CLINICAL CALORIMETRY.

XLV. PROLONGED MEAT DIETS WITH A STUDY OF KIDNEY FUNCTION AND KETOSIS.*

By WALTER S. McCLELLAN and EUGENE F. Du BOIS.

(*From the Russell Sage Institute of Pathology in Affiliation with the Second Medical (Cornell) Division of Bellevue Hospital, New York.*)

(Received for publication, February 13, 1930.)

CONTENTS.

INTRODUCTION.

Two normal men volunteered to live solely on meat for one year, which gave us an unusual opportunity of studying the effects of this diet. The term "meat," as used by us, included both the lean and the fat portions of animals. The subjects derived most of their calories from fat and the diet was quite different from what one, who uses the term "meat" as including chiefly lean muscle, would expect. Rubner (1) called attention to the fact that a man cannot live on meat alone because of the

* These studies were supported in part by a research grant from the Institute of American Meat Packers.

Reported in abstract before The Thirteenth International Physiological Congress at Boston, August 21, 1929.

physical limitation of the apparatus of mastication. He was evidently considering only lean meat as fat offers little difficulty.

It is well known that the Eskimos have lived on an almost exclusive meat diet for generations. Certain explorers in the North also have subsisted for long periods on meat. Dr. Vilhjalmur Stefansson in particular has demonstrated that it is feasible for travelers in the arctic region to "live off the country," which means living on meat alone. The experiences of Stefansson and his companions have been given in his book "The Friendly Arctic" (2). He spent over 11 years in arctic exploration, during 9 years of which he lived almost exclusively on meat. Stimulated by this experience, Stefansson and Andersen, the latter a member of one of the expeditions, voluntarily agreed to eat nothing but meat for 1 year while they continued their usual activities in the temperate climate of New York.

LITERATURE.

The literature apparently contains no report concerning metabolic observations on subjects who lived exclusively on meat for long periods.

August and Marie Krogh, in 1908 (3), studied the dietary of the Greenland Eskimo. On the basis of the total annual food consumption of a section of Greenland, as collected by Rink in 1855, they estimated that the daily diet contained approximately 280 gm. of protein, 135 gm. of fat, and 54 gm. of carbohydrate. Thomas (4), finding no elevation of blood pressure and rarely any evidence of renal disease in the examination of 142 Eskimos, concluded that a carneous diet under strenuous living conditions does not produce renal or vascular disease. Heinbecker, in 1927 (5), found that the Baffin Island Eskimo, on a similar diet to that of the Greenland Eskimo, showed a normal carbohydrate tolerance, normal amounts of non-protein nitrogen in the blood, and no acetonuria. Fasting induced acetonuria in 3 days. In a recent discussion of high and low protein diets, Du Bois (6) referred to Catlin's statement that buffalo meat was the "staff of life" of the Central Plains' Indians. He cited also Head's account of subsisting on the native diet of beef and water while crossing the South American Pampas. All of these races are noted for their endurance of exertion and hardships.

Thomas (4) found no rickets or scurvy among the Greenland Eskimos, but a large incidence of these diseases among the Labrador Eskimos who live mostly on preserved food including dried potatoes, flour, canned foods, and cereals. Stefansson (7) reported three patients with scurvy on his last expedition, one of whom was our subject, Andersen. These cases were caused by eating canned foods with only a small amount of cooked meat, and were cured by eating raw meat. Lieb, in 1922 (8), carefully examined

Stefansson and stated that he found no evidence of injury from the prolonged and exclusive use of meat. He mentions the experience of two other men who lived mainly on meat for shorter periods.

Plan of Investigation.

The general scope of the investigation was outlined in 1926 and 1927 by an advisory committee of scientists of which Dr. Raymond Pearl of Johns Hopkins University, Baltimore, was chairman. The main portion of the work was carried on while the two subjects lived and ate in the metabolism ward of the Russell Sage Institute of Pathology in Bellevue Hospital, New York. The study was a cooperative one and several papers on various phases of the work have already been published. Short reports on the clinical features and general laboratory findings have been made by Lieb (9) and by McClellan (10). The excretion of acetone bodies has been discussed in papers on ketosis by McClellan, Spencer, Falk, and Du Bois (11) and by McClellan and Toscani (12). The chemical studies on the constituents of the blood have been presented by Lieb and Tolstoi (13) and by Tolstoi (14, 15). References to the above papers will be made later in this report.

A series of three papers, of which this is the first, will present the observations made in the ward, calorimeter, and laboratories of the Russell Sage Institute of Pathology.

