m. Reading</u>				<u>4 p.m. Reading.</u>			
	Syst.	Diast.	Pulse	Pulse	Syst.	Diast.	Pulse	Pulse
Pre water	108	67	41	70	112	62	50	72
	110	65	45	77	106	57	49	-
	113	66	47	-	112	60	52	72
Water	109	51	58	72	111	54	57	-
	95	56	39	68	102	55	47	63
Post Water	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-
	104	63	41	72	108	59	49	-
	105	51	54	75	102	56	46	72

Readings by Dr. Kinloch, Lecturer on Public Health,
University, Aberdeen.

Subject was on a constant high protein diet. On one water day three litres of water were taken between 1 p.m. and 5 p.m. Readings were taken at 9 a.m. before the first meal, at 1 p.m. and at 5 p.m. Readings were not taken at 5 p.m. on the first pre water day nor at 5 p.m. on the third post water day.

TABLE 6 (See page 15.)

	<u>9 a.m. Reading.</u>				<u>1 p.m. Reading.</u>			
	Syst. Diast.		Press.	Pulse	Syst. Diast.		Press.	Pulse
Pre water	106	56	50	64	112	60	52	72
	106	58	48	64	112	58	54	76
Water	105	58	47	63	109	59	50	80
Post water	100	58	42	62	106	58	48	80
	109	58	51	68	108	58	50	72
	108	60	48	64	108	56	52	82

5 p.m. Reading.

	Syst.	Diast.	Pulse	Press.	Pulse.
Pre water	-	-	-	-	-
	112	60	52	72	
Water	114	63	51	62	
Post water	111	48	63	76	
	110	55	55	72	
	-	-	-	-	

EXPERIMENT 1 March 1919 (Table 7.)

On each of three water days two litres of water were taken between 11 a.m. and 3 p.m. Readings were taken at 11 a.m. and 3.30 p.m. No readings were taken after the 11 a.m. reading on the third water day until the 3.30 p.m. reading on the third post water day.

TABLE 7. (See page 15.)

	<u>11 a.m. Reading.</u>				<u>3.30 p.m. Reading.</u>			
	Pulse				Pulse			
	Syst.	Diast.	Press.	Pulse.	Syst.	Diast.	Press.	Pulse
Pre water	114	74	40	-	111	67	44	-
	112	72	40	-	109	70	39	-
Water	116	68	48	-	111	67	44	-
	108	70	38	-	116	68	48	-
	102	66	36	-	-	-	-	-
Post water	-	-	-	-	102	58	44	-
	110	68	42	60	108	67	41	54
	108	56	52	58	112	63	49	60

On the water day three litres of water were taken between 12.30 p.m. and 3 p.m. Readings were taken at 10 a.m., 12.30 p.m., 3 p.m. and 4.30 p.m.

TABLE 8 (See page 16)

10 a.m. Reading.

12.30 p.m. Reading.

	Syst. Diast. Pulse Pressure			Syst. Diast. Pulse Press		
Pre water	105	65	40	106	74	32
	116	73	43	117	73	44
Water	115	72	43	116	75	41
Post water	113	70	43	113	70	43

3 p.m. Reading.

4.30 p.m. Reading.

	Syst. Diast. Pulse Pressure			Syst. Diast. Pulse Press		
Pre Water	106	65	41	111	72	39
	112	73	39	112	73	39
Water	109	75	34	109	72	37
Post water	105	67	38	103	73	30

Readings by Dr. Melvin, Lecturer in Experimental Physiology University, Aberdeen.

On the water day three litres were taken between 9 a.m. and 11.30 a.m. and 1.5 litres were taken on the previous evening between 6 p.m. and 7 p.m. Readings taken at 12 noon and 4.30 p.m. No readings were taken on the first and second post water days.

