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ORIGINAL ARTICLES

MANAGEMENT OF PATIENTS WITH CHRONIC RENAL  
DISEASE.<sup>1</sup>

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It needs only a glance at current medical periodicals to show the amount of time and energy being devoted to the study of kidney function today. In fact, some may have been inclined to believe that the 'phthalein test and the electrocardiograph are the only methods now employed in the investigation of patients in our hospitals. So much work may surely, by this time, be expected to have produced some results which the practitioner of medicine can use for the good of his patients. It has been my fortune during this period of the development of functional tests, both at the Presbyterian Hospital, New York, and during the last year at the Johns Hopkins Hospital, to have for my associates a group of men actively interested in this field. During the last year, especially, Dr. Mosenthal and Dr. Rowntree and their co-workers in our clinic have, by their laboratory studies, quite definitely modified our practice in the wards. I shall give our present views on the practical management of the different types of chronic renal disease which are commonly met in general practice. I say "practical management of the patient," because, except in the rarest instances, we have no real treatment of the disease. We

<sup>1</sup> Read before the Academy of Medicine, New York City, November 4, 1915.  
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must not let the fascination of growing insight into the complexities of function blind us to the fact that the problem of fundamental importance in any disease is the problem of its cause. It is devoutly to be hoped that our knowledge may be increased along this line. The study of the relation of focal infections to renal disease is a promising movement, but a vast material must be worked over critically before we can reach conclusions. Except for certain cases of renal involvement in secondary syphilis, possibly rare cases of nephritis due to malaria, lead poisoning, pregnancy, or some focus of streptococcus infection, we can not speak of an effective causal therapy of chronic nephritis.

For the most part, treatment has in the past been purely schematic and based on a conventional diagnosis. Since this treatment usually involved violent interference with the habits of a lifetime, even though it did not use dangerous drugs, we can not regard it as a harmless procedure. To tell every patient with albuminuria or hypertension to stop eating red meat, or still worse, as I have actually seen done, to go on a milk diet, is evidence either of colossal ignorance or of inexcusable mental laziness. Nothing is clearer to me, however, in dealing with patients who have a chronic disease than the amount of thought and tact necessary to accomplish the readjustment of their life to the necessary limitations which they must be taught to recognize. This is a field which the internist has to himself, and it should be our pride to develop it in detail as carefully as the surgeon has developed his operative technique. Here is where the functional test becomes indispensable.

The treatment of chronic disease has two aims: the prolongation of life, and the amelioration of the discomforts due to the disease. These two aims are achieved by two types of treatment: (1) safeguarding treatment, which aims to protect a weakened function from further damage by overstrain; (2) symptomatic treatment, directed toward the amelioration of the symptoms which depend upon disordered function. While a correct anatomical diagnosis is always desirable it is not of special importance in determining treatment along either of these lines. What is fundamental is the accurate estimation of the kind and degree of functional damage.

Chronic renal disease presents an endless variety of symptom combinations, but certain clinical types occur with such frequency that we are all called on to meet the problem of their management; and they present themselves, in a way, as specific practical problems. I propose to consider them as such:

1. Patients in whom albumin and casts in the urine are the only evidence of disease. This is a large group. These patients come to us, both family practitioners and consultants, from the life insurance examiners; or if we have careful patients, and are careful examiners, we discover them among our supposedly healthy clients. They are found among the children in the clinics. Their problem is the

last problem we have to work out in a convalescent from known acute nephritis or from a pregnancy albuminuria. The last two instances give the key to the important question that must be answered for every patient in this group, namely, Are the albumin and casts in the urine the last remaining evidences of a healing renal lesion? A searching inquiry must be made into the history for evidences of a mild unrecognized scarlet fever, a tonsillitis, or other infection, recent pregnancy, syphilis, the administration of salvarsan, or some intoxication which might have led to acute renal disease without noticeable symptoms. If such possible cause can be found, or even suspected, especially in the case of young people, then a period of rest in bed and milk or bland diet should be given a thorough trial. If treatment, as of true acute nephritis, results in steady subsidence of the albuminuria, then it should be persisted in just as though the patient had a known acute nephritis. No sacrifice is too great for any patient to make which may prevent the subsequent development of chronic diffuse nephritis, leading to the secondary contracted kidney in later life. If, however, there is no suspicion of a past or existing infection, and if a week in bed on milk diet has no appreciable effect upon the albumin and casts, then bed and milk diet are an unwarrantable hardship, because they are sacrifice without result. If persisted in, the result will very likely be the sacrifice of the physician.

In children the next problem is the differentiation of postural albuminuria. This is much commoner than is usually supposed, and marked albuminuria without casts, or with rare casts, in a child should always suggest the possibility of its being this peculiar type. For an excellent discussion of this subject I can recommend the article by Langstein in *Pfaundler and Schlossman's Handbuch*,<sup>2</sup> for interesting special pleading on the two sides of the question, the monographs of Politzer and of Jehle.<sup>3</sup>

Testing the separate urines passed at different times of day, and the effect of standing fifteen to thirty minutes in marked lordotic position, will often clear up the diagnosis promptly. The large amount of protein precipitable by acetic acid in the cold has been, in my experience, an important feature of the albuminous urine in these cases. The treatment of these children should, I believe, be along the lines of general invigoration, with medical gymnastics for the improvement of posture. Their diet should be ample, not restricted. In some the suspicion of true nephritis is strong, though there is marked postural albuminuria. Such cases should be more cautiously handled.

<sup>2</sup> Langstein, L., Die orthotische Albuminurie, Handbuch, Pfaundler und Schlossman, 1910, iv, 30. F. C. W. Vogel, Leipzig.