PROTOCOLS.

V. Stefansson was an arctic explorer, aged 48, Canadian, and single. He had had measles at 10 years and mumps in early adult life and had survived typhoid fever, complicated by pneumonia as well as two attacks of pleurisy, which occurred in 1918, while on the arctic coast of Canada. For the past 10 years he had required occasional catharsis for moderate constipation, but except for infrequent colds, had not been ill during this period.

Physically, he was a well developed man, although his muscles were soft and somewhat flabby. His teeth contained many fillings and a mild gingivitis was present. The heart, lungs, and abdomen were normal. No changes in the blood vessels were detected.

Preliminary observations while on a mixed diet were started in the metabolism ward, February 13, 1928. Stefansson took his meals in the ward but slept at home. On February 26, 1928, he was admitted to the ward and on February 28, started on the meat diet. At our request he began eating lean meat only, although he had previously noted, in the North, that very lean meat sometimes produced digestive disturbances. On the 3rd day nausea

and diarrhea developed. When fat meat was added to the diet, a full recovery was made in 2 days. This disturbance was followed by a period of persistent constipation lasting 10 days. The subject had a craving for calf brain of which he ate freely. On March 12, poor appetite, nausea, and abdominal discomfort were present and a second but milder attack of diarrhea occurred which responded quickly to a proper proportionment of lean and fat meat. Because of the intestinal disturbance, the food intake for this period was below the average. Between March 21 and April 9, duplicate food samples were not saved for analysis. During this period the man's appetite was excellent. From April 10 to 19, duplicate diets were saved and complete analyses made. The subject left the hospital April 20 and continued the meat diet at home. One gastrointestinal disturbance occurred during the summer, from eating infected meat when abdominal pain, nausea, and vomiting were suffered for 36 hours. A table companion suffered from a similar but more severe attack. While on the meat diet, the explorer had two attacks of pharyngitis, one in the summer and one in December, 1928, while lecturing in the Middle West. Each attack subsided quickly without complications.

For the concluding observations Stefansson lived at home, where his diets were carefully checked by one of our own dietitians, but he came to the metabolism ward for calorimeter observations and blood studies. This terminal period of 8 days ended March 8, 1929, when he had completed 375 days on an exclusive meat diet. Then followed two periods of 1 week each —the first on a high fat diet, and the second on a general mixed diet. The investigations were concluded March 22, 1929.

K. Andersen was a fruit grower, born in Denmark, aged 38, and single, who had spent 5 years in arctic exploration and since 1920 worked an orange grove in Florida. His appendix had been removed 15 years previous.

The younger man was a thin, well developed adult with strikingly tanned skin and almost bald. The natural teeth which he still possessed—nine lower and seven upper—showed much repair, and he wore a denture replacing the four upper incisors. No gingivitis was evident. A soft, puffing, systolic sound was heard over the heart at mid-inspiration only, which was classed as a cardiorespiratory murmur.

Andersen entered the ward January 6, 1928, and started with a preliminary period on a mixed diet. The meat diet began January 24. No intestinal disturbances occurred. Intensive study on the effect of this régime continued for 90 days—until April 22, 1928. Our subject then left the hospital and, until the terminal observations, lived in a suburb, where he took plenty of exercise, while spending part of his time writing. In April and in August he had mild attacks of pharyngitis which lasted 2 to 3 days each. He reentered the ward on January 4, 1929, for our concluding studies. Meat was continued for 3 weeks, until January 24, making a total of 367 days on this diet. The next 3 weeks included three periods during which he received a variety of diets, all high in fat content. February 13 and 14, he had a mild pharyngitis. On the morning of February 15, he took 100 gm. of glucose for a glucose tolerance test. That evening he

had pain in the right chest, a severe chill, and rapidly rising temperature. The next day the sputum was rusty in color, the temperature was 40.0° (104°F.), and signs of consolidation were present over the right lower lobe. A diagnosis of lobar pneumonia was made. The infecting organism was the pneumococcus, Type II. Commencing 18 hours after the onset, Dr. Felton's concentrated polyvalent pneumococcus serum (Types I and II) was given in large amounts, and the temperature returned to normal at the end of 72 hours. Pain and general discomfort persisted for 5 days. General toxemia was slight, and convalescence was uneventful. While this infection lasted, the diet, mainly fluids at first, was rich in carbohydrate. Urine collections were continued throughout these periods but fecal specimens were not saved because medicated enemata were used. Following his convalescence, a period of 10 days on mixed diet, ending March 20, 1929, terminated the observations on Andersen. He left the hospital in good physical condition.