TABLE 9.(See page 16)

	<u>12 noon Reading</u>				<u>4.30 p.m. Reading.</u>			
	Syst.	Diast.	Pulse	Pulse	Syst.	Diast.	Pulse	Pulse
Pre water	102	62	40	52	102	61	41	60
	112	68	44	60	104	62	42	60
Water	111	70	41	50	101	61	40	66
	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-
Post water	106	61	45	50	97	56	41	48
	106	67	39	48	101	61	40	60

S E R I E S C. Subject J.I.A.I.EXPERIMENT 1 May 1919 (Table 10.)

On the water day three litres were taken between 10.40 a.m. and 3 p.m. Readings were taken at 10 a.m., 12 noon and 4 p.m.

TABLE 10 (See page 17)

<u>10 a.m. Reading.</u>					<u>12 noon Reading.</u>			
	Syst.	Diast.	Pulse		Syst.	Diast.	Pulse	
			Press.	Pulse.			Press.	Pulse.
Pre water	125	75	50	54	125	75	50	55
	123	72	51	72	126	76	50	58
Water	124	74	50	59	134	84	50	64
Post water	127	63	64	60	123	69	54	54

4 p.m. Reading.

	Syst.	Diast.	Pulse	Pressure.	Pulse.
Pre water	120	70	50		72
	127	77	50		62
Water	118	64	54		60
Post water	126	69	57		66

On the water day four litres were taken between 10.45 a.m. and 3.40 p.m. Readings were taken at 12 noon and 4 p.m. No readings were taken at 4 p.m. on the second post water day.

TABLE 11 (See pages 16 & 17)

	<u>12 noon Reading</u>				<u>4 p.m. Reading.</u>			
	Syst.	Diast.	Pulse	Pulse	Syst.	Diast.	Pulse	Pulse
Pre water	121	70	51	-	122	66	56	72
	121	69	52	60	120	67	53	60
	125	69	56	60	119	68	51	58
Water	115	74	41	60	126	64	62	72
Post water	117	65	52	60	116	64	52	60
	120	67	53	-	-	-	-	-

EXPERIMENT 3 June 1919 (Table 12)

On the first water day four litres were taken between 10.20 a.m. and 3.15 p.m. On the second water day two litres were taken between 10.15 a.m. and 10.30 a.m. Readings were taken at 12 noon and 4 p.m. Only the 12 noon readings were taken on the first pre water day and no readings were taken on the second post water day.

TABLE 12. (See page 17.)

<u>12 Noon Reading.</u>					<u>4 p.m. Reading.</u>			
	Pulse					Pulse		
	Syst.	Diast.	Press.	Pulse.	Syst.	Diast.	Press.	Pulse
Pre water	120	72	48	54	120	72	48	64
	121	71	50	60	118	63	55	63
	122	71	51	60	124	58	66	-
Water	116	68	48	-	129	48	81	-
	116	64	52	50	117	62	55	60
Post water	117	55	62	60	-	-	-	-
	-	-	-	-	-	-	-	-
	118	68	50	60	118	60	58	60
	119	69	50	54	118	65	53	72
	120	66	54	52	126	62	64	72

S E R I E S D. Subject F.W.L.EXPERIMENT 1 (Table 13).

On the water day three litres of water were taken between
12.30 p.m. and 3.10 p.m. Readings were taken at 12.30 p.m.,
3 p.m. and 4.30 p.m.

TABLE 13. (See page 18)

	<u>12.30 p.m. Reading.</u>				<u>3 p.m. Reading.</u>			
	Pulse				Pulse			
	Syst.	Diast.	Press.	Pulse.	Syst.	Diast.	Press.	Pulse.
Pre water	131	82	49	77	131	82	49	62
	148	86	62	60	141	84	57	54
Water	137	88	49	60	136	88	48	60
Post water	142	87	55	54	136	78	58	77

4.30 p.m. Reading.

	Syst.	Diast.	Pulse Pressure.	Pulse
Pre water	137	79	58	60
	134	83	51	56
Water	136	88	48	54
Post water	134	87	47	50

EXPERIMENT 2 May 1919 (Table 14.)