<sup>3</sup> Ren juvenum, Beiträge zur Kenntnis der orthostatischen Albuminurie, Berlin und Wien, 1913, Urban und Schwarzenburg; Die Albuminurie, Julius Springer, Berlin, 1914.

When one has clearly recognized and separated from the patients in whom albuminuria has been accidentally discovered these two preceding types, residual albuminuria after acute nephritis and postural albuminuria, there remain the large number of patients in whom the cause of the albuminuria is not evident. In them it is of first importance to exclude inflammation of the urinary tract, stone, tumors, and other non-nephritic causes of albuminuria, the treatment of which is local and surgical. Then the search must be made for a remote focus of infection in tonsils, sinuses about the teeth, in the gall-bladder, in the prostate or seminal vesicles, and any such focus should be eradicated in the hope that from it as a portal of entry has come the infection responsible for the renal damage. Possible toxic causes, especially the inorganic poisons, should be in mind. I have seen albuminuria produced by the therapeutic use of arsenic for instance. In childhood and adolescence, albuminuria without casts and not definitely postural may exist without subsequent evidence of any serious injury to the kidney, and may be more lightly regarded than albuminuria in adult life.

The effect of exercise, cold baths, and so on upon the albuminuria should be studied. I have the records of one patient, who more than thirty years ago, was refused life insurance because of large numbers of hyaline casts in the urine. He came to my father, who discovered that life insurance examinations had always been made in the afternoon, after he had done some lively boxing, and had a cold shower. His urine was perfectly normal at all other times. Twenty-six years afterward he was still free from evidence of chronic nephritis, and, I believe, is still living. Such a patient either needed no advice at all, or to be told to avoid the combination of very active exercise and a cold bath. If exercise produces marked albuminuria with casts it should certainly be reduced.

Apart from wholly temporary albuminuria, however, it is wise for the physician to consider albumin and casts as the evidence of a definite renal lesion, to be watched over long periods of time in the interest of both science and the patient, but not necessarily calling for either a bad prognosis or much interference with the patient's life. Barringer's<sup>4</sup> studies of life insurance statistics show that the persistent presence of granular casts indicates a higher probability of progressive renal disease. Even so, these individuals may enjoy apparently perfect health for ten years or more. It is even more important to watch their blood-pressure than their urine. If this begins to rise, then the development of symptoms is to be looked for. A tendency toward nocturnal polyuria or to fixation of specific gravity is an almost certain danger sign. These point to beginning inability of the kidney to concentrate urea, and therefore connote

<sup>4</sup> The Prognosis of Albuminuria with or without Casts, *Arch. Int. Med.*, 1912, ix, 657-664.

anatomical damage which has reached the stage of seriously compromising the large factor of safety of the kidneys. Until hypertension, nocturnal polyuria, or other symptoms arise, symptomatic treatment is quite unnecessary. Safeguarding treatment is important, but must not go beyond what is of proved efficacy.

Severe physical strain, such as competitive athletics, rough hunting trips and so on, should clearly be avoided. Exposure to cold and wet is also unwise. The wearing of woolen underwear has long been regarded as desirable. Alcoholic and other excesses should naturally be warned against, also the immoderate use of tobacco. The common mild infections, such as tonsillitis, should be much more carefully treated than in normal individuals and the effect on the urine carefully observed.

As to diet, von Noorden<sup>5</sup> has shown that considerable quantities of pepper, mustard, and other condiments are renal irritants. He always held that creatinin was dangerous, and recent work, well summed up and amplified by Myers and Lough,<sup>6</sup> has proved that creatinin retention may be very striking in severe nephritis. Therefore, soups, which are unimportant as sources of energy, and spices may wisely be excluded from the diet. Gourmands should clearly have their excessive appetite restrained, and obese patients should be moderately reduced. If the 'phthalein test is normal I see no reason for a restriction of protein, either qualitatively or quantitatively, below a moderate normal intake. One limitation not immediately necessary, I believe, should be made for the sake of training the patient in case it may become imperative later. Patients who regularly use a large amount of salt with their food—that is the people who habitually put salt on before they have tasted the dish—should be told to reduce their use of added salt at table to foods which come from the kitchen unsalted. Without this training, treatment of subsequent edema in them will meet with serious obstacles. One special category under this heading comprises the diabetics with albuminuria. For them, unless the 'phthalein test shows an excretion below 40 per cent., or there are definite symptoms, such as edema, the treatment is the dietetic treatment of diabetes and the albuminuria should not be allowed to interfere with this.

2. Patients with hypertension, with or without a trace of albumin, and with slight subjective symptoms or none at all. These patients we all recognize at a glance. Since the introduction of blood-pressure measurements into practice they have come into prominence, often, from the stand-point of their comfort, an undesirable prominence. They are usually just middle age. Many of them

<sup>5</sup> Clinical Treatises on the Pathology and Therapy of Disorders of Metabolism and Nutrition—Nephritis, New York, 1903.

