PROTEIN IN NEPHRITIS*

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For many years it was believed that protein had a deleterious effect on the kidneys, and protein restriction was advised in cases of nephritis. This belief was based in part on experimental work and in part, no doubt, on clinical experience at the bedside. Claude Bernard¹ observed albuminuria after feeding large amounts of raw eggs, and Watson² reported that renal degeneration occurred in animals after feeding them on a high protein diet.

Animal Experiments

In 1919 Newburgh³ produced renal lesions in the rabbit by means of a diet which contained a high protein content. On egg-white the rabbits developed acute and subacute nephritis, and on soya bean and on casein renal lesions were again observed. Polvogt, McCollum, and Simmonds,⁴ believing that the deficiencies in Newburgh's diet might be the cause of the kidney lesions, fed rats on a well-constituted diet which also contained a high proportion of protein; all their rats developed kidney lesions, the glomeruli themselves being little involved. Osborne and his associates⁵ found the kidneys normal in rats, except for hypertrophy, after a high protein diet, but when they used the Polvogt diet their rats developed severe focal lesions. Evans and Risley⁶ also observed kidney lesions on a high protein diet in animals.

On the other hand, Drummond, Crowden, and Hill⁷ fed a high protein diet to rats and cats, and observed no degenerative changes in the kidneys as the result of the diet. Addis⁸ and his co-workers obtained similar results. Miller,⁹ Jackson and Riggs,¹⁰ and Reader and Drummond¹¹ were also unable to detect any lesions in the kidneys as a result of a high protein diet.

Approaching the subject from a slightly different angle, Jackson and Moore¹² found that though their high protein diet did not cause renal lesions in normal rats, if one kidney was first removed severe damage was produced in the remaining kidney. These results are in agreement with Smith and Moise¹³ but in disagreement with Anderson,¹⁴ who found no renal damage in rabbits after 60 to 70 per cent. of kidney substance had been removed and a high protein diet instituted. MacLean, Forest Smith, and Urquhart¹⁵ found that a high protein diet produced no renal lesions in the rabbit provided that some green food was given in the diet, but that the rabbits died of nephritis if green food was persistently withheld.

These experiments have shown that although it is possible to produce kidney damage in animals by means of diets such damage may not be the result of an excessive amount of protein in the diet. The damage may possibly be the result of some dietetic deficiency.

Clinical Experience

Turning to the human subject, Squier and Newburgh¹⁶ stated that excessive feeding of protein to patients with some degree of renal damage caused the appearance in the urine of red blood cells, and increased albuminuria. Further, red blood cells were found in the urine of normal men when given excessive amounts of protein in their diet. Addis¹⁷ gave normal human subjects one and a half pounds of beefsteak, and observed no material change in the number of red cells normally present in the urine. Keutmann and McCann¹⁸ studied four subjects with

haemorrhagic Bright's disease, and reported that no increase in the haematuria occurred after as much as 200 grams of protein daily. In two subjects, however, they found that the amount of urinary protein was increased.

CASE REPORTS

In one of my cases, a girl with chronic nephritis who had slight haematuria, the protein after being varied between 30 and 70 grams daily was kept at 30 grams and the number of red cells in the urine was counted roughly by a method somewhat similar to that described by Addis.¹⁹ During this low protein phase the red cells in the twelve-hourly night specimen fell from 240 million to 70 million, but I must add that this was probably a coincidence, as when on this low protein diet previously no decrease in the blood present had been noted. A diet of 150 grams a day was then given and the red cells counted as before. The number varied between 3 million and 78 million, but never rose above the latter number, and was usually nearer the former. The guaiac reaction, which became negative when the patient was on the low protein diet, remained negative.

In another case, that of a man with a systolic blood pressure of over 200 mm. and with no albumin in the urine or blood, a diet containing 150 grams of protein daily for three and a half weeks did not cause the appearance of red blood cells in the urine on any day.