On the first water day one litre was taken between 10 a.m. and 12 noon. On the second water day three litres were taken between 10 a.m. and 1 p.m. and on the third day three litres were taken between 12 noon and 1.15 p.m. Readings were taken at 10 a.m., 12.30 p.m. and 4 p.m. The 4 p.m. reading on the second post water day was not taken.

TABLE 14 (See page 19)

	<u>10 a.m. Reading.</u>				<u>12.30 p.m. Reading.</u>			
			Pulse				Pulse	
	Syst.	Diast.	Press.	Pulse	Syst.	Diast.	Press.	Pulse.
Pre water	135	72	63	66	135	75	60	60
	138	71	67	66	137	75	62	66
	136	70	66	84	134	77	59	60
Water	139	74	65	72	139	92	47	55
	130	70	60	78	136	89	47	60
	136	70	66	72	136	80	56	60
Post water	138	76	62	66	129	79	50	54
	131	69	62	72	130	80	50	60

4 p.m. Reading.

	Syst.	Diast.	Pulse Pressure.	Pulse.
Pre water	133	70	63	72
	-	-	-	-
Water	133	78	55	59
	129	75	54	66
	128	71	57	72
	132	78	54	63
	127	75	52	84
	-	-	-	-

EXPERIMENT 3. May 1919 (Table 15.)

On the water day six litres were taken between 12 noon and 5 p.m. Readings were taken at 12.30 p.m. and 4 p.m.

TABLE 15. (See page 19)

		<u>12.30 p.m. Reading.</u>				<u>4 p.m. Reading.</u>			
		<u>Pulse</u>				<u>Pulse</u>			
		<u>Syst.</u>	<u>Diast.</u>	<u>Press.</u>	<u>Pulse</u>	<u>Syst.</u>	<u>Diast.</u>	<u>Press.</u>	<u>Pulse</u>
Pre water	{	130	75	55	62	133	76	57	60
		133	78	55	64	127	79	48	72
Water		133	79	54	61	129	75	54	60
Post Water	{	126	75	51	60	123	73	50	66
		126	71	55	64	129	70	59	68

EXPERIMENT 1. Very low protein diet.

Diet. In grams -

Apple	100	Protein	27
Banana	150	Fat	70
Potato	400	Carbo-hydrate	325
Butter	75		
Sugar	75		
Cocoa	10		
Bread	200		

Subject aet.33; weight at beginning of exp. 67.8, at end 65.8 kilos

The diet was continued for a preliminary period of eight days.

On the 9th, 10th and 11th days three litres extra of water were drunk. The experiment was stopped on the 12th day.

The results of the first six days are omitted, the only points of interest being a continuous loss of weight, an excretion of nitrogen in excess of the intake and a uniform decrease of creatinine from 1.367 to 1.320 grams per day.

TABLE

Day of Exper.	Wt. kilos.	Urine c.c.	Tot.N grs.	Urea N.grs.	N.H. ₃ N.grs.	Amino Acid N.grs.	Creat- inine grs.	Creat- inine grs.	Tot.N as urea.	p.c. of Re-
7	65.97	412	6.300	4.151	0.259	0.113	1.320	-	65.9	Exd. diet.
8	65.97	405	6.300	4.157	0.185	0.143	1.328	-	65.9	do
9	65.80	2830	8.610	6.629	0.231	0.163	1.330	-	76.9	3 lit H ₂ O
10	66.02	3545	6.325	4.534	0.266	0.161	1.315	-	71.6	extra
11	65.80	3602	6.125	4.388	0.280	0.108	1.313	-	71.6	do

EXPERIMENT II. Moderately low protein diet.

Diet. In grams -

Oatmeal	100		
Bread	300	Protein	48
Butter	80		
Apple	70	Fat	93
Cocoa	10		
Sugar	100	Carbohydrate	346
Milk	300 c. c.		