<sup>6</sup> The Creatinin of the Blood in Nephritis: Its Diagnostic Value, Arch. Int. Med., 1915, xvi, 536.

are obese, many diabetic. The functional disturbance is so clear-cut, and the anatomical basis in their arterioles so remote from observation, that we usually classify them under the functional category of hypertension. The vast majority certainly have changes in their renal vessels and in the arterioles elsewhere; but the clinical type which I have in mind here does not have renal symptoms. The development of nocturnal polyuria, of severe headaches, especially explosive headaches with vomiting; in patients who have not been subject to migraine, of retinal lesions, or of edema, takes the patient immediately out of this category. Slight cardiac or neurasthenic symptoms are common. Safeguarding treatment is the entire problem of their management. In the first rank must come safeguarding from all avoidable influences which raise blood-pressure in the normal man; next, safeguarding the myocardium and, to a certain extent, the cerebral vessels and the kidneys. The worst hypertensive influence is mental strain, and especially emotional strain. Its avoidance necessarily calls for readjustment of the every-day life for the man in business or for the woman in the home, and the details of this should be worked out with care and sympathy. Distinctly the worst advice is to tell a man of important affairs to give up business completely; but for the manual laborer change of occupation may be imperative. It is of great importance to secure adequate normal sleep. In addition, I believe that the strain of a hard day's work can be greatly reduced by a short break in the middle of the day for absolute rest, or, better yet, for a little exercise, followed by rest. With more marked myocardial symptoms a few days in bed will work wonders, often reducing blood-pressure greatly. Tobacco in excess is clearly a poison both to vessels and to cardiac mechanism. Whether two or three mild cigars a day may be smoked while the patient is sitting quietly after meals must be determined in the individual case. Their effect upon blood-pressure should be observed. If the patient is perfectly miserable without them it may wisely influence the physician. Excessive athletics may be dangerous to both heart and vessels, but I believe that, as a rule, these patients may take more exercise than is usually allowed them—even women who have not previously been accustomed to it. The functional response of the myocardium is the determining factor, and can often be improved by proper exercise. Slight dyspnea on exertion may become less or disappear with gradual training. Mild anginoid pain on exertion, however, calls for great care, and the patient should always stop when it is felt. When exercise cannot be allowed, massage is helpful. The reduction of obesity is a highly important measure. Limitation of diet follows much the same lines as in the preceding class of patients, but physiological economy in nutrition should usually be insisted on, and meals should not be bulky. Moderation in the use of salt, I think, is quite important. The abuse of fluid is clearly dangerous

for them, as von Noorden has insisted. High blood-pressure is no indication of nitrogen retention, as Folin, Denis, and Seymour<sup>1</sup> have shown, and protein should not be restricted merely because of hypertension. Luxur consumption clearly should be, and it is possible that some patients will be, better without meat. On the other hand I am sure that others may be made worse by the loss of appetite that an unpalatable diet produces.

Alcoholic drinks are condemned by von Noorden in these patients. I am not convinced that every patient who has taken wine temperately all his life should be deprived of it absolutely. One should judge by its effects on the circulation. If it causes marked flushing of the face or palpitation it should clearly be avoided; but if it leads to greater enjoyment of meals and to relaxation after it may be permitted. It is needless to say that it should be used sparingly and in dilute form.

Climatic has seemed to me not without its influence. The majority of these patients have more symptoms during cold weather, and the combination of cold and high wind taxes the heart maximally. For those who live in the North a winter vacation in a warm climate is desirable. For all of them a long break in their work once or twice a year is most helpful. Turkish baths or other sweating procedures benefit some. Vasodilators should not be used except in emergencies, and aconite, I believe, is worthless.

3. Patients with hypertension and outspoken myocardial insufficiency. This is one of the largest groups to be found in the medical wards of every hospital, and these patients are equally common in private practice. They present primarily the problem of treatment of a circulatory disease. For them both safeguarding and symptomatic treatment are essential. The symptoms demanding treatment in the majority are dyspnea, edema, and the whole picture of cardiac failure with chronic passive congestion of the viscera. A small number have anginoid pain on exertion or severer attacks of angina pectoris. For the latter the essential safeguarding treatment is rest, never permitting enough exercise to produce an attack. Symptomatic treatment consists in the use of vasodilators to cut short or to ward off an attack when exertion must be made. Fresh nitroglycerin tablets dissolved on the tongue and not swallowed have always fulfilled the indications in my experience, and are free from the disagreeable publicity which the breaking of an amyl nitrite pearl entails. Vasodilators have their most important use in these people, who owe Lauder Brunton a great debt of gratitude for the introduction of the nitrites into medicine. Theobronine may be valuable in some cases. It is not necessary for me to go into the treatment of angina in further detail.

<sup>1</sup> The Non-protein Nitrogenous Constituents of the Blood in Chronic Vascular Nephritis (Arteriosclerosis) as Influenced by the Level of Protein Metabolism, Arch. Int. Med., 1913, xiii, 224.

The patients with ordinary myocardial failure do not present a simple problem of circulatory therapeutics. Their study by the nephritic test meal, originally advocated by Schlager and Hedinger, and which Mosenthal<sup>8</sup> has adapted and amplified with such excellent results in our clinic, has shown the importance of the special functional changes, depending upon chronic passive congestion of the kidney in retaining salt, and thus in producing at least the edema if not other symptoms of the disease. Every case of this type should, I believe, be given such a test, and should have a phenolsulphonephthalein test as a preliminary to treatment. If, in addition, the blood urea and the Ambard coefficient can be determined, very valuable information may be gained. The 'phthalein output is usually low, often under 30 per cent., sometimes minimal. If normal, or nearly so, and the test meal shows no lowering of the nitrogen concentration in the urine and no marked nitrogen lag, then it is rarely necessary to determine the blood nitrogen. Only in moribund patients can important retention exist. It is also essential to recognize the presence or absence of fibrillation of the auricles as a guide to the use of digitalis. Clark's<sup>9</sup> study of venous pressure in our wards, using Hooker's simple method, has also given us valuable indications of the need for digitalis.