E. F. D. B. was a physician, American, married, aged 45, and in excellent health. During observation, he lived at home and came to the ward for his meals and the calorimeter studies. This subject went through a preliminary period on a general diet lasting 4 days, then for 10 days he ate nothing but meat. His appetite was poor and he required a number of days in which to adjust himself to the strange diet.

Nature of Diet.

The meat used included beef, lamb, veal, pork, and chicken. The parts used were muscle, liver, kidney, brain, bone marrow, bacon, and fat. While on lecture trips V. S. occasionally ate a few eggs and a little butter when meat was not readily obtainable. The carbohydrate content of the diet was very small, consisting solely of the glycogen of the meat. The men, except during short periods of special observation, ate as much as they wanted and proportioned the lean meat to the fat as they desired. V. S., in 31 days of special diet in the ward in which he was free from digestive disturbances, took an average of 0.81 kilos of meat per day while K. A. for 110 days averaged 0.79 kilos per day. The protein content of the diet ranged from 100 to 140 gm., the fat, from 200 to 300 gm., and the carbohydrate from 7 to 12 gm. The caloric value varied from 2000 to 3100 calories per day. 15 to 25 per cent of the calories were derived from protein, 75 to 85 per cent from fat, and 1 to 2 per cent from carbohydrate. Details concerning the food eaten are presented in Table I. The data for the meat periods were obtained from analyses of portions of meat which duplicated as closely as possible the meat actually eaten. Details

TABLE I.

Food and Urine Analyses.

All data are given in average daily values.

Period No.	No. of days.	Food.				Urine.				Remarks on diet.
		Protein.	Fat.	Carbohydrate.	Calories from protein.	Volume.	Acidity.	Nitrogen.	Acetone bodies.	
Subject K. A.										
		gm.	*gm.*	*gm.*	*per cent*	*cc.*	*cc.*	*gm.*	*gm.*	
1	8	61.8	122.4	164.1	12.4	1194	155	8.3	0.0	Mixed.
2	10	138.2	231.5	8.4	20.6	1162	531	20.3	6.17*	Meat.
3	10	124.1	202.2	7.7	21.1	1013	470	19.1	5.09	"
4	10	126.3	252.7	8.7	17.8	1182	493	17.9	5.16	"
5	9	116.0	281.2	8.1	15.2	1220†	517	17.6	4.98	"
6	11	117.8	243.8	9.2	17.4	1247†	523	16.8	5.53	"
7	10	122.6	223.8	10.2	19.2	1097	546	17.8	5.47	"
8	10	114.4	215.8	8.7	18.6	1074	513	18.1	4.62	"
9	10	126.9	216.5	10.4	20.2	1120	581	19.3	5.10	"
10	10	110.4	162.3	8.9	22.7	1490	503	18.4	3.18	"
										Elapsed time, 8 mos.
11	10	133.5	208.2	10.2	21.7	1303		22.2	2.85	Meat.
12	10	135.2	198.1	9.6	22.7	1354		21.7	2.48	"
13	7	45.9	227.6	4.9	8.1	1124		10.9	7.18	High fat, low protein.
14	7	45.0	233.4	34.7	7.4	922		8.2	6.20	" " " " and carbohydrate.
15	7	103.1	206.7	8.1	17.8	1532		16.8	5.06	Meat.
16	12	50.4	111.4	160.3	10.9	1949		14.7	0.0‡	Mixed diet, pneumonia.
17	12	90.8	202.8	280.5	10.9	1700		11.9	0.0	" " convalescent.
18	10	78.1	144.6	207.9	12.7	1645		9.2	0.0	Mixed.
Average for Periods 2–12.....	110	124.1	221.1	9.1	19.6					Meat periods.

Subject V. S.										
1	5	80.0	149.8	200.4	12.9	1260	278	10.8	0.0	Mixed.
2	4	181.0	152.2	11.8	33.6	1373§	601	28.3	0.63	Meat (lean).
3	9	101.6	188.6	7.4	18.9	1072†	573	18.1	6.22	Meat.
4	9	85.7	116.0	5.7	24.2	962	369	16.2	4.81	"
5	10					1092	395	16.6	3.00	" not analyzed.
6	10					1114	555	21.1	1.47	" " "
7	10	148.0	217.5	10.8	22.7	1219	642	22.1	1.39	" Elapsed time, 10 mos.
8	8	99.4	188.4	6.6	18.6	1364		18.2	0.45	Last period of meat.
9	7	74.4	236.0	34.7	11.6	854		11.0	0.42	High fat, low carbohydrate.
10	7	80.1	148.0	208.6	12.8	1653		9.0	0.0	Mixed.
Average for Periods 2–4, 7, 8.....	40	117.1	175.8	8.2	22.3					Meat periods.
Subject E. F. D. B.										
1	4	No data for food intake.				1270		12.2	0.0	Mixed.
2	5					1454		20.2	1.43*	Meat.
3	5					1422		22.3	1.16	"
4	4					1100		13.4	0.0‖	Mixed.