Subject act.22; weight at beginning of exp.57.8, at end 57.7 kilos.

The diet was continued for a preliminary period of seven days.

On the 8th, 9th and 10th days three litres extra of water were

drunk. On the 11th 12th and 13th days the diet was continued

without extra water. The first five days are omitted from the

table, as they show no points of interest. The first post water

day is also omitted, as the analysis showed the day's collection

to have been contaminated.

TABLE II.

<u>TABLE III.</u>										
	Body		Tot.	Urea	N.B.g	Amino	Creat-	Creat-	p.c.	
	wt.	Urine	N.	N.	N.	Acid	inine	ine	of	
Day	kilos.	c.c.	grs.	grs.	grs.	N.grs.	grs.	grs	Tot.N	Remarks
									as	
									urea	
6	57.7	600	9.07	6.10	0.342	0.1834	1.350	-	67.3	Fixed Diet
7	57.7	670	8.77	5.95	0.347	0.1788	1.421	-	67.8	"
8	58.4	2980	9.83	6.90	0.459	0.3633	1.360	-	70.2	3 lit.H ₂ O extra.
9	58.2	3105	8.96	6.12	0.465	0.1827	1.360	-	68.3	
10	58.2	3400	9.24	6.41	0.459	0.1970	1.377	-	69.4	
12	57.7	880	9.38	6.44	0.336	0.1970	1.343	-	67.6	Fixed diet
13	57.7	870	9.46	6.59	0.403	0.1480	1.350	-	69.7	"

EXPERIMENT III.Moderately high protein diet.

Diet. In grams -

Sugar	100		
"Plasmon"	60	Protein	160
Cheese	200		
Dried skimmed Milk	50	Fat	73
Bread	400		
Cocoa	20	Carbohydrate	359
Butter	50		
Apple	100		

Subject same as Exp. II, act. 22; weight at beginning of exp. 57.2, at end 57.4 kilos.

On the 5th, 6th and 7th days three litres extra of water were drunk. On the third post water day the diet was stopped. The table gives the results from the third day.

TABLE III.

p.c.

Day	Body wt. kilos.	Urine c.c.	Tot. N. grs.	Urea N. grs.	N.E.3 N. grs.	Amino Acid N.grs.	Creat- inine grs.	Creat- ine grs.	p.c. of Tot.N as urea	Remarks
3	57.2	1220	17.53	13.98	0.468	0.1274	1.377	-	79.7	Fixed diet
4	57.3	1040	17.47	14.03	0.392	0.1060	1.381	-	80.3	"
5	58.8	3450	19.04	14.54	0.609	0.1000	1.332	-	76.4	3 lit. H O on
6	58.8	3895	19.06	15.87	0.566	0.1081	1.405	-	83.3	2
7	58.9	2730	18.72	14.99	0.549	0.1172	1.343	-	80.1	"
8	57.6	1350	19.49	16.26	0.426	0.2744	1.400	-	83.4	Fixed Diet
9	57.4	1220	20.12	16.67	0.440	0.0792	1.340	-	82.9	"

EXPERIMENT IV.Very high protein diet.

Diet. In grams -

Dried skimmed Milk	600	Protein	319
Cheese	300		
Bread	300	Fat	153
Water	3 litres	Carbohydrate	179

Subject set. 21; weight at end of exp. 57 kilos.

In this experiment the diet was continued for 15 days.

On the 5th and on the 9th, 10th and 11th days 9.6 litres of water were drunk in addition to the water used in preparing the food.