All these patients require rest in bed, or in a chair if they are orthopneic, as the essential safeguarding treatment for the heart. Those with auricular fibrillation must receive effective digitalis treatment. Choice of the preparation and the method of administration, as between strophanthin intravenously or intramuscularly, infusion or tincture of digitalis, the powdered leaf of *digipuratum*, being determined by the details of the case and the habits of the physician. Those without auricular fibrillation, but with marked edema and a congested liver, should, I believe, also be placed on digitalis. Many of them will respond as well as the fibrillating cases; others will not. Toxic effects must be watched for and heeded, as some patients with regular rhythm are made worse by digitalis. If it does not succeed alone with proper diet, then one of the caffeine diuretics—theocoin, about twelve grains a day, or diuretin, about forty grains, in divided doses—should be given not oftener than every other day. It is very important to have the fluid intake and urine output accurately measured, and it is helpful to have the daily weight recorded. Diuresis from digitalis by the ordinary administration by mouth should not be expected before forty-eight hours. The diuresis of the caffeine group of drugs, however, should be observed on the chart of the day of administration, and may

<sup>8</sup> Renal Function as Measured by the Elimination of Fluids, Salt, and Nitrogen, and the Specific Gravity of the Urine, *Arch. Int. Med.*, 1915, xvi, 733.

<sup>9</sup> A Study of the Diagnostic and Prognostic Significance of Venous Pressure Observations in Cardiac Disease, *Arch. Int. Med.*, 1915, xvi, 587.



then persist for one or two days longer. The next doses should be given when the diuresis ceases.

### NEPHRITIC TEST DIET.

For.....

Date.....

All food is to be salt-free food from the diet kitchen.

Salt for each meal will be furnished in weighed amounts.

All food or fluid not taken must be weighed or measured after meals and charted in the spaces below.

Allow no food or fluid of any kind except at meal times.

Note any mishaps or irregularities that occur in giving the diet or collecting the specimens.

#### Breakfast, 8 A.M.:

Boiled oatmeal, 100 gms.	.....
Sugar, 1 to 2 teaspoonfuls.	.....
Milk, 30 c.c.	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Coffee, 160 c.c.	.....
Sugar, 1 teaspoonful	} -200 c.c.
Milk, 40 c.c.	
Milk, 200 c.c.	
Water, 200 c.c.	.....

#### Dinner, 12 Noon:

Meat soup, 150 c.c.	.....
Beefsteak, 100 gms.	.....
Potato (baked, mashed or boiled)	.....
130 gms.	.....
Green vegetables as desired	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Tea, 150 c.c.	} -200 c.c.
Sugar, 1 teaspoonful	
Milk, 20 c.c.	
Water, 250 c.c.	.....
Pudding (tapioca or rice), 110 gms.	.....

#### Supper, 5 P.M.:

Two eggs cooked in any style	.....
Two slices bread (30 gms. each)	.....
Butter, 20 gms.	.....
Tea, 150 c.c.	} -200 c.c.
Sugar, 1 teaspoonful	
Milk, 20 c.c.	
Fruit (stewed or fresh), 1 portion.	.....
Water, 300 c.c.	.....

8 A.M. No food or fluid is to be given during the night or until 8 o'clock the next morning (after voiding), when the regular diet is resumed.

Patient is to empty bladder at 8 A.M., and at the end of each period, as indicated below. The specimens are to be collected for the following periods in properly labeled bottles, to be furnished by the chemical division of the medical clinic: 8 A.M. to 10 A.M.; 10 A.M. to 12 N.; 12 N. to 2 P.M.; 2 P.M. to 4 P.M.; 4 P.M. to 6 P.M.; 6 P.M. to 8 P.M.; 8 P.M. to 8 A.M.

Specimens are to be left in the ward until called for at 8.30 A.M. by an attendant from the chemical laboratory.

## REPORT ON NEPHRITIC TEST MEAL.

Name.....

Date.....

Time of day.	Cubic centimeters	Specific gravity.	NaCl.		Per cent.	N.	Time and c.c. of fluid intake.
			Per cent.	Grams.		Grams.	
8 to 10 . . .	153	1.016	1.32	2.62	.89	1.26	
10 to 12 . . .	150	1.019	1.25	1.95	.74	1.15	
12 to 2 . . .	194	1.012	.64	1.24	.59	1.14	
2 to 4 . . .	260	1.014	.77	2.00	.56	1.46	
4 to 6 . . .	114	1.020	.99	1.13	.95	1.08	
6 to 8 . . .	238	1.010	.43	1.02	.52	1.23	
Total day . . .	1115	.....	....	9.36	....	7.32	
Night, 8 to 8 . .	375	1.020	.63	2.36	1.23	4.61	
Total 24 hours .	1490	.....	....	11.72	....	11.93	
Intake . . .	1760	.....	....	8.5	....	13.4	
Balance . . .	+270	.....	....	-3.22	....	+1.47	

*Impression.* Normal reaction to the nephritic test meal. Note the variations occurring in the fluid output and the specific gravity, which are in inverse ratio; the night urine, which is small in amount and shows a high specific gravity and a high percentage of nitrogen, and the approximately normal output of water, salt, and nitrogen.

Regulation of the diet is one of the most essential features of treatment. Thanks to our functional studies we can now base this upon the individual requirements of the case, not upon so-called general principles. The three factors to be considered are the fluid, the salt, and the nitrogen intakes. Practically all of these patients require limitation of their fluid intake, the degree of limitation depending upon the observed lag in water output and the amount of edema. It is scarcely possible, however, to discuss the water exchanges separately from the salt, since in these patients they are concurrent. The most distinctive result of the test meal in myocardial insufficiency, without renal involvement other than chronic passive congestion, is a low-water output with fairly high specific gravity, nearly always 1020, extremely low salt concentration and total output, and, in contrast, a normal nitrogen excretion brought about by the high concentration of this substance in the urine. The greater the degree of accompanying contraction of the kidney the more the specific gravity tends to be fixed and at a low level, nocturnal polyuria to become marked, and the concentration of the nitrogen, especially in the night urine, to fall far below the normal. With any of these features in evidence it is necessary to further test the functional capacity of the kidney for nitrogen by the determination of the blood urea and, best, by the comparison of this with the urinary urea in the Ambard formula. Whether this is better expressed, as in the recent admirable work of McLean, of the Rockefeller Institute, as an index of urinary

excretion, on the basis of a normal standard of reference of 100, or by Ambard's coefficient, the normal value for which is 0.06 to perhaps 0.09, is not clear to me. It is desirable that we should not have to burden our minds with any unnecessary arbitrary numerical values. Since Ambard's coefficient is already widely used the desirability of another set of values for expressing the same functional test should be clearly demonstrated before being adopted. The new values have mnemonic simplicity in that 100 is ideal perfection and the calculation is much simplified, but the range of normal values, from 80 to over 200, is rather wide.