* First 3 days omitted from average.
† Urine averages for periods of 10 days.
‡ Acetone present 1st day of period. Sugar present first 4 days.
§ Urine averages for period of 3 days.
‖ Acetone present 1st day of period.

of these analyses will be found in the following paper of this series. The remainder of the data was calculated from the tables of food analysis, published by Rose (16). In Period 4, V. S. was far below his average intake on account of the intestinal disturbances previously described.

In this experiment, it was found that boiled meat was preferred to fried. Broiled steaks and chops were used,—V. S. choosing lamb frequently while K. A. ate beef almost exclusively. The meat was usually cooked lightly and the bone marrow eaten raw. Raw frozen meat was requested as a variation but no method of freezing it was available. The men generally took three but sometimes four meals daily. A sample menu for the day, given in raw weights follows.

Breakfast: lean beef, 190 gm.; fat, 100 gm.
Dinner: liver, 200 gm.; fat, 75 gm.
Supper: lean beef, 200 gm.; marrow, 70 gm.

The meat was usually cut from the bone and trimmed before weighing and cooking. In Period 7, V. S. ate "from the bone" which was the method of choice of both men, but this made the sampling of meat for analysis more difficult. The meat used during the first 3 months was selected from freshly killed animals; for the remainder of the time refrigerated meat from local markets was eaten.

The meat diet contained about 25 per cent of the amount of calcium found in the average mixed diet, while phosphorus and sulfur were present in larger quantities than usual. Table salt was allowed as desired but the men consumed only 1 to 5 gm. daily including that used in the cooking. As meat is one of the foods contributing to the acid portion of a ration, the diet was acid in the extreme but no calculation of the acid-base balance was made.

The daily intake of liquids—coffee, black tea, meat broths, and water, varied from 1 to 2 liters. When K. A. had pneumonia, however, he took 2.5 to 3.5 liters per day.

Did these men adhere strictly to the diet? We can answer in the affirmative with confidence for three reasons. First, the subjects were under close observation during a large part of the intensive studies. Second, in every individual specimen of urine which was tested during the intervals when they were living at

home, acetone bodies were present in amounts so constant that fluctuations in the carbohydrate intake were practically ruled out. Finally, the high character of the subjects is a guarantee that they faithfully followed the prescribed diet.

Effect of Diet on Clinical Condition.

General.—Both men were in good physical condition at the end of the observation. There were no subjective or objective evidences of any loss of physical or mental vigor. The teeth showed no deterioration and gingivitis had disappeared. There was, however, an increase in the deposit of tartar on teeth of V. S. Bowel elimination was undisturbed—V. S. required no extra catharsis and K. A. was regular throughout. The stools were

TABLE II.

Weights Given in Kilos.

Subject.	Beginning of observation.	Start of meat diet.	After 1 wk.	After 1 mo.	After 2 mos.	After 1 yr.	Pneumonia.		End of observations.
							Onset.	After recovery.	
V. S.	73.0	72.2	70.2	68.0	69.0	69.4			69.7
K. A.	60.0	59.4	58.3	58.5	60.5	58.0	55.6	56.1	56.6
E. F. D. B.	76.5	76.0	73.2						

smaller than usual, well formed, and had an inoffensive, slightly pungent odor. No flatus was noted.

Nutrition.—All three subjects lost weight during the 1st week of the meat diet—V. S., 2.0 kilos; K. A., 1.1 kilos; and E. F. D. B., 2.8 kilos. V. S. lost 2.2 kilos more in the next 3 weeks because of reduced intake at the time of his intestinal disturbance. After the 1st month both V. S. and K. A. regained part of the weight which they had lost and continued through the year with little variation. K. A. lost 2.4 kilos during the 3 weeks following the meat diet as the diets high in fat caused a loss of appetite resulting in diminished intake. Table II shows the weights of the subjects at various stages of the observation. The loss of weight in the 1st week is explained by a shift in the water content of the body which was adjusting itself to the different type of food eaten. The other losses of weight were definitely associated with dimin-

ished food intake. There was no evidence, as judged by weight, that the meat diet was detrimental to nutrition.