TABLE IV.p.c.
of

Day	Urine c.c.	Tot. Urea N. grs.	N. N. grs.	N.H. N. 3 grs.	Amino Acid N.grs.	Creat- inine grs.	Creat- ine grs.	Tot.N. as urea	Remarks
1	1930	39.82	33.59	0.250	0.241	1.660	-	84.4	Fixed diet
2	1930	40.24	33.83	0.241	0.249	1.480	-	84.1	"
3	2130	42.19	33.90	0.246	0.264	1.563	-	80.4	"
4	2260	42.88	35.03	0.206	0.324	1.554	-	79.8	"
5	7400	40.19	36.41	0.477	0.103	1.535	-	90.6	9.6 lits.H 6
6	2150	34.60	31.71	0.202	0.348	1.588	-	91.4	Fixed diet 2
7	2110	38.19	35.36	0.283	0.267	1.650	-	92.6	"
8	2040	40.22	36.58	0.299	0.398	1.604	-	91.0	"
9	8370	40.19	37.05	0.576	0.268	1.586	-	92.2	9.6 lits.H 6
10	8500	40.57	36.68	0.563	0.436	1.459	-	90.4	" 2
11	8070	39.24	36.12	0.499	0.387	1.547	-	92.1	"
12	2440	34.16	31.23	0.252	0.348	1.687	-	91.6	Fixed diet
13	2150	36.34	33.46	0.353	0.279	1.605	-	92.1	"
14	2160	36.89	33.96	0.345	0.265	1.619	-	92.1	"
15	2300	40.40	37.18	0.361	0.363	1.642	-	92.0	"

EXPERIMENT V.

Diet creatine-free, containing:-

Protein	110
Fat	67
Carbohydrate	325

In this experiment nitrogenous equilibrium had not been attained before the increased water intake. Its results are omitted in discussing the effects of water on the excretion of total nitrogen.

TABLE V.

Urine cc.	Tot. N. grs.	Urea N. grs.	N.H. N. 3 grs.	Amino Acid N.grs.	Creat- inine grs.	Creat- inine grs.	p.c. of Tot.N. grs.	Remarks.
1298	10.885	8.458	0.322	0.243	1.330	-	77.7	Fixed Diet
898	12.810	9.940	0.280	0.261	1.340	0.02	77.6	"
3741	13.583	10.962	0.378	0.257	1.340	0.02	80.7	3 lits. H ₂ O extra 2
4020	13.02	10.596	0.406	0.229	1.385	-	81.4	

EXCRETION OF SALTS.

SECTION II.

No. of hrs.	Calcium	Magnesium	Potassium as Kcl.	Sodium as Nacl.	Chlorides as Nacl.	Phosphates as P O . g. 5
4	0.0096	0.0101	0.59	1.684	1.827	0.165
4	0.028	0.0103	1.151	1.205	1.74	0.2
16	0.2054	0.097	1.209	3.297	2.61	1.245
4	0.017	0.0095	0.4303	1.1897	0.87	0.165
4	0.0389	0.0054	0.5379	1.7961	1.218	0.24
4	0.0335	0.0101	0.086	0.586	0.58	0.245
12	0.1578	0.0205	.4626	2.4654	1.0092	0.85
4	0.0143	0.002	.2958	0.6662	0.5104	0.74
4	0.0407	0.0038	.3228	1.1172	0.464	0.87
4	0.03	0.0065	0.2286	1.2114	0.522	0.475
12	0.1332	0.0704	0.4336	1.8164	0.696	1.045
4	0.0468	0.002	0.1948	0.7022	0.348	0.245
4	0.0545	0.0031	0.2012	0.9448	0.506	0.655
4	0.04	0.0047	0.2162	1.898	0.551	0.36
12	0.1078	0.0313	0.355	2.401	1.044	1.65
8	0.0954	0.0043	0.3077	2.0723	1.16	0.55
4	0.0664	0.0096	0.3496	1.8084	0.928	0.485
12	0.1411	0.0292	0.2582	2.4738	1.392	1.14

Three litres extra water was taken on fourth day.

BIBLIOGRAPHY.