A high Ambard or a falling index of urea excretion, or blood nitrogen above the normal, indicates the need for limitation of the protein intake. Ambard considers the normal constant 0.07. Unpublished observations by Lewis, in our clinic, show that 0.09 is more nearly the upper normal limit. There is considerable difference of opinion as to the figure for urea which may be found in the blood of healthy persons, but our experience coincides with McLean's<sup>10</sup> that 50 mgs. per 100 c.c. is possible with very high protein diet. Apart from this, 40 mgs. should never be exceeded. The urea nitrogen is practically one-half of this. The total non-protein nitrogen should rarely pass 40 mgs. per 100 c.c. under any circumstances. The small range found by Folin and Denis<sup>11</sup> in absolutely healthy individuals, 22 to 26 mgs., is too ideal a standard to apply to patients. The practical means for accomplishing this limitation vary from a low protein diet, which can never be an exclusive milk diet, to the introduction of short periods of nitrogen starvation in the worst cases. In such periods carbohydrate food should be given freely to spare protein. A satisfactory low-protein diet devised by Mosenthal for use in our wards follows:

#### THE JOHNS HOPKINS HOSPITAL.

##### LOW PROTEIN DIET.

###### Breakfast:

Sherry, 30 c.c.

Baked apple, stewed prunes, orange.

"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch).

Cream, 15 c.c.

###### Dinner:

Sherry, 30 c.c.

Potato, baked or mashed.

String beans, cabbage, carrots, lettuce, onions, tomatoes, cucumber pickles.

Fruit cornstarch pudding, fruit tapioca pudding.

###### Supper:

Same as dinner. (Salt, sugar and butter may be used as desired, and need not be weighed.)

<sup>10</sup> The Numerical Laws Governing the Rate of Excretion of Urea and Chlorides in Man, Jour. Exp. Med., 1915, xxii, 212, No. 2; 1915, xxii, No. 3.

<sup>11</sup> Protein Metabolism from the Standpoint of Blood and Tissue Analysis—Sixth Paper, Jour. Biol. Chem., 1913, xiv, No. 1.

## NITROGEN CONTENT OF FOODS USED IN LOW PROTEIN DIET.

Article of food.	Percentage of nitrogen.
Cream . . . . .	0.41
Cereal:	
"Hominy cornstarch cereal" (two-thirds hominy, one-third cornstarch) . . . . .	.13
Fruit:	
Baked apple . . . . .	.04
Orange . . . . .	.16
Stewed prunes . . . . .	.14
Vegetables:	
Cabbage . . . . .	.16
Carrots . . . . .	.10
Lettuce . . . . .	.24
Onions . . . . .	.17
Cucumber pickle . . . . .	.10
Baked potato . . . . .	.48
Mashed potato . . . . .	.40
String beans . . . . .	.23
Tomatoes . . . . .	.23
Desserts:	
Blackberry cornstarch pudding . . . . .	.05
Prune cornstarch pudding . . . . .	.07
Apple tapioca pudding . . . . .	.02
Peach tapioca pudding . . . . .	.06

Failure to eliminate salt makes essential the reduction of the salt intake to a figure below the twenty-four-hour output. Where much edema exists a rigorous salt-poor diet containing less than 3 grams, if possible getting the amount down to 1 gram, is most desirable at the start. Since these patients with myocardial insufficiency and marked edema require strict limitation of fluids as well the Karell diet is ideal. As is known, this consists of 800 c.c. of milk in the twenty-four hours as the only food or fluid allowed. Karell was a Russian physician who introduced this diet as a somewhat empirical cure for dropsy fifty years ago. We now possess entire theoretical justification for its use as a rational measure of safeguarding treatment, which is also highly effective in the cure of a most distressing symptom. It has the great virtue of simplicity. It can be carried out in households where an accurate salt-poor diet of any other kind would be impossible. Disappearance of edema usually begins after two or three days in this myocardial group of patients, and is little short of magical. When diuresis is abundant and the dropsy disappearing rapidly the amount of milk can be gradually increased up to 1500 c.c., and then other appropriate foods gradually added. It is desirable to determine the degree of restoration of the power of the kidney to excrete salt before allowing return to a full diet. All such patients should be warned against the abuse of salt for the future, and must never take large volumes of fluid or bulky meals. I think tobacco should be forbidden, but I am not sure that a little alcohol is harmful.

After recovery from the urgent symptoms the return to physical activity must be by very gradual stages and carefully supervised. Massage, resistance movements, and hydrotherapeutic procedures are all helpful here. Fibrillating cases must, if they show any tendency to a rate above the normal, take small doses of digitalis more or less constantly, the dosage to be determined by observation.