Blood Pressure.—The meat diet did not cause any elevation in the blood pressure of these two men despite the popular view that meat is a definite factor in producing such a result. V. S. maintained a systolic pressure of 105 mm. and a diastolic pressure of 70 mm. throughout the entire period. K. A. registered 140 mm. systolic and 80 mm. diastolic pressure at the beginning and 120 mm. systolic and 80 mm. diastolic pressure at the end of the year. The individual variations in pressure during the year were not significant.

Mental Attitude Toward Diet.—The two explorers who had lived on similar diets before, exhibited no mental reserve while eating meat exclusively. When the proportions of foodstuffs were correct, they ate with relish and no disturbances occurred. The third subject, a laboratory worker, had some difficulty in accustoming himself to such a diet and it required nearly a week to make the adjustment. He appeared to have some doubt regarding the outcome. This may have been due both to a lack of experience with such a diet and to the fact that his responsibilities were more pressing than those of other subjects.

Activity.—The men led somewhat sedentary lives. V. S. was writing, lecturing, and taking short walks daily. K. A. did some writing and walked 3 to 5 miles daily. Their response to muscular exertion was studied three times during the early part of the observations. The test consisted of running about $2\frac{1}{4}$ miles in approximately 20 minutes. Records of blood pressure and pulse rate while lying down were made before and after the run and were continued until both blood pressure and pulse rate returned to the resting levels. The blood pressure returned to its previous level in 10 to 15 minutes but in all three subjects the pulse rate required approximately 30 minutes to reach its resting level. No significant variation in response to this test was detected after 2 months of the meat diet.

According to their own reports the men carried on their usual activities without any increase of fatigue while taking meat. No unusual discomfort from the heat during the summer months was noted.

Intestinal Function.—The men were not troubled by consti-

pation more than when eating mixed diets. The diet was small in bulk and well absorbed (see the following paper of this series). In one instance, when the protein was relatively high, diarrhea developed. Fat aided in the regulation of the bowels. High fat diets have been used with success at the Mayo Clinic in the treatment of constipation (Smith (17, 18)). A detailed analysis of the second period of V. S. has been made to determine, if possible, whether any dietary factor was the cause of his intestinal upset (see protocols). Table III presents the food data for each day of this period. During the first 2 days his diet approximated that of the Eskimos, as reported by Krogh and Krogh (3), except that

TABLE III.

Daily Food Intake of V. S. during Period 2.

Date.	Intake.				Per cent of calories from:			Nitrogen.		Remarks.
	Protein.	Fat.	Carbohydrate.	Calories.	Protein.	Fat.	Carbohydrate.	Food.	Urine.	
1928	*gm.*	*gm.*	*gm.*					*gm.*	*gm.*	
Feb. 28	270	141	17	2489	44.6	52.6	2.8	43.2	24.5	Started meat diet.
" 29	257	137	16	2395	44.0	53.2	2.8	41.2	35.2	Weakness, nausea, and diarrhea.
Mar. 1	104	157	7	1916	22.2	76.3	1.5	16.6	25.2	
" 2	93	174	7	2028	18.8	79.8	1.4	14.9	21.3	Nausea and diarrhea absent.

he took only one-third as much carbohydrate. The protein accounted for 45 per cent of his food calories. The intestinal disturbance began on the 3rd day of this diet. During the next 2 days he took much less protein and more fat so that he received about 20 per cent of his calories from protein and 80 per cent from fat. In these two days his intestinal condition became normal without medication. Thereafter the protein calories did not exceed 25 per cent of the total for more than 1 day at a time. The high percentage of calories from protein may have been a factor in the production of the diarrhea.

Vitamin Deficiency.—No clinical evidence of vitamin deficiency

was noted. The mild gingivitis which V. S. had at the beginning cleared up entirely, after the meat diet was taken.

Effect of Diet on Urinary Constituents.

The daily determinations on the urine included volume, acidity, specific gravity, total nitrogen, total acetone bodies, albumin, and glucose. The Kjeldahl method was used for the total nitrogen and the method of Van Slyke (19) for computing the acetone bodies. The acidity was measured by the amount of 0.1 N alkali required to neutralize the 24 hour amount. A tabulation of these data by periods, computed as averages per day, is presented in Table I.