In the first case it appeared as if slow improvement was continuing in spite of the protein in the diet being excessive. On the other hand, improvement might have been greater had there been less protein in the diet. In two of their cases Keutmann and McCann did observe an increase in the albumin present.

Restriction of Proteins

Strouse and Kelman²⁰ found that no impairment of renal function and no increase of the non-protein nitrogen followed the administration of 150 grams of protein daily. Others have observed increases of the non-protein nitrogen following a high protein diet, and as urea is excreted by the kidneys it seems reasonable, when the kidneys are having difficulty with excretion, to give a restricted protein diet, as the aim is to throw as little work on the kidneys as possible. Rennie,²¹ in a study of ninety-eight cases of acute nephritis, came to the conclusion that a sufficiency of protein in the diet did not militate against the disappearance of non-protein nitrogen retention, and he believed protein to have no harmful effects. MacAdam,²² Callis,²³ and Aldrich and Boyle²⁴ have put forward the claims of a high protein diet in chronic glomerulonephritis, and the present tendency is to include a liberal supply of protein in the diet on the grounds that it causes no damage to the kidneys and improves the general health of the patient. The presence of a basic or neutral ash is regarded by some writers as being of more importance than the amount of protein in the diet.

Until we are more certain of the part played by diet in nephritis it is safest to advise some restriction of protein, not only in acute glomerulonephritis but also in chronic glomerulonephritis during acute exacerbations, and when the renal tests show impairment of kidney function to be present. Restrictions must be to some extent in accordance with the ability of the kidneys to excrete the end-products of protein, and I think about two-thirds of a gram per kilogram of body weight should be the minimum amount allowed. Even in cases of impending uraemia it is doubtful whether a lower protein diet is of real help. Fishberg²⁵ mentions 40 grams as the minimum amount which he advises, and this is, on an average, in adults about two-thirds of a gram per kilogram. Where there is no urea retention the protein allowed should be one gram per kilogram, and if a patient shows no improvement on such a moderate diet I think

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it is justifiable to increase the protein, particularly if there is oedema present, and observe if any benefit is derived from it.

Estimating Renal Function

In estimating the functional capacity of the kidneys Fishberg²⁶ lays great stress on Volhard's maximum specific gravity test and on the blood urea. The latter is the best test to determine whether the kidneys are excreting the end-products of protein metabolism in a satisfactory manner. If it is normal then presumably the protein allowed in the diet is not excessive, whereas if it is raised then protein restriction becomes necessary. The specific gravity test is simple, and is briefly the maximum ability of the kidneys to concentrate urine as judged by the specific gravity. The test performed by Fishberg is as follows.

SPECIFIC GRAVITY TEST

The patient empties the bladder and drinks no water from 8 p.m. on the previous night, and at 8 a.m., 9 a.m., and 10 a.m. the urine is passed and the specific gravity tested. If in one of these specimens the specific gravity is not 1020 or more, the functional capacity of the kidneys is below normal, but though this test may prove the kidney function to be below normal, polyuria, which is often present, may permit the kidneys to excrete the protein end-products in a satisfactory manner, in which case there may be no rise in the blood urea. This is the "compensated kidney," and where polyuria is present this excretion of protein end-products may be assisted by a liberal amount of water in the diet, assuming, of course, that there is no oedema. The specific gravity test is thus a test of kidney function, and the blood urea a test of whether the kidneys are compensated. This test loses much of its value if oedema is present.

Tests such as the urea clearance test and the phenolphthalein test may be more valuable, but the specific gravity test is one which can be carried out by any practitioner. The blood urea should be estimated from time to time.