4. General edema without notable myocardial insufficiency the prominent symptom. This group of patients is much smaller than the preceding, and is met more frequently in hospital wards than in private practice. A considerable proportion of these dropsical patients have a subacute or chronic diffuse nephritis—that is a true inflammatory lesion of the kidney involving glomeruli, tubules, and interstitial tissue. This was what Dr. Delafield called chronic diffuse nephritis with exudation. Their urine is highly albuminous, and contains casts of all kinds. The common name given this type of disease, chronic parenchymatous nephritis, is altogether a misnomer. A number of them, under careful treatment, prove to be cases of very protracted acute nephritis, and will eventually make a functional recovery. Others develop increasing renal insufficiency with uremia and enter the next group, which I shall describe later. A few patients of this type, with the most obstinate edema and low blood-pressure, prove at autopsy to have amyloid kidneys. Still others are examples of a degenerative lesion of the tubular epithelium, not an inflammatory process. The cause of this we do not know, but its similarity to the effects of certain inorganic poisons makes a chronic intoxication plausible. The pregnancy kidney is a special example of this type. Following Friedrich Müller, Volhard and Falck<sup>12</sup> in their recent book use the term nephrosis to describe these non-inflammatory cases. Their diagnostic criteria are the absence of blood elements in the urine and the absence of a rise in blood-pressure. Those who are interested in the pathology of renal disease I would refer to this admirable anatomical and clinical monograph. Vidal,<sup>13</sup> on the other hand, adopts a purely functional classification. While I do not believe the functional disturbances permit of so clean-cut a subdivision of renal disease as he makes, and should be personally dissatisfied with a diagnosis which did not rest upon an anatomical basis, still this particular type has so predominant a disturbance of the salt and water excretion as to justify his name salt-retention nephritis. Certainly for treatment this is the essential feature to recognize, and Vidal and Javal's<sup>14</sup> work on the effects of withholding and feeding salt in such cases has been one of the great recent advances in practical therapeutics. When tested, either by the nephritic

<sup>12</sup> Die Brightsche Nierenkrankheit, Berlin, Julius Springer, 1914.

<sup>13</sup> Les Grands Syndromes du Mal de Bright, Jour. med. français, Paris, 1911, v, 18-33.

<sup>14</sup> La cure de déchloruration, Paris, J. & H. Baillière, 1906.

test meal or by the addition to a constant diet of an added ten grams of salt, these patients all show a striking failure to excrete sodium chloride. The salt concentration in the urine is often as low as 0.1 per cent., and the daily output not over one gram for long periods. With this the amount of urine is naturally very small and the retained water and salt accumulate in the subcutaneous tissues or serous sacs. Whether in all these cases the power of the kidney to excrete salt is primarily affected is very doubtful. It is highly probable that in many an increased affinity of the tissues for water, is equally important with the state of the kidney. For practical purposes of treatment it makes no difference. Salt and water are being retained. The 'phthalein test and the ability to excrete nitrogen may show unimpaired kidney function in every other respect. The potassium iodide test of Schlayer shows tremendous delay in excretion, but to me has no practical significance. The important point to determine is the degree of impairment of the ability to excrete water and salt. One patient may put out five grams of sodium chloride a day, another only one gram. For the first a diet containing three grams will lead to disappearance of the edema; for the other the most rigorous salt-poor diet will be without effect. Treatment should always begin by a period of very low salt and water intake to promote rapid absorption of the dropsical effusions. When this has been accomplished the response to increased water intake should first be tested and fluid pushed as fast as it can be excreted. The response to added salt should later be tested from time to time and the intake gradually increased, with care to keep always below the tolerated amount. Bed is desirable until normal function is restored. The problem of further treatment is that of the convalescence from acute nephritis. Local foci of infection should be looked for and the patient safeguarded from exposure, strain, and all injurious surroundings.

Patients with very low salt outputs and obstinate edema require accessory dehydrating measures, of which sweat baths have, in my experience, been the most effective. Purging may be of some value. In one patient hot packs were promptly followed by diuresis, the absorption of an obstinate edema of nineteen months' standing, and a prompt rise in the salt concentration of the urine. Retention with recurrence of edema was immediate upon cessation of the packs, and again disappeared upon their resumption. Such an influence is hard to explain, but suggests an alteration in the kidney circulation, acting upon the lesion itself. Borderline cases between this group and the preceding require a suitable combination of cardiac therapy with that just outlined.

5. Advanced renal insufficiency, uremic symptoms superimposed upon one of the foregoing types. We all recognize this as the classical picture of the end-stage of chronic Bright's disease. It is much easier to recognize than to define. Uremia can best be considered

with Ascoli as the varied disturbances, chiefly of the central nervous system, seen clinically in association with disease of the kidney or obstruction of the urinary tract and not dependent upon gross anatomical lesions of the brain. The differentiation of the severe headache of uremia and that due to cerebral vascular disease or of a uremic from an organic coma or hemiplegia may be very difficult. Lumbar puncture sometimes gives the clue, and should be resorted to. The gradually developing uremia which I have in mind here, however, with increasing headache, attacks of vomiting, respiratory disturbance, irritability, delirium, or drowsiness, gradually passing into terminal coma, scarcely permits of confusion, except with similar toxic states, as in the end-stages of liver disease. Changes in the optic nerve or retina are practically always present in true uremia, and the functional tests show what we may well consider as quantitative renal insufficiency. The test meal can be safely used only in the early stages, and then should frequently have its protein content reduced. It will show nocturnal polyuria, fixation of the specific gravity at a fairly constant, sometimes an absolutely constant, level, which is low in proportion to the severity of the renal insufficiency. It indicates inability of the kidney to excrete the normal constituents in anything but low concentration. The functional picture is constant in advanced contracted kidney, but may vary from week to week in diffuse nephritis. In our experience both nitrogen and NaCl concentrations have been equally reduced. Frothingham and Smillie<sup>15</sup> have found this also. This makes Widal's distinction between nitrogen-retention nephritis and salt-retention nephritis invalid. Sodium chloride excretion may be affected as an isolated functional disturbance, but nitrogen excretion seems only to be affected in quantitative renal insufficiency in company with all of the other functions except that of water excretion, which may remain intact. This NaCl retention does not necessarily lead to edema. The patients often have great thirst, considerable polyuria, and loss of weight, with dryness of the skin and tissues. This dry salt retention emphasized by the French school is of much theoretical interest. The 'phthalein test is of diagnostic, prognostic, and therapeutic importance. The excretion is diminished in proportion to the degree of renal insufficiency, and, as a rule, parallels closely the Ambard coefficient and the degree of increase of the non-protein nitrogen of the blood. When blood analyses are not possible it is the best practical measure of the probable degree of nitrogen retention, so-called. Agnew<sup>16</sup> has shown that in experimental renal lesions the blood nitrogen remains normal when the 'phthalein output is over 40 per cent. for the