While meat was eaten, the average output of urine varied from 900 to 1500 cc. There were indications that some of the changes in urine volume were associated with changes in the amount of carbohydrate in the tissues. With two of the subjects (V. S. and E. F. D. B.) the urine volume was greater in Period 2, when carbohydrate was first omitted, than it was in the preceding period. In all three subjects it was at its lowest level in the period when carbohydrate was first added. A carbohydrate diet seems to favor retention of water in the body. The increased output of K. A. in Periods 16 and 17 paralleled the greater intake of fluids during his pneumonia.

The specific gravity ranged from 1012 to 1032 with the majority of the readings above 1020. The acidity of the urine showed a 2- to 3-fold increase during the meat diet as compared with the acidity of the preliminary period on mixed diet. This finding reflects the distinctly acid nature of the diet.

The average daily nitrogen excretion per period varied from 16.2 to 28.3 gm. V. S. showed the maximum excretion for a single day of 35.2 gm., on February 29, 1928, when eating purely lean meat. The acetone bodies in daily averages per period remained between 0.4 and 7.2 gm. K. A. showed the maximum excretion for one day of 12.3 gm., on February 13, 1928. No albumin, casts, or blood cells were found at any time.

Glucose appeared in the urine of K. A., February 15, 1929, and was present for 4 days. The daily amounts were 9.9, 17.0, 10.7, and 5.0 gm. This finding coincided with the giving of 100 gm. of glucose for a tolerance test and with the first 3 days of his pneumonia.

Effect of Diet on Kidneys.

Newburgh and his associates (20, 21) have reported that meat in large amounts is irritating to the kidneys of both animals and human beings. The clinical tests carried out on two of our subjects (V. S. and K. A.) revealed no evidence of irritation to the kidneys nor of damage to the kidney function. In the absence of microscopical studies of the kidneys themselves, one cannot say that no changes took place. Attention has been called to the fact that the diet was not particularly high in protein, being only 30 to 50 per cent above the average protein intake of the men when they partook of mixed diets.

The observations on which the above statements are based include the following.

TABLE IV.
Van Slyke Urea Clearance Tests.

Subject.	Date.	Blood urea N.	Excretion as per cent of normal.	Remarks.
	1929	*mg. per 100 cc.*	*per cent*	
K. A.	Feb. 13	12.6	105	End of meat diet.
	Mar. 15	18.5	42	After 4 wks. on mixed diet and after pneumonia.
V. S.	" 7	15.5	102	End of meat diet.
	" 19	11.3	76	After 2 wks. on mixed diet.

1. Examination of Urine.—No albumin, blood cells, or casts were observed at any time. The specific gravity showed good concentration throughout the year.

2. Phenolsulfonephthalein Excretion.—K. A. excreted 55 per cent of the dye in 2 hours and 10 minutes at the beginning and 62 per cent at the end. V. S. excreted 50 per cent at the beginning, but the concluding observation was not completed.

3. Urea Clearance Tests.—This test, which determines the amount of blood cleared of urea per minute, based on the urea excreted by the kidneys in the same time, has been described by Möller, McIntosh, and Van Slyke (22). Two tests were made on V. S. and two on K. A. by Dr. R. R. Hannon of The Rockefeller Institute Hospital to whom we are indebted for the following

data (Table IV). The first test on each subject, made at the end of 1 year on the meat diet, showed an excretion of urea which was above the average for normal men on mixed diets. The second test, made after a period on mixed diets was below the normal range for K. A. and at low normal for V. S.—the second test on K. A. was carried out after he had had pneumonia. A decrease in function following a period of hyperfunction has been noted in other conditions.

4. Blood Constituents.—Tolstoi (14) found no increase in the non-protein content of the blood of our subjects. He noted a slight increase of the uric acid nitrogen during the first 3 months, which was not present in the remainder of the observations. There was no change in the other non-protein nitrogenous constituents. Therefore, it may be stated that no retention of nitrogen occurred as a result of the meat diet. Baumgartner and Hubbard (23) found slight elevations of the urea nitrogen in the blood of two men who received diets containing 100 to 120 gm. of protein. This was noted early in their studies which lasted from 4 to 6 months. As the level was normal during the later months, they concluded that the diet did not damage the kidneys.

5. Size.—Roentgenographic studies of the kidneys by Dr. H. M. Imboden, at the beginning and the end of the meat diet, gave no evidence of kidney hypertrophy.

Effect of Diet on Fat Metabolism.