Protein in Hyperpiesis

I shall pass now to the question of protein in hyperpiesis and in chronic nephritis with hypertension but without evidence of failing kidney function. It is probable that protein has very little to do with high blood pressure, and that protein restriction is unnecessary in these cases providing the kidney function is good. Nuzum, Osborne, and Sansum²⁷ noted that their rabbits when on the high protein diet of McCollum and Polvogt developed hypertension. This was the diet which caused well-marked kidney lesions. Anderson¹⁴ did not find any rise in blood pressure after a high protein diet either in normal rabbits or in rabbits in which 60 to 70 per cent. of the kidney substance had been destroyed before the commencement of the protein diet.

In man, Mosenthal²⁸ studied nine cases with high blood pressure for periods of from eight to sixty-seven days, and came to the conclusion that it was exceptional for a high protein diet to increase the blood pressure or a low protein diet to lower it. Strouse and Kelman²⁹ were unable to note any relationship between protein intake and blood pressure, and similar conclusions were arrived at by Keutmann and McCann¹⁸ and by Squier and Newburgh.¹⁶ Then there is the well-known case of the explorer Stefansson²⁹ who lived a total period of nine years out of eleven years on meat without any rise in blood pressure. McClellan and Du Bois³⁰ studied two men who were on a high meat diet for a year; one of these was Stefansson, and at the end of the year no rise of blood pressure was noted. Thomas³¹ examined the Greenland Eskimos, who eat their fish and meat preferably raw, and the highest pressure noted in 142 adults, between

40 and 60 years, was a systolic pressure of 170 and a diastolic pressure of 100. The Labrador Eskimos, on the other hand, prefer their meat cooked, and their diet includes tinned foods; they are prone to renal and vascular disease.

I have myself failed to observe any reduction of blood pressure amongst my own cases of hyperpiesis when treated by a diet having a very low protein content. I treated eight patients with systolic blood pressure of over 200 mm. on a diet containing only 30 grams of protein daily, and then changed it to a diet containing 150 grams of protein, and I failed to observe any significant changes of blood pressure which I could attribute to the effects of the diet. There were, of course, normal variations in the blood pressure, and in assessing the results of diet one has to take this into account. Rest in bed produces in many cases a striking lowering of blood pressure, and before trying the effect of diet this fall was excluded by first putting the patient to bed for several days. With a few exceptions the observations on man have been for only a comparatively short time, and it is wrong to attempt to draw hard-and-fast conclusions; *inter alia*, Harris, Aldred, and Hawthorne English,³² have observed a rise in blood pressure in cases on a high protein diet. However, it appears to be the case that protein, at any rate in normal quantities, has little or no effect on the blood pressure of man. I say in normal amounts, as Benedict³³ found that by under-feeding normal healthy young adults he was able to lower the blood pressure, but in some cases a secondary anaemia developed.

Protein and Nephrosis

Whatever dietetic measures one adopts in hyperpiesis it is unnecessary to make tiresome restrictions in the protein content unless there is evidence that there is disease of the kidneys present; it is advisable to test out the kidney function in all cases of high blood pressure where renal insufficiency is suspected. This applies particularly to pale-looking patients. Volhard³⁴ classes these as "pale hypertension," and regards this group as renal in origin. If the function is found to be below normal then some protein restriction is probably advisable.

In cases of chronic glomerulonephritis known as the nephrotic type, a high protein diet is advocated in the hope of making good the loss of protein in the urine and increasing the serum protein. These patients are often made worse by protein restriction, and many of them improve when put on a high protein diet; in some the oedema is lessened. A few of these cases are regarded by some writers as being quite distinct from chronic glomerulonephritis, and are believed to be degenerative in origin. These are the genuine lipoid nephroses. Without going into any of these debatable points, one may say that even in some of the so-called true nephroses nephritis finally develops. In all these cases, before starting the patient on a high protein diet, it is advisable to test the renal function, and here again the simple specific gravity test may furnish valuable information. A urea clearance test, however, should be carried out in these cases. Lashmet and Newburgh³⁵ have improved the simple specific gravity test, but in doing so have made it not quite so simple to carry out.

Conclusion

In closing, let me restate briefly the position of protein in nephritis.