<sup>15</sup> A Study of Different Nitrogenous Diets in Chronic Nephritis, *Arch. of Inter. Med.*, 1915, xv, 204.

<sup>16</sup> Comparative Study of Phenolsulphonephthalein Elimination and the Incoagulable Nitrogen of the Blood in Cardiorenal Diseases, *Arch. Int. Med.*, 1913, xiii, 485.

two hours. The most advanced cases excrete mere traces. All subsequent observers have confirmed the importance of Rowntree and Geraghty's<sup>17</sup> test in the prognosis and management of these cases.

The Ambar<sup>18</sup> coefficient is always raised and is unquestionably the most accurate measure of the degree of impairment of the urea excretion, though data in a large number of cases are not yet available. Widal's figures for blood urea remain the nearest approach to a prognostic standard if one remembers that they were obtained by the hypobromite method and represent more nearly total non-protein nitrogen. With 50 to 100 mgs. per 100 c.c. a long survival is possible, though prognosis must be guarded. With more than 100 mgs. no case lived over two years nor over one year if 200 mgs. were found. Over 500 mgs. were only found just before death. Certainly, in our experience, no case with over 300 mgs. of total non-protein nitrogen per 100 c.c. or an Ambar above 0.4 lived many weeks. On the other hand, Foster<sup>19</sup> has shown that low blood nitrogen does not insure a good prognosis.

Treatment of the severest renal insufficiency is purely symptomatic and not a cheerful duty. The distressing paroxysms of dyspnea and of Cheyne-Stokes breathing usually demand special relief. The low alveolar  $\text{CO}_2$  shows acidosis, but alkali has not relieved the symptom. For many patients morphin alone is effective, but it is a two-edged sword—it occasionally precipitates the rapid onset of anuria with coma, and once begun has to be used in increasing doses. Nothing requires more judgment on the part of the physician. Chloral hydrate in 5 or 10 grain doses, alone or combined with moderate doses of bromides, is sometimes very effective and should always be given a trial. Insomnia is commonly bound up with the onset of dyspnea on first lying down or with the recurrence of dyspneic paroxysms through the night. One serious practical mistake made by many physicians is to insist on these sufferers going to bed. Instead they should be encouraged to sleep in a chair until one is sure that he can promise them a real sleep in bed. Bed soon acquires for them a mental association with respiratory distress, and acts by suggestion as well as directly. The breaking up of this suggestion through a few good nights in a chair may make possible the return to restful sleep in bed. In some of the milder cases I have had great success by the use of a vasodilator just before retiring. For this purpose I prefer sodium nitrite, the effects of which are more lasting. It should be given about fifteen minutes before bedtime.

The gastro-intestinal disturbances, I believe, are of central nervous origin or eliminative. I feel sure that water and NaCl

<sup>17</sup> An Experimental and Clinical Study of the Functional Activity of the Kidney by Means of Phenolsulphonephthalein, *Jour. Phar. and Exp. Ther.*, 1910, i, 579.

<sup>18</sup> *Physiologie Normale et Pathologique des Urins*, 1914, Paris, F. Gittler.

<sup>19</sup> Functional Test of the Kidney in Uremia, *Arch. Int. Med.*, 1913, xii, 432.



are removed by vomiting and perhaps a little of the retained nitrogen. Treatment is apt to be very ineffectual. Lavage of the stomach and of the bowel are worth trying, but for the most part it is a problem in the use of general sedatives.

Diet is usually reduced to a minimum by the patient, for anorexia is the rule. In the severer degrees of insufficiency only starvation can hinder the nitrogen accumulation, and nothing prevents the terminal rise in blood nitrogen. In the early cases a very low nitrogen diet is strictly indicated with nitrogen starvation on days of severe symptoms, giving as much carbohydrate as possible. We have had a few remarkable improvements from this treatment. More frequently it is merely a choice of evils. The amount of fluid should depend upon the urinary output, and should be limited only by this or by the occurrence of edema. Vomiting, of course, will entail self-limitation. Of direct measures to reduce the retention of poisons, bleeding takes first place, but bleeding increases the anemia, which is so apt to be a feature of the intoxication. In a few recent cases repeated bleedings with consecutive transfusion have produced definite symptomatic improvement, and at times seemed to hold the blood nitrogen down. We have hoped that Abel's<sup>20</sup> operation of plasmapheresis might prove useful in these cases. It consists in bleeding into a non-clotting solution, separation of plasma and corpuscles by centrifugation, removal of the plasma, and reinjection of the corpuscles suspended in Locke's solution. One case done with hirudin, which was quite harmless to Abel's dogs, had a violent febrile reaction with shock, but recovered later and was considerably improved. We are cautiously testing the procedure further, using citrate, but have no successes to report as yet.