The diet used in these investigations contained a large proportion of fat calories and striking effects were noted in the utilization of this foodstuff. On the 1st day of the meat diet, acetone bodies were excreted in the urine showing that the amount of carbohydrate oxidized had already become insufficient to assure the complete combustion of the fat. Increasing amounts of acetone bodies were eliminated daily until the 4th day after which they remained nearly uniform in the case of K. A. but decreased steadily with V. S., throughout succeeding periods. Chart I shows the amounts of acetone bodies excreted in given periods. K. A. had a sustained level all through the first 3 months but at the end of the year, in Periods 11 and 12, he excreted about one-half as much as during the earlier intervals. In Period 13 the fat was proportionately higher than previously, due to the restriction of

protein. Here occurred the highest excretion of acetone bodies, an average of 7.2 gm. per day for a week. The acetonuria persisted while the subjects were receiving 5 per cent or less of their food calories from carbohydrate, but promptly disappeared when diets containing 30 per cent of the calories in carbohydrate were started—lasting only 4 hours in V. S., 12 hours in E. F. D. B., and 36 hours in K. A. The longer time required in the case of K. A. may have been due to the pneumonia which developed at that time.

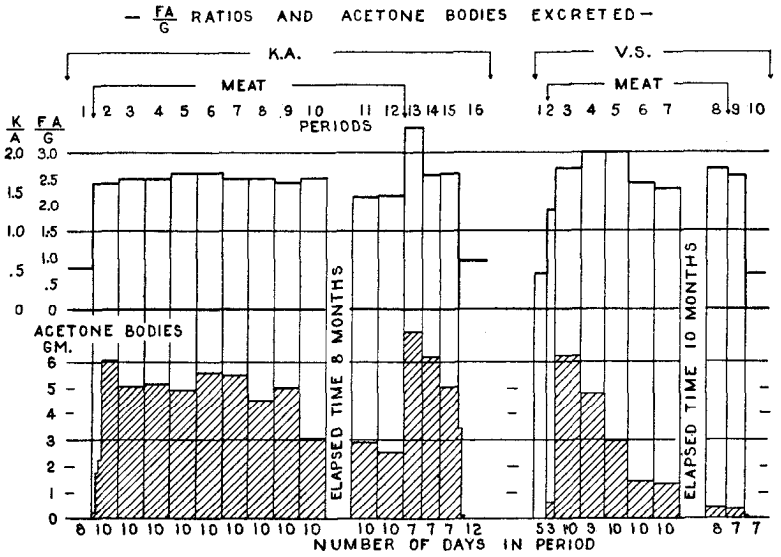

CHART I. A comparison of the fatty acid-glucose ratios and the acetone bodies excreted.

The blood showed a visible lipemia when the fat intake was at the higher levels and the cholesterol varied from 200 to 800 mg. per 100 cc. of blood reaching the higher values when the lipemia was noted (Tolstoi (14)). Total blood fats and blood acetone bodies were not determined.

Computation of the fatty acid-glucose ratios was made, using the Woodyatt formula (24). The estimated food metabolized was the basis of this analysis. Detailed data of the early periods

of the meat diet and the method of estimating the foodstuffs metabolized have been reported by McClellan and others (11) with a discussion of the threshold of ketosis in various conditions. The completed computation is presented in Chart I. It was found that acetone bodies were present in the urine when the FA:G ratios were above 1.5, but that the amount of acetone bodies excreted revealed no definite relation to the FA:G ratio. In K. A., the quantity showed a tendency to decrease even though the ratio remained relatively uniform and in V. S., the excretion decreased rapidly even while he was utilizing about the same amount of fat. In E. F. D. B., the excretion of acetone bodies remained low throughout the 10 days. These individual variations are difficult to explain. The subject, K. A., who had the high sustained ketosis, was the smallest of the three and had less subcutaneous fat than either of the others.

A comparison of the data supplied in Periods 8 and 9 of V. S. shows that for the protection of the body against ketosis, glucose derived from ingested protein is equivalent to glucose derived from carbohydrate food. In Period 8, when taking the meat diet, he was metabolizing foodstuffs with a FA:G ratio of 2.68 and excreting 0.45 gm. of acetone bodies per day. In Period 9, the diet was changed and contained less protein and 35 gm. of carbohydrate, which approximately equaled the available glucose contained in the omitted protein. The ratio for Period 9 was 2.54, and 0.42 gm. of acetone bodies were excreted daily.

No symptoms were noted, which could be attributed to the mild ketosis. There was no depression of mental faculties and no significant change in the carbon dioxide-combining power of the blood. We had no way of telling whether or not any changes had occurred in the walls of the blood vessels, but as far as clinical observations and special tests revealed, no injuries resulted from the prolonged mild ketosis.