- Abderhaldane and Bloch (1907) Zeitsch physiol. Chem. 53. 464
- Abelous Ribaut, Soulie and Troujan (1906) C.R. Soc. de Biol. 1. 463
- Barger and Dale (1909) Proc. physiol. Soc. May 1909.
- " " (1910) Jl. Physiol. 41. 19.
- Bayliss and Starling. Cited by Starling Principles of Human Physiology 1912. 1129
- Burns and Orr (1914) B.M.J. Sept. 19th. 505.
- Dale and Dixon (1909) Jl. Physiol. 39. 25
- Dale and Laidlaw (1910) Jl. Physiol. 41. 318
- Dennig (1901) Zeitsch f. diatet und physikal Therapie 1.281
Cited by Von Noorden.
- Dixon and Taylor (1907) B.M.J. 1907 2. 1150
- Dubelir (1891) Zeitsch Biol. 28. 237
- Emerson (1902) Beitr. Chem. Physiol. Path. 1. 50 cited by Barger.
- Folin (1904) Zeitsch. physiol. Chem. 41. 223
- Forster Zeitsch Biol. 47. 538
- Fowler and Hawk Jl. of Exper. Med. 12. 388.
- Frankel (1877) Archiv. path. Anot. Physiol. 71.117.
- Gaskell (1880) Jl. Physiol 3. 48
- Glax cited by Huggard. Handbook of Climatic Treatment 1906.
- Graube Zeitsch f. diatet und physikal Therapie 7. 255.
Cited by Von Noorden.
- Gruber (1901) Zeitsch Biol. 42. 419.
- Hay Jl. /

- Hay JI. of Anat and Physiol. 17. 436
- Heilner (1906) Zeitsch Biol. 47.538
- Hooker (1911) Amer. JI. Physiol. 28. 361
- Howe Mattill and Hawk (1911) JI. of Biol. Chem. 10. 417
- Huchard Maladies du coeur et des vaisseaux 1893 p.96.
Cited by Russell.
- Jerusalem and Starling (1910) JI. Physiol. 40. 279
- Jones JI. of Physiol. 8. 1
- Kerotkoff (1905) Mittheilungen der Kaiserl Milit-Mediz.
Akad S. St.Petersburg 11. 365 Cited by
MacWilliam and Melvin Heart 5. 153.
- Kronecker (1874) Cited by Bayliss. Principles of General
Physiology 1915. 314.
- MacWilliam, Mackie and Murrey (1904) JI. Physiol. 30. 38
- MacWilliam, Melvin and Murray (1914) Proc. Phys. Soc. March 1914.
- Mayer (1880) Zeitsch klin. Med. 2. 35
- Mott and Halliburton (1899) Proc. Physiol. Soc. Feb. 1899
- Neumann (1899) Cited by Von Noorden Path. of Met. 1. 403.
- Plimmer Practical Organic and Biochemistry 1915. 544. 546
- Plimmer and Skelton (1914) Biochem. J. 8. 70
- Rosenheim (1909) JI. Physiol. 38. 337
- Russell (1907) Arterial hypertonus sclerosis and blood pressure
33 et seq.
- Salkouskie and Munk (1877) Archiv. path. Anat. Physiol. 71. 408
- Salmon (1905) Cited by Van Noorden Path. of Met. 1. 409
- Seegen (1871) Cited by Munk. Archiv. path. Anat. Physiol. 94. 436
- Senator/

Senator Folia Therapeutica April 1907 p.37

Starling (1) Principles of Human Physiology 1912 1131.

(2) " " " " 815

Strauss Zeitsch f. diatet und physikal Therapie 7. 388
Cited by Von Noorden

Straub (1899) Zeitsch Biol. 37, 537.

Von Noorden (1) Metabolism and practical medicine Vol.3 897 et seq.

(2) 3. 934 et seq.

(3) 1.402

Von Slyke and Hart Amer. Chem. Jl. 30. 8

Voit (1860) cited by Munk Archiv. path. Anat. Physiol. 94. 436

Winterstein and Kunz (1909) Zeitsch. physiol. Chem. 59. 138