Bleeding has its greatest value in the case of sudden convulsive seizures. These so-called acute uremic or eclamptic convulsions have, in my experience, occurred in patients who did not have advanced renal insufficiency with marked nitrogen retention. The removal of at least 500 or 600 c.c. of blood is regularly indicated and recovery is common. I have known a number of such patients to live for several years after severe convulsions. I believe that the causation of these convulsions is analogous to that of the convulsions which occasionally mark the onset of acute scarlatinal nephritis, and has nothing in common with the causation of the chronic uremia which accompanies advanced renal insufficiency. Many are undoubtedly due to cerebral vascular disease. Sweating occasionally seems to benefit the patient.

The most important treatment in uremic cases is of associated myocardial insufficiency, when it exists. The superposition of chronic passive congestion on moderately damaged kidneys may

<sup>20</sup> Plasma Removal with Return of Corpuscles (Plasmapheresis), *Jour. Phar. and Exp. Ther.*, 1913, v, 625.

precipitate severe renal insufficiency. In other words a person who has lost the part of his reserve kidney tissue which constitutes the factor of safety, and is, roughly, about two-thirds of the total, may be thrown into the severest renal insufficiency by purely functional disturbance of the kidney circulation, as he may also be by the occurrence of an acute intoxication or infection leading to fresh anatomical lesions of an acute type. The prognosis when myocardial insufficiency is marked is always much better, because the element of functional disturbance may be recovered from under appropriate treatment of the heart, while gradually increasing renal insufficiency, due to progressive destruction of the kidney tissue, must have an absolutely hopeless outlook.

Of equal importance, but less generally appreciated, is the urgent necessity for the treatment of any associated obstruction of the urinary tract. Back pressure from an enlarged prostate with even moderate residual urine, combined with an only slightly damaged kidney, may rapidly lead to severe renal insufficiency, with uremia. The recent work of the genito-urinary surgeons in this field should be familiar to all medical men. The extent of the damage to function is demonstrated by the phenolsulphonephthalein test, as Rowntree and Geraghty<sup>21</sup> early showed in patients from Dr. Young's urological clinic, and Mosenthal has found the same indications in the study of such patients with his test meal. I have personally seen what was apparently advanced contracted kidney, with extreme hypertension and serious uremic symptoms, in a man, aged seventy-six years, transformed to a comparatively benign arteriosclerosis of the kidney, with hypertension, after the relief of back pressure by removal of the prostate. The patient was restored to practically ordinary health and working ability for a man of his years. In elderly men especially the possibility that urinary obstruction is the chief cause and renal disease the accessory cause for renal symptoms should never be out of mind. Pyelitis and pyelonephritis may produce similar pictures. Modern surgery in such conditions may make medical management superfluous.

A final word as to the possibility of surgical treatment in uncomplicated nephritis. Reginald Harrison first proposed this nineteen years ago, calling attention to the possibility of mechanical damage to the kidney circulation by pressure of the unyielding fibrous capsule upon a swollen edematous kidney. He proposed the relief of this mechanical factor by incision of the capsule. Five years afterward the late Dr. Edebohl, of New York, proposed to restore a damaged kidney circulation by decapsulation and the production of a collateral circulation between the cortex of the kidney and the surrounding tissues, and somewhat later Sippel advocated decap-

<sup>21</sup> The 'Phthalein Test: An Experimental and Clinical Study of Phenolsulphonephthalein in Relation to Renal Function in Health and Disease, *Arch. Int. Med.*, 1912, ix, 284.

sulation of the kidney for puerperal eclampsia. The whole subject has been recently well reviewed by Ruge in the *Ergebnisse der Chirurgie und Orthopädie*.<sup>22</sup> He makes it clear, in spite of considerable contradiction in the interpretation of the results obtained, that we medical men should more carefully consider the possibility of improvement by nephrotony or decapsulation in certain cases both of acute and chronic nephritis which do not respond satisfactorily to our usual measures. The need for better methods of treatment is plain. The field is peculiarly one for coöperative studies. I have personally witnessed a number of failures, but two cases stand out in my experience which I would record in this connection:

Both had persistent edema, hypertension, retinal lesions, and uremic symptoms extending over months, under my observation, in St. Luke's Hospital, New York. Both made an eventual complete functional recovery, being left only with albumin and casts in the urine and a moderate elevation of blood-pressure. Even the retinal lesions disappeared and both were well seven years later. Both had decapsulation performed. In one the improvement followed so closely as to suggest that the operation was its cause. The other had been decapsulated before she came to us, and improvement was so long delayed as to make the relation wholly improbable. I have seen no other recoveries after decapsulation in patients with severe renal insufficiency. I am inclined to believe that these two patients had a protracted subacute diffuse nephritis, and that the inflammatory process subsided without assignable cause, though possibly some remote focus of infection ceased to act as a portal of entry. In the first I feel sure, however, that the operation, probably by relieving tension within the capsule and improving the blood flow through the kidney, at least hastened the recovery. One would not anticipate any advantage from operation on advanced contracted kidneys.

In conclusion, may I emphasize the obvious summing up of the whole matter. Improved methods of investigation now permit of the much more accurate analysis of the various factors entering into the production of the complicated symptomatic pictures of chronic renal disease. Such analysis makes possible the more exact adjustment of treatment to the needs of the individual case and the relief of the patient from burdensome and unnecessary restrictions. In spite of all this it brings us not one whit nearer the real goal of treatment, prevention, or cure of the disease. If we ever achieve this it will be through new knowledge of the causes of these obscure but frequent affections, and every attempt to approach this problem from a new view-point should be enthusiastically welcomed by every medical man.

<sup>22</sup> Ueber den daseitigen Stand einiger Nephritisfragen und der Nephritischirurgie. loc. cit., 1913, vi, 565; see also Jour. Am. Med. Assn., October 2, 1915, lxx, 1188.