SUMMARY AND CONCLUSIONS.

1. Two men lived on an exclusive meat diet for 1 year and a third man for 10 days. The relative amounts of lean and fat meat ingested were left to the instinctive choice of the individuals.

2. The protein content varied from 100 to 140 gm., the fat from

200 to 300 gm., the carbohydrate, derived entirely from the meat, from 7 to 12 gm., and the fuel value from 2000 to 3100 calories.

3. At the end of the year, the subjects were mentally alert, physically active, and showed no specific physical changes in any system of the body.

4. During the 1st week, all three men lost weight, due to a shift in the water content of the body while adjusting itself to the low carbohydrate diet. Thereafter, their weights remained practically constant.

5. In the prolonged test, the blood pressure of one man remained constant; the systolic pressure of the other decreased 20 mm. and the diastolic pressure remained uniform.

6. The control of the bowels was not disturbed while the subjects were on prescribed meat diet. In one instance, when the proportion of protein calories in the diet exceeded 40 per cent, a diarrhea developed.

7. Vitamin deficiencies did not appear.

8. The total acidity of the urine during the meat diet was increased to 2 or 3 times that of the acidity on mixed diets and acetonuria was present throughout the periods of exclusive meat.

9. Urine examinations, determinations of the nitrogenous constituents of the blood, and kidney function tests revealed no evidence of kidney damage.

10. While on the meat diet, the men metabolized foodstuffs with FA:G ratios between 1.9 and 3.0 and excreted from 0.4 to 7.2 gm. of acetone bodies per day.

11. In these trained subjects, the clinical observations and laboratory studies gave no evidence that any ill effects had occurred from the prolonged use of the exclusive meat diet.

BIBLIOGRAPHY.

1. Rubner, M., in von Leyden, E., Handbuch der Ernährungstherapie, Leipsic, **1**, 42 (1903).
2. Stefansson, V., The friendly arctic, New York (1927).
3. Krogh, A., and Krogh, M., A study of the diet and metabolism of Eskimos, Bianco Luno, Copenhagen (1913).
4. Thomas, W. A., *J. Am. Med. Assn.*, **88**, 1559 (1927).
5. Heinbecker, P., *J. Biol. Chem.*, **80**, 461 (1928).
6. Du Bois, E. F., *J. Am. Diet. Assn.*, **4**, 53 (1928).
7. Stefansson, V., *J. Am. Med. Assn.*, **71**, 1715 (1928).

8. Lieb, C. W., *J. Am. Med. Assn.*, **87,** 25 (1926).
9. Lieb, C. W., *J. Am. Med. Assn.*, **93,** 20 (1929).
10. McClellan, W. S., *Klin. Woch.*, **9,** 931 (1930).
11. McClellan, W. S., Spencer, H. J., Falk, E. A., and Du Bois, E. F., *J. Biol. Chem.*, **80,** 639 (1928).
12. McClellan, W. S., and Toscani, V., *J. Biol. Chem.*, **80,** 653 (1928).
13. Lieb, C. W., and Tolstoi, E., *Proc. Soc. Exp. Biol. and Med.*, **26,** 324 (1929).
14. Tolstoi, E., *J. Biol. Chem.*, **83,** 753 (1929).
15. Tolstoi, E., *J. Biol. Chem.*, **83,** 747 (1929).
16. Rose, M. S., Laboratory handbook for dietetics, New York, revised edition (1925).
17. Smith, F. W., *Proc. Staff Meetings Mayo Clinic*, **2,** 166 (1927).
18. Smith, F. W., *J. Am. Med. Assn.*, **88,** 628 (1927).
19. Van Slyke, D. D., *J. Biol. Chem.*, **32,** 455 (1917).
20. Newburgh, L. H., *Medicine*, **2,** 77 (1923).
21. Squier, T. L., and Newburgh, L. H., *Arch. Int. Med.*, **28,** 1 (1921).
22. Möller, E., McIntosh, J. F., and Van Slyke, D. D., *J. Clin. Inv.*, **6,** 427 (1928).
23. Baumgartner, E. A., and Hubbard, R. S., *Clifton Med. Bull.*, **13,** 52 (1927).
24. Woodyatt, R. T., *Arch. Int. Med.*, **28,** 125 (1921).

CLINICAL CALORIMETRY: XLV. PROLONGED MEAT DIETS WITH A STUDY OF KIDNEY FUNCTION AND KETOSIS

Walter S. McClellan and Eugene F. Du Bois

J. Biol. Chem. 1930, 87:651-668.