In acute nephritis, and in chronic nephritis without oedema, protein in ordinary amounts does not cause actual damage to the kidneys and possibly restrictions on that account are unnecessary, but protein gives work to

the kidneys, and if these are damaged it is safest, in our present state of knowledge, to restrict proteins somewhat.

Such restrictions must never be carried to the extreme limits formerly advocated, and two-thirds of a gram per kilogram of body weight may be regarded as a minimum.

In the nephrotic type of case a high protein diet is usually indicated.

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Sir H. Lindo Ferguson, C.M.G., M.D., F.R.C.S.I., has retired from the active staff of Dunedin Hospital and Medical School, following his withdrawal from the chair of ophthalmology in the University of Otago. He was associated with the hospital for fifty-two years as ophthalmic surgeon and had been dean of the Medical Faculty of the University for the last twenty-two years. He qualified at Dublin in 1880, and he is believed to have been the first trained ophthalmic surgeon to settle in New Zealand, and his fame drew patients from as far as Australia. At the official opening of the new administration block of Dunedin Hospital on March 23rd a warm tribute was paid by Professor J. B. Dawson, chairman of the honorary visiting staff and professor of obstetrics, to Sir Lindo Ferguson's period of service to the institution, which was a record of hospital service that had been seldom, if ever, equalled. In this new century of amazing advances in medical science, he said, Sir Lindo had retained a clearness of vision, an acuity of mind, and a capacity to select and assimilate the best of the new doctrines which many of his younger colleagues might well emulate. Sir Lindo is an honorary Fellow of the American College of Surgeons and a Fellow of the Royal Australian College of Surgeons.

THE RENAL FUNCTION IN DISEASE*

BY

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About a hundred years ago Richard Bright¹ gave us clinical descriptions of kidney disease which in many respects are difficult to surpass to-day. Physiology has since supplied by Cushny² hypothesis of renal function, which, though probably not acceptable in its entirety, is still considered to be the basis of what we know of the secretion of urine. Nearly forty years ago Rose Bradford³ made some experiments on the kidney which have since become classical, and Verney⁴ and Winton⁵ have recently added a great deal to our knowledge of the behaviour of the kidney under varying conditions. The present paper is an attempt to bring the findings of the physiologists into line with the observations that can be made at the bedside.

Physiology of Renal Secretion

The arrangement of the glomerulus and its tubule and their blood supply is represented schematically in the diagram.

The afferent arteriole enters at A, and breaks up into capillaries which form the glomerulus. Through these capillaries and the membrane lining Bowman's capsule, water and substances in solution pass from the blood stream into the tubule, but the membranes are (normally) impermeable to protein and, of course, to the blood cells. The capillaries reunite to form the efferent vessel, E, which again breaks up into capillaries over the cells of the renal tubule. These again unite into venules, V, which eventually join to form the renal vein.

According to the Cushny theory a simple process of filtration occurs in the capsule, and from this filtrate the cells of the tubule secrete back into the blood stream a fluid of constant composition, a saline solution containing the water and salts necessary to the blood in their correct proportions. The most attractive feature of this hypothesis is that it relieves one of the necessity for supposing that the renal cells themselves have some unique power of varying their secretion according to the needs of the body at the moment. Special mechanisms probably exist for the excretion of excess of water and for the synthesis of ammonia and hippuric acid.

The urine may therefore be looked upon as the waste material from the blood filtrate; its composition depends primarily upon the composition of the blood.

Reserve Forces of the Kidney

Nevertheless the kidney is capable of increasing its normal rate of activity in two distinct ways, and each of these brings about changes in the composition of the urine. In the first place the number of nephrons in the normal kidney is far more than is necessary under ordinary circumstances, and we know that they undergo alternating periods of rest and activity, the blood supply to the resting glomeruli being practically shut off or possibly shunted through the artery of Ludwig. The ability